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***Aloe vera* for prevention and treatment of infusion phlebitis (Review)**

Zheng GH, Yang L, Chen HY, Chu JF, Mei L

Zheng GH, Yang L, Chen HY, Chu JF, Mei L.
Aloe vera for prevention and treatment of infusion phlebitis.
Cochrane Database of Systematic Reviews 2014, Issue 6. Art. No.: CD009162.
DOI: [10.1002/14651858.CD009162.pub2](https://doi.org/10.1002/14651858.CD009162.pub2).

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[Intervention Review]

Aloe vera for prevention and treatment of infusion phlebitis

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Editorial group: Cochrane Vascular Group.

Publication status and date: Edited (no change to conclusions), published in Issue 3, 2017.

Citation: Zheng GH, Yang L, Chen HY, Chu JF, Mei L. *Aloe vera* for prevention and treatment of infusion phlebitis. *Cochrane Database of Systematic Reviews* 2014, Issue 6. Art. No.: CD009162. DOI: [10.1002/14651858.CD009162.pub2](https://doi.org/10.1002/14651858.CD009162.pub2).

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ABSTRACT

Background

Up to 80% of hospitalised patients receive intravenous therapy at some point during their admission. About 20% to 70% of patients receiving intravenous therapy develop phlebitis. Infusion phlebitis has become one of the most common complications in patients with intravenous therapy. However, the effects of routine treatments such as external application of 75% alcohol or 50% to 75% magnesium sulphate (MgSO₄) are unsatisfactory. Therefore, there is an urgent need to develop new methods to prevent and alleviate infusion phlebitis.

Objectives

To systematically assess the effects of external application of *Aloe vera* for the prevention and treatment of infusion phlebitis associated with the presence of an intravenous access device.

Search methods

The Cochrane Peripheral Vascular Diseases Group Trials Search Co-ordinator (TSC) searched the Specialised Register (last searched February 2014) and CENTRAL (2014, Issue 1). In addition the TSC searched MEDLINE to week 5 January 2014, EMBASE to Week 6 2014 and AMED to February 2014. The authors searched the following Chinese databases until 28 February 2014: Chinese BioMedical Database; Traditional Chinese Medical Database System; China National Knowledge Infrastructure; Chinese VIP information; Chinese Medical Current Contents; Chinese Academic Conference Papers Database and Chinese Dissertation Database; and China Medical Academic Conference. Bibliographies of retrieved and relevant publications were searched. There were no restrictions on the basis of date or language of publication.

Selection criteria

Randomised controlled trials (RCTs) and quasi-randomised controlled trials (qRCTs) were included if they involved participants receiving topical *Aloe vera* or *Aloe vera*-derived products at the site of punctured skin, with or without routine treatment at the same site.

Data collection and analysis

Two review authors independently extracted the data on the study characteristics, description of methodology and outcomes of the eligible trials, and assessed study quality. Data were analysed using RevMan 5.1. For dichotomous outcomes, the effects were estimated by using risk ratio (RR) with its 95% confidence interval (CI). For continuous outcomes, mean differences (MD) with 95% CIs were used to estimate their effects.

Main results

A total of 43 trials (35 RCTs and eight qRCTs) with 7465 participants were identified. Twenty-two trials with 5546 participants were involved in prevention of *Aloe vera* for phlebitis, and a further 21 trials with 1919 participants were involved in the treatment of phlebitis. The included studies compared external application of *Aloe vera* alone or plus non-*Aloe vera* interventions with no treatment or the same non-*Aloe vera* interventions. The duration of the intervention lasted from one day to 15 days. Most of the included studies were of low methodological quality with concerns for selection bias, attrition bias, reporting bias and publication bias.

The effects of external application of fresh *Aloe vera* on preventing total incidence of phlebitis varied across the studies and we did not combine the data. *Aloe vera* reduced the occurrence of third degree phlebitis (RR 0.06, 95% CI 0.03 to 0.11, $P < 0.00001$) and second degree phlebitis (RR 0.18, 95% CI 0.10 to 0.31, $P < 0.00001$) compared with no treatment. Compared with external application of 75% alcohol, or 33% $MgSO_4$ alone, *Aloe vera* reduced the total incidence of phlebitis (RR 0.02, 95% CI 0.00 to 0.28, $P = 0.004$ and RR 0.43, 95% CI 0.24 to 0.78, $P = 0.005$ respectively) but there was no clear evidence of an effect when compared with 50% or 75% $MgSO_4$ (total incidence of phlebitis RR 0.41, 95% CI 0.16 to 1.07, $P = 0.07$ and RR 1.10 95% CI 0.54 to 2.25, $P = 0.79$ respectively; third degree phlebitis (RR 0.28, 95% CI 0.07 to 1.02, $P = 0.051$ and RR 1.19, 95% CI 0.08 to 18.73, $P = 0.9$ respectively; second degree phlebitis RR 0.68, 95% CI 0.21 to 2.23, $P = 0.53$ compared to 75% $MgSO_4$) except for a reduction in second degree phlebitis when *Aloe vera* was compared with 50% $MgSO_4$ (RR 0.26, 95% CI 0.14 to 0.50, $P < 0.0001$).

For the treatment of phlebitis, *Aloe vera* was more effective than 33% or 50% $MgSO_4$ in terms of both any improvement (RR 1.16, 95% CI 1.09 to 1.24, $P < 0.0001$ and RR 1.22, 95% CI 1.16 to 1.28, $P < 0.0001$ respectively) and marked improvement of phlebitis (RR 1.97, 95% CI 1.44 to 2.70, $P < 0.001$ and RR 1.56, 95% CI 1.29 to 1.87, $P = 0.0002$ respectively). Compared with 50% $MgSO_4$, *Aloe vera* also improved recovery rates from phlebitis (RR 1.42, 95% CI 1.24 to 1.61, $P < 0.0001$). Compared with routine treatments such as external application of hirudoid, sulphonic acid mucopolysaccharide and dexamethasone used alone, addition of *Aloe vera* improved recovery from phlebitis (RR 1.75, 95% CI 1.24 to 2.46, $P = 0.001$) and had a positive effect on overall improvement (marked improvement RR 1.26, 95% CI 1.09 to 1.47, $P = 0.0003$; any improvement RR 1.23, 95% CI 1.13 to 1.35, $P < 0.0001$). *Aloe vera*, either alone or in combination with routine treatment, was more effective than routine treatment alone for improving the symptoms of phlebitis including shortening the time of elimination of red swelling symptoms, time of pain relief at the location of the infusion vein and time of resolution of phlebitis. Other secondary outcomes including health-related quality of life and adverse effects were not reported in the included studies.

Authors' conclusions

There is no strong evidence for preventing or treating infusion phlebitis with external application of *Aloe vera*. The current available evidence is limited by the poor methodological quality and risk of selective outcome reporting of the included studies, and by variation in the size of effect across the studies. The positive effects observed with external application of *Aloe vera* in preventing or treating infusion phlebitis compared with no intervention or external application of 33% or 50% $MgSO_4$ should therefore be viewed with caution.

PLAIN LANGUAGE SUMMARY

Aloe vera for prevention and treatment of infusion phlebitis

Infusion phlebitis is acute inflammation of a vein in the presence of intravenous therapy. In modern medical practice, more than 80% of inpatients will receive intravenous therapy during their admission, and about 20% to 70% of them may develop infusion phlebitis. Therefore infusion phlebitis is the most common complication of intravenous therapy. However, routine treatments for prevention or treatment of phlebitis such as external application of 75% alcohol or 50% to 75% magnesium sulphate ($MgSO_4$) are unsatisfactory.

This review examined 35 randomised controlled trials and eight quasi-randomised controlled trials with 7465 participants. Twenty-two trials with 5546 participants were involved in looking at prevention of phlebitis with *Aloe vera*, and a further 21 trials with 1919 participants were involved in looking at *Aloe vera* for the treatment of phlebitis. The included trials mainly compared external application of fresh *Aloe vera* alone or with another non-*Aloe vera* treatment such as a wet compress of 75% alcohol or 33%, 50% or 75% $MgSO_4$ with no treatment or the same non-*Aloe vera* treatment. The duration of intervention lasted from one day to 15 days. Most of the included studies were of low methodological quality with concerns for selection bias, attrition bias, reporting bias and publication bias. The incidence of phlebitis at varying degrees of severity as well as the resolution rate and level of improvement of phlebitis were investigated.

The available evidence suggests that external application of fresh *Aloe vera* alone or combined with other non-*Aloe vera* treatment may be effective for the prevention and treatment of infusion phlebitis resulting from the intravenous therapy. The conclusions should be cautiously interpreted due to the low methodological quality of the included trials.

BACKGROUND

Description of the condition

Intravenous therapy is the giving of substances directly into a vein. Intravenous therapy may be used to correct electrolyte imbalances, deliver medications, for blood transfusion, or as fluid replacement. In modern medical practice up to 80% of hospitalised patients receive intravenous therapy at some point during their admission (Tager 1983; Tjon 2000). Compared with other routes of administration, the intravenous route is the fastest way to deliver fluids and medications throughout the body. The devices for intravenous therapy usually include a hypodermic needle, peripheral venous cannula or intravenous catheter and this is the most common invasive procedure among patients admitted to hospital (Waitt 2004). It is estimated that 200 million peripheral intravenous devices are placed each year in America alone (Maki 2008; Mermel 2001), while one in three inpatients have at least one peripheral venous catheter in situ (Boyd 2011). Medication, fluids, nutrition, and blood products can all be given via the peripheral intravenous route, and the plastic catheter may stay in situ long term. Although common, these practices are not devoid of complications, which may increase duration of hospital stay and admission cost (Waitt 2004). The complications that occur frequently in patients with peripheral intravenous therapy include infusion phlebitis, infection, infiltration or extravasation, fluid overload, hypothermia, electrolyte imbalance and embolism. Infusion phlebitis is in almost all cases a biochemical reaction to the mechanical irritation caused by the presence of the intravenous catheter (Maki 1991). The remaining cases may be chemical or infectious. Studies have shown that 20% to 70% of patients receiving peripheral intravenous therapy develop phlebitis (Hershey 1984; Monreal 1999; Tully 1981). In China, according to statistics, about 80% of the patients with intravenous therapy develop varying degrees of infusion phlebitis (Tang 2001).

Description of the intervention

Aloe or *Aloe vera* is a genus containing many species of flowering succulent plants with a rosette of large, thick, fleshy leaves (Klein 1988). *Aloe vera* species are frequently cultivated as ornamental plants both in gardens and in pots. *Aloe* has been known and used for centuries for its health, beauty and skin care properties. Two thousand years ago, the Greek scientists regarded *Aloe vera* as the universal panacea and the Egyptians called *Aloe* the plant of immortality (Surjushe 2008). It has a long history of use as an anti-inflammatory herbal application for burns and for a variety of conditions in traditional medicine (Hutter 1996). Today, *Aloe vera* is still used as a herbal medicine. *Aloe vera* is used either internally or externally in humans and has some medicinal effects which have been supported by scientific and medical research (Vogler 1999). As a herbal medicine, *Aloe vera* juice is commonly used internally to relieve digestive discomfort (Langmead 2004) and externally to relieve skin discomforts such as minor burns, wounds and various skin conditions such as eczema and scabies (Feily 2009; Oyelami 2009; Visuthikosol 1995). The topical or external applications usually use *aloe*-derived products, which include *aloe vera* cream, *aloe vera* mucilage, *aloe vera* gel etc. (Vogler 1999). However, crude *aloe vera* components such as fresh *aloe vera* leaf, fresh *aloe vera* stem, and *aloe vera* juice are also used as adjuvant treatment to treat skin disorders (Peng 2009; Zhang 2010).

How the intervention might work

Aloe vera contains 75 potentially active constituents including vitamins, enzymes, minerals, sugars, lignin, saponins, salicylic acids and amino acids (Shelton 1991), some of which have several pharmacological actions. These include the carboxypeptidase that inactivates bradykinin, salicylates and substances that inhibit local vasoconstriction (Klein 1988). The anti-inflammatory compound called C-glucosyl chromone has been isolated from gel extracts (Hutter 1996). It has been proven that fresh *Aloe vera* can promote the attachment and growth of normal human cells in vitro and enhance the healing of wounded monolayers of cells (Winters 1981) whereby *Aloe vera* gel not only increased the collagen content of the wound but also changed the collagen composition and increased the degree of collagen cross linking (Chithra 1998). Some studies have shown that pure *Aloe vera* is effective in preserving skin circulation following frostbite injury (McCauley 1990) and in accelerating wound healing (Fulton 1990) and increasing the breaking strength of resulting scar tissue in patients (Heggers 1996). In addition, *Aloe vera* can stimulate fibroblasts, which produce the collagen and elastin fibres, making the skin more elastic and less wrinkled; and *Aloe vera* has cohesive effects on the superficial flaking epidermal cells by sticking them together, to soften the skin (West 2003). To summarise, the mechanism of action of *Aloe vera* includes healing properties, anti-inflammatory activity, effects on the immune system, moisturising and anti-aging effects and antiseptic effects (Surjushe 2008). *Aloe* may therefore be beneficial for the prevention and treatment of infusion phlebitis.

Why it is important to do this review

Infusion phlebitis is acute inflammation of a vein in the presence of and directly connected to an intravenous access device. It may be influenced by the pH and osmotic pressure of the solution, the size of the vein used, the size and material of the catheter, and the infusion period (Kuwahara 1998); and may be the most common complication of intravenous therapy. Especially during cancer chemotherapy, the toxicity of and irritation caused by the chemotherapy drugs can directly lead to phlebitis and even tissue necrosis. Yoh et al reported that the incidence of phlebitis after a six-minute infusion of vinorelbine was 16% to 33% (Yoh 2007). Phlebitis not only brings great physiological and psychological suffering to the patients but also reduces the treatment effect and prolongs the process of treatment. The infusion phlebitis may initially manifest itself in the form of pain, erythema and swelling, warmth, hardening and thickening of the skin in the injection area (Schmid 2000). However, it can quickly develop into more serious symptoms such as severe local tissue ulceration and necrosis, even leading to serious limb dysfunction, and could ultimately cause thrombus formation and pyrexia. This is most likely to be caused by the pH and osmotic pressure of the solution, the mechanical irritation of the catheter or chemical irritation of the drugs (Emiko 2009). Therefore, infusion phlebitis does not only increase the psychological burden of the patient it also affects the quality of care. The routine or traditional methods for prevention and treatment of infusion phlebitis are varied, for example self care, anti-inflammatory medication, cortisone preparations, rubbing or flushing the site with 75% alcohol or 0.9% saline solution, and compresses with 50% to 75% magnesium sulphate, but none are completely effective (Curran 1990; Nakayama 2002; O'Grady 2002). There is an urgent need to develop new methods to prevent and alleviate infusion phlebitis.

In clinical settings in China, it is common for *Aloe vera* to be externally applied to prevent and treat infusion phlebitis (Cao 2008; Hu 2006; Lu 2008; Yang 2008). Studies on its effectiveness have small sample sizes and the real effect is difficult to confirm. This systematic review of randomised and quasi-randomised trials was conducted to clarify its efficacy.

OBJECTIVES

To systematically assess the effects of external application of *Aloe vera* for the prevention and treatment of infusion phlebitis associated with the presence of an intravenous access device.

METHODS

Criteria for considering studies for this review

Types of studies

Randomised controlled trials (RCTs) and quasi-randomised controlled trials (qRCTs) which evaluated *Aloe vera* used alone or in combination with other treatments for infusion phlebitis were included irrespective of blinding, publication status and language. We excluded non-randomised studies. Randomised cross-over trials and cluster-RCTs were eligible.

Types of participants

We included participants, regardless of gender, age or ethnic origin, who suffered from phlebitis of a peripheral limb vein that was associated with the presence of an intravenous access device, or who were at risk of developing phlebitis because of insertion of an intravenous access device. Peripheral limb veins are frequently used for siting intravenous access devices, including the dorsal venous network of the hand, veins of the forearm, veins of the cubital fossa, and dorsalis pedis veins.

Types of interventions

We included trials that compared topical external application of any type of *Aloe vera* (fresh *Aloe vera* slice or fresh *Aloe vera* juice) or aloe-derived products, or *Aloe vera* plus non-*Aloe vera* treatments, at the site of punctured skin with no treatment, routine treatment or the same non-*Aloe vera* treatment at the same site. We excluded trials without a definite duration of treatment. In addition, we excluded those trials in which *Aloe vera* plus other non-*Aloe vera* treatments were used in the treatment group and the same non-*Aloe vera* treatments were not used in the control group.

Types of outcome measures

Primary outcomes

1. The incidence of phlebitis (for preventive effect) as assessed by the total incidence of phlebitis. We also assessed the incidence of third degree and second degree phlebitis.
2. The rate of resolution of phlebitis (for treatment effect) as assessed by the total improvement rate of phlebitis. We also assessed the recovery rate and marked improvement rate of phlebitis.

Secondary outcomes

1. The duration of successful placement of a venous catheter, defined as the length of time which the venous catheter, such as the needle, was retained in the vein after infusion.

2. Symptom improvement of phlebitis.

3. Health-related quality of life, using quality of life measures as reported by the study authors.

4. Adverse effects: any adverse events as a result of the use of *Aloe vera* for treatment or prevention, such as toxic response, anaphylaxis, etc.

Search methods for identification of studies

There were no restrictions on the basis of date or language of publication.

Electronic searches

The Cochrane Peripheral Vascular Diseases Group Trials Search Co-ordinator (TSC) searched the Specialised Register (last searched February 2014) and the Cochrane Central Register of Controlled Trials (CENTRAL) (2014, Issue 1), part of *The Cochrane Library* (www.thecochranelibrary.com). See Appendix 1 for details of the search strategy used to search CENTRAL. The Specialised Register is maintained by the TSC and is constructed from weekly electronic searches of MEDLINE, EMBASE, CINAHL, AMED, and through handsearching relevant journals. The full list of the databases, journals and conference proceedings which have been searched, as well as the search strategies used, are described in the Specialised Register section of the Cochrane Peripheral Vascular Diseases Group module in *The Cochrane Library* (www.thecochranelibrary.com).

In addition, the TSC searched MEDLINE (Appendix 2), EMBASE (Appendix 3) and Allied and Complementary Medicine (AMED) (Appendix 4).

The following trial databases were searched by the TSC for details of ongoing and unpublished studies using the term "aloe vera":

- World Health Organization International Clinical Trials Registry Platform (<http://apps.who.int/trialsearch/>);
- ClinicalTrials.gov (<http://clinicaltrials.gov/>);
- Current Controlled Trials (<http://www.controlled-trials.com/>).

Author searches

The review authors searched the following Chinese databases for published and unpublished studies:

- Chinese BioMedical Database (1980 to 28 February 2014) (<http://www.imicams.ac.cn/>);
- Traditional Chinese Medical Database System (1984 to 28 February 2014) (<http://cowork.cintcm.com/engine/windex.jsp>);
- China National Knowledge Infrastructure (1994 to 28 February 2014) (<http://acad.cnki.net/kns55/default.aspx>);
- Chinese VIP Information (1989 to 28 February 2014) (<http://cstj.cqvip.com/>);
- Chinese Medical Current Contents (1994 to 28 February 2014) (<http://210.34.66.109/esource/showdb.jsp?ID=6>);
- Chinese Academic Conference Papers Database and Chinese Dissertation Database (1994 to February 2014) (<http://acad.cnki.net/kns55/brief/result.aspx?dbPrefix=CMFD>);
- China Medical Academic Conference (1994 to 28 February 2014) (<http://acad.cnki.net/kns55/Navigator.aspx?ID=CPFD>);

- WangFang database (1987 to 28 February 2014) (<http://www.wanfangdata.com.cn/>).

The search strategies which were used are listed in [Appendix 5](#) to [Appendix 12](#).

Searching other resources

We searched the bibliographies of all relevant publications for further studies. One review author (Zheng GH) contacted authors and experts in the field of surgical nursing (Guan FG, Zhao RH) for any information about unpublished studies.

Data collection and analysis

Selection of studies

Two review authors (Chen HY and Chu JF) independently screened the abstract, title, or both sections of every record retrieved according to the inclusion criteria. The full text of literature with any unclear information in the title or abstract was retrieved for clarification. We investigated all potentially relevant articles as full text. We selected the most complete publication or pooled the data if there were two or more publications relating to one trial. Any disagreements were resolved by discussion.

Data extraction and management

Mei LJ and Yang L independently extracted data using a data extraction form and the results were checked for accuracy by a third author (Zheng GH). Disagreements were resolved by discussion. In the case of duplicate publications and companion papers of a primary paper, we maximised the yield of information by simultaneous evaluation of all available data. The information that was extracted from each included report included the following.

1. Basic information: study design, title, authors, publication status.
2. Participant characteristics: mean age, proportion of each gender, sample number.
3. Methodological description: method of randomisation, method of concealment of allocation, exclusions post-randomisation, blinding, losses to follow up.
4. Intervention characteristics: type of intervention (prevention or treatment), routes of administration, period of treatment, duration of follow up.
5. Outcomes: primary and secondary outcomes, safety outcomes.
6. Other: infusion given, site of vein, type of catheter, risk factors for phlebitis.

Assessment of risk of bias in included studies

Two review authors (Zheng GH, Yang L) independently assessed the risk of bias of each trial by using the tool developed by The Cochrane Collaboration ([Higgins 2011](#)) and the following criteria were used. Disagreements were resolved by consensus.

1. Was the allocation sequence randomly generated?
2. Was the treatment allocation adequately concealed?
3. Was knowledge of the allocated interventions adequately prevented during the study?

4. Were incomplete outcome data adequately addressed?

5. Are reports of the study free of suggestion of selective outcome reporting?

6. Was the study apparently free of other problems that could put it at a high risk of bias?

Measures of treatment effect

Dichotomous outcomes

We expressed dichotomous data (for example the rate of resolution of phlebitis, incidence of phlebitis) as the risk ratio (RR) with its 95% confidence interval (CI). We pooled data using the fixed-effect model or the random-effects model when heterogeneity among studies was obvious. We did not calculate the risk difference (RD) or include the number needed to treat (NNT) in the analysis because this was not feasible with the data available. We did not perform the evaluation of adverse events because the data were unavailable in the included studies. If adverse events data are available in future updates we will calculate the number needed to harm (NNH).

Continuous data

We analysed continuous outcomes by using mean differences (MD) with 95% CIs.

Unit of analysis issues

The primary analysis was based on per individual randomised. Cross-over trials and cluster-randomised trials were not found for this review. For trials with more than two intervention groups, we combined groups to create a single pair-wise comparison ([Higgins 2011a](#)).

Dealing with missing data

We attempted to obtain relevant missing data from the authors of the included trials, if feasible, and carefully performed evaluations of important numerical data such as the number of screened and randomised participants as well as the intention-to-treat (ITT) and per protocol (PP) populations.

Assessment of heterogeneity

We tested the heterogeneity between the included trials by examining the I^2 statistic, quantifying inconsistency across studies, to assess the impact of heterogeneity on the meta-analysis ([Higgins 2003](#)). We analysed the study components such as the participants, diseases, interventions, comparisons and outcomes if obvious heterogeneity ($I^2 > 75\%$) was found, and explained the source of heterogeneity by subgroup analysis and sensitivity analysis. We used a random-effects model meta-analysis as an overall summary if the heterogeneity among trials was considered acceptable ($85\% > I^2 > 50\%$). If heterogeneity was substantial ($I^2 > 85\%$) we did not pool the data and produced a narrative qualitative summary.

Assessment of reporting biases

We used funnel plots to assess publication bias when a sufficient number of studies were included (at least 10 studies) as recommended by the *Cochrane Handbook for Systematic Reviews of Interventions* 5.1.0 ([Higgins 2011](#); [Sterne 2001](#)).

Data synthesis

For the predefined outcomes which were available, measured similarly, and of sufficient quality we statistically summarised the pooled effects and performed statistical analyses according to the statistical guidelines referenced in the current version of the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011a).

We performed a meta-analysis of the data using a fixed-effect model prior to a random-effects model only if the test of heterogeneity was not significant. However, if heterogeneity was substantial ($I^2 > 85\%$), we did not perform a meta-analysis at all and a narrative, qualitative summary was carried out.

Subgroup analysis and investigation of heterogeneity

We carried out the following subgroup analyses to explore possible sources of heterogeneity, for primary outcomes only.

1. Duration of treatment (such as *Aloe vera* used for three, five or seven days, etc).

2. Types of *Aloe vera* products (such as a thin slice or the juice of *Aloe vera* and Aloe-derived products).

Sensitivity analysis

Where possible, we performed the following sensitivity analyses to explore the effect of potential biases.

1. Repeating the analysis excluding unpublished studies.
2. Repeating the analysis taking account of study quality.
3. Reanalysing the data using different statistical methods.
4. Repeating the analysis excluding qRCTs.

RESULTS

Description of studies

For a detailed description of the studies, see [Characteristics of included studies](#); [Characteristics of excluded studies](#).

Results of the search

See [Figure 1](#).

Figure 1. Study flow diagram.

Figure 1. (Continued)

43 studies included in quantitative synthesis (meta-analysis)
Randomised controlled trials: n = 35
Quasi-randomised controlled trials: n = 8

Included studies

A total of 43 studies (35 RCTs and eight qRCTs) with 7465 participants were included in the review (Cao 2008; Chen 2009; Chen 2010; Chen 2012; Deng 2010; Deng 2012; Dong 2001; Dong 2008; Gao 2007; Gao 2012; Hou 2010; Hu 2009; Ji 2007; Jin 2010; Li 2003; Li 2006; Li 2009; Li 2011; Liang 2004; Liu 2003; Liu 2006; Liu 2012; Liu 2012b; Lu 2004; Pan 2008; Peng 2009; Ren 2008; Tan 2002; Tang 2011; Wang 2006; Wang 2008; Wang 2010; Wang 2010b; Wu 2009; Xiao 2008; Yang 2008; Yao 2009; Yu 2006; Zhang 2010; Zhang 2013; Zheng 2010; Zhong 2011; Zhou 2006).

The number of participants in each trial ranged from 40 (Chen 2009) to 3000 (Hu 2009). The age of participants ranged from 18 to 75 years old except for one study where the age of participants ranged from one month to three years old (Gao 2007). All included studies were conducted in China, and were performed in the hospital setting.

Various formulations of *Aloe vera* or aloe-derived products were used in the included studies. A slice of fresh aloe 5 cm to 15 cm long and 3 cm wide was most commonly used and reported on in 31 included studies. Six studies used fresh aloe leaf divided into pieces 15 cm to 20 cm long and 5 cm to 10 cm wide (Hou 2010; Hu 2009; Pan 2008; Wang 2010b; Xiao 2008; Zhang 2010). Other aloe vera products used were the juice of fresh aloe leaf in three included studies (Deng 2010; Jin 2010; Ren 2008), aloe glue in two studies (Chen 2010; Li 2011), and dry aloe linimentum in one study (Lu 2004).

Twenty-two studies with 5546 participants involved the use of *Aloe vera* for prevention of phlebitis (Cao 2008; Chen 2012; Dong 2008; Hou 2010; Hu 2009; Ji 2007; Li 2011; Liang 2004; Liu 2003; Liu 2006; Liu 2012b; Pan 2008; Peng 2009; Ren 2008; Tan 2002; Wang 2006; Wu 2009; Xiao 2008; Yao 2009; Yu 2006; Zhang 2010; Zheng 2010). Of these 22 studies, 13 trials with 4272 participants compared *Aloe vera* alone in the treatment group with no treatment in the control group (Cao 2008; Dong 2008; Hu 2009; Li 2011; Liu 2006; Liu 2012b; Pan 2008; Peng 2009; Tan 2002; Xiao 2008; Yao 2009; Yu 2006; Zheng 2010), and two trials with 248 participants compared *Aloe vera* alone with 50% MgSO₄ (Ren 2008; Zhang 2010). Two trials with 200 participants compared *Aloe vera* versus 33% MgSO₄ (Chen 2012; Hou 2010). One trial with 66 participants compared *Aloe vera* alone with potato slices (Wu 2009). One trial with 150 participants compared *Aloe vera* alone with 75% alcohol (Liang 2004). One trial with 147 participants compared aloe plus an ice bag compress with an ice bag compress plus 75% MgSO₄ (Liu 2003). One study was a three-arm trial with 320 participants comparing *Aloe vera* versus potato slice versus no treatment (Wang 2006). The remaining trial with 142 participants compared *Aloe vera* plus saline (NaCl₂)

plus dexamethasone with NaCl₂ plus dexamethasone in the control group (Ji 2007).

The therapeutic effect of *Aloe vera* for phlebitis was evaluated in 21 studies involving 1919 participants (Chen 2009; Chen 2010; Deng 2010; Deng 2012; Dong 2001; Gao 2007; Gao 2012; Jin 2010; Li 2003; Li 2006; Li 2009; Liu 2012; Lu 2004; Tang 2011; Wang 2008; Wang 2010; Wang 2010b; Yang 2008; Zhang 2013; Zhong 2011; Zhou 2006). Of these, 10 studies with 880 participants compared aloe alone in the treatment group with 50% MgSO₄ in the control group (Chen 2010; Deng 2010; Deng 2012; Gao 2007; Li 2003; Li 2009; Liu 2012; Tang 2011; Wang 2010; Yang 2008), and three studies with 422 participants compared *Aloe vera* alone with 33% MgSO₄ (Dong 2001; Gao 2012; Li 2006). The remaining eight studies compared *Aloe vera* alone or *Aloe vera* plus other treatment, such as sulphanilamide pyrimidine, potato, sulphonic acid mucopolysaccharide cream, in the treatment group versus the same 'other treatment' in the control group (Chen 2009; Jin 2010; Lu 2004; Wang 2008; Wang 2010b; Zhang 2013; Zhong 2011; Zhou 2006).

Excluded studies

In total 60 studies were excluded on the basis of their full text versions. Reasons for exclusion were as follows: self-controlled clinical trial (Zou 2004), an incorrect control used (the non-*Aloe vera* treatment used in the treatment group but not used in the control group) in 50 studies (Cao 2007; Dai 2007; Deng 2001; Deng 2009; Gong 2004; Gu 2013; Guo 2009; Hu 2011; Huang 2005; Huang 2009; Jiang 2007; Li 2003b; Li 2006b; Li 2010; Li 2011b; Liang 2011; Lin 2009; Lu 2004b; Lu 2007; Lu 2008; Lu 2010; Lu 2010b; Lu 2011; Ma 2008; Ma 2009; Mo 2008; Peng 2002; Shao 2008; Shen 2013; Shi 2013; Su 2011; Tang 2008; Tang 2008b; Wang 2004; Wang 2010c; Wang 2011; Wang 2012; Wang 2013; Wei 2012; Wu 2010; Xu 2007; Xu 2008; Yan 2012; Yang 2010; Ye 2008; Ye 2011; Zhang 2004; Zhang 2008; Zhu 2010; Zhuang 2008), and an unclear intervention duration in nine studies (Chen 2007; Huang 2013; Lei 2012; Liu 2009; Zhang 2003; Zhang 2005; Zhang 2006; Zhang 2011; Zhou 2001). Although we were able to contact one of the authors, we did not obtain more information to judge the duration of the intervention.

Risk of bias in included studies

Of the 43 included studies, all included studies were judged as at high risk of bias because one or more main aspects of the bias assessment was labelled high or unclear risk of bias. We tried to contact the original study authors but we received no response from most of them. See Figure 2 and Figure 3.

Figure 2. Risk of bias summary: review authors' judgements about each risk of bias item for each included study.

	Random sequence generation (selection bias)	Allocation concealment (selection bias)	Blinding of participants and personnel (performance bias)	Blinding of outcome assessment (detection bias)	Incomplete outcome data (attrition bias)	Selective reporting (reporting bias)	Other bias
Cao 2008	+	+	-	?	+	+	+
Chen 2009	?	?	-	?	?	?	+
Chen 2010	?	?	-	?	?	?	+
Chen 2012	?	?	-	?	?	?	?
Deng 2010	-	-	-	?	?	?	+
Deng 2012	?	?	-	?	?	?	?
Dong 2001	?	?	-	?	?	?	?
Dong 2008	?	?	-	?	?	?	+
Gao 2007	-	-	-	?	?	?	?
Gao 2012	?	?	-	?	?	?	?
Hou 2010	-	-	-	?	?	?	+
Hu 2009	-	-	-	?	?	?	+
Ji 2007	?	?	-	?	?	?	?
Jin 2010	+	?	-	?	?	?	?
Li 2003	?	?	-	?	?	?	?
Li 2006	?	?	-	?	?	?	?
Li 2009	?	?	-	?	?	?	+
Li 2011	?	?	-	?	?	?	+
Liang 2004	?	?	-	?	?	?	+
Liu 2003	?	?	-	?	?	?	?

Figure 2. (Continued)

Liu 2003	?	?	-	?	?	?	?
Liu 2006	-	-	-	?	?	?	+
Liu 2012	?	?	-	?	?	?	?
Liu 2012b	?	?	-	?	?	?	?
Lu 2004	?	?	-	?	?	?	+
Pan 2008	?	?	-	?	?	?	?
Peng 2009	?	?	-	?	?	?	+
Ren 2008	?	?	-	?	?	?	+
Tan 2002	?	?	-	?	?	?	+
Tang 2011	+	?	-	?	?	?	?
Wang 2006	-	-	-	?	?	?	+
Wang 2008	?	?	-	?	?	?	+
Wang 2010	?	?	-	?	?	?	?
Wang 2010b	+	?	-	?	?	?	+
Wu 2009	?	?	-	?	?	?	?
Xiao 2008	-	-	-	?	?	?	?
Yang 2008	?	?	-	?	?	?	?
Yao 2009	?	?	-	?	?	?	+
Yu 2006	?	?	-	?	?	?	+
Zhang 2010	-	-	-	?	?	?	?
Zhang 2013	?	?	-	?	?	?	?
Zheng 2010	?	?	-	?	?	?	+
Zhong 2011	?	?	-	?	?	?	+
Zhou 2006	?	?	-	?	?	?	+

Figure 3. Risk of bias graph: review authors' judgements about each risk of bias item presented as percentages across all included studies.

Allocation

Four studies with adequate sequence generation used random digit tables or computer random digit generators (Cao 2008; Jin 2010; Tang 2011; Wang 2010b). Eight studies were of qRCT design and judged as at high risk of bias because of alternate allocation using the participant's birthdays or admission sequences (Deng 2010; Gao 2007; Hou 2010; Hu 2009; Liu 2006; Wang 2006; Xiao 2008; Zhang 2010). In the other studies the method was unclear because of a lack of useful information reported in the study papers.

Adequate allocation concealment, by sealed opaque envelopes, was used in one study (Cao 2008). The eight qRCTs were judged to be at high risk of bias for allocation concealment as described above (Deng 2010; Gao 2007; Hou 2010; Hu 2009; Liu 2006; Wang 2006; Xiao 2008; Zhang 2010). The remainder of the studies were judged to be at unclear risk of bias because of insufficient reporting.

Blinding

Blinding of participants and nurses was not possible due to the external application of *Aloe vera*. Therefore, we assessed blinding as at high risk of bias in all included studies. No included studies reported the blinding of outcome assessors, and we judged this risk of bias to be unclear because of a lack of sufficient information reported in the papers.

Incomplete outcome data

The flow of participants was not reported in any of the included studies so we were uncertain whether or not the reported outcome data were appropriate. One study reported that the withdrawal and attrition rates between the treatment and control groups were similar (Cao 2008) and this study was therefore judged to be at low risk of bias. For the remaining 42 studies it was not clear how many were randomised and how many withdrawn following randomisation.

Selective reporting

No study protocols were available for any of the included studies. Therefore, it was difficult to judge whether selective reporting

bias existed in the studies. Only for Cao 2008 it was clear that the expected outcomes were reported. We judged the remaining studies to be at unclear risk of bias.

Other potential sources of bias

The baseline information were considered to be similar between the comparison groups in 23 (Cao 2008; Chen 2009; Chen 2010; Deng 2010; Dong 2008; Hou 2010; Hu 2009; Li 2009; Li 2011; Liang 2004; Liu 2006; Lu 2004; Peng 2009; Ren 2008; Tan 2002; Wang 2006; Wang 2008; Wang 2010b; Yao 2009; Yu 2006; Zheng 2010; Zhong 2011; Zhou 2006) of the included studies. The remaining 20 studies (Chen 2012; Deng 2012; Dong 2001; Gao 2007; Gao 2012; Ji 2007; Jin 2010; Li 2003; Li 2006; Liu 2003; Liu 2012; Liu 2012b; Pan 2008; Tang 2011; Wang 2010; Wu 2009; Xiao 2008; Yang 2008; Zhang 2010; Zhang 2013) were judged as at unclear risk of bias because they lacked a detailed description of the baseline information.

Effects of interventions

Primary outcomes

Of the 43 studies that met the selection criteria, 22 studies reported the prophylactic effect of *Aloe vera* (Cao 2008; Chen 2012; Dong 2008; Hou 2010; Hu 2009; Ji 2007; Li 2011; Liang 2004; Liu 2003; Liu 2006; Liu 2012b; Pan 2008; Peng 2009; Ren 2008; Tan 2002; Wang 2006; Wu 2009; Xiao 2008; Yao 2009; Yu 2006; Zhang 2010; Zheng 2010) by measuring the total incidence of phlebitis, which was divided into first degree, second degree and third degree phlebitis according to the severity of the symptoms.

In the pooled analysis of the prophylactic effect we included the numbers of patients with first degree and second degree phlebitis in the outcome 'incidence of second degree phlebitis', and the numbers of patients with third, second and first degree phlebitis in the outcome total incidence of phlebitis.

Twenty-one studies reported the treatment effect of *Aloe vera* (Chen 2009; Chen 2010; Deng 2010; Deng 2012; Dong 2001; Gao 2007; Gao 2012; Jin 2010; Li 2003; Li 2006; Li 2009; Liu 2012; Lu 2004; Tang 2011; Wang 2008; Wang 2010; Wang 2010b; Yang

2008; Zhang 2013; Zhong 2011; Zhou 2006) by using the resolution rate of phlebitis (or total improvement rate of phlebitis). Patients were divided into those with recovery, marked improvement and improvement as the outcomes.

In this review we did not select the improvement outcome alone for analysis because we considered that the outcomes recovery, marked improvement and improvement were correlative. For example, a study showing a high number of participants with the recovery outcome will accordingly show a low number of participants with the outcomes marked improvement or improvement. Therefore, we assumed a cumulative effect of the marked improvement and improvement outcomes, and ruled that the outcome marked improvement contained the patients with recovery plus those with a marked improvement; and the outcome of total improvement contained the numbers showing recovery plus those with marked improvement plus improvement in the pooled analysis of the treatment effect.

Prevention of infusion phlebitis

Total incidence of phlebitis

The total incidence of phlebitis was directly reported in four studies (Chen 2012; Hou 2010; Liang 2004; Peng 2009), and calculated by the review authors by using the formula: all grades of phlebitis = first degree phlebitis plus second degree phlebitis plus third degree phlebitis, in the other studies (Cao 2008; Dong 2008; Hu 2009; Ji 2007; Li 2011; Liu 2006; Liu 2012b; Pan 2008; Ren 2008; Tan 2002; Wang 2006; Wu 2009; Xiao 2008; Yao 2009; Yu 2006; Zhang 2010; Zheng 2010). The results showed that *Aloe vera* decreased the total incidence of phlebitis when compared with no other intervention at different intervention periods; the risk ratio (RR) with three and seven days intervention duration was 0.44 (95% CI 0.29 to 0.66) and 0.28 (95% CI 0.11 to 0.68) respectively. The total incidence at five days of intervention showed an I^2 of 93%, which was higher than the pre-planned cut-off for pooling data. However, due to limitations of the software we were unable to switch off the totals for individual subgroups (Analysis 1.1). An overall pooled analysis was not performed because of the obvious heterogeneity among the included studies (Analysis 1.1). Compared with external application of a potato slice (Wang 2006; Wu 2009), *Aloe vera* had no obvious advantage for reducing the total incidence of phlebitis with the pooled RR being 0.90 (95% CI 0.58 to 1.40, $P = 0.65$, $I^2 = 0\%$, Analysis 2.1). However, significant differences were observed with *Aloe vera* for preventing all grades of phlebitis compared with external application of 75% alcohol (Liang 2004) and 33% MgSO₄ (Chen 2012; Hou 2010) with a RR of 0.02 (95% CI 0.0 to 0.28, $P = 0.004$, Analysis 6.1) and 0.43 (95% CI 0.24 to 0.78, $P = 0.005$, Analysis 3.1) respectively. Compared with 50% MgSO₄ (Ren 2008; Zhang 2010), external application of *Aloe vera* had no obvious advantage for the total incidence of phlebitis and the pooled RR was 0.41 (95% CI 0.16 to 1.07, $P = 0.07$, $I^2 = 76\%$, Analysis 4.1). One trial (Liu 2006) compared *Aloe vera* plus an ice bag with an ice bag plus 75% MgSO₄ and the effect on the prevention of all grades of phlebitis was not significant (RR 1.10, 95% CI 0.54 to 2.25, $P = 0.79$, Analysis 5.1).

Incidence of second degree phlebitis

Fourteen studies (Cao 2008; Dong 2008; Hu 2009; Ji 2007; Li 2011; Liu 2006; Liu 2012b; Pan 2008; Tan 2002; Wang 2006; Xiao 2008; Yao 2009; Yu 2006; Zheng 2010) with a combined total of 4585 participants compared *Aloe vera* with no other intervention

and reported the numbers of participants with second degree phlebitis. The application of *Aloe vera* alone had a significant effect on preventing second degree phlebitis (including first degree phlebitis) with a pooled RR of 0.18 (95% CI 0.10 to 0.31, $P < 0.0001$, $I^2 = 70\%$, Analysis 1.2). There was no significant difference between *Aloe vera* and a potato slice on second degree phlebitis (Wang 2006; Wu 2009) (RR 1.14, 95% CI 0.49 to 2.67, $P = 0.76$, Analysis 2.2). A significant difference was observed between *Aloe vera* and 50% MgSO₄ (Ren 2008; Zhang 2010) (RR 0.26, 95% CI 0.14 to 0.50, $P < 0.0001$, Analysis 4.2). The comparison of *Aloe vera* plus an ice bag with external application of 75% MgSO₄ plus an ice bag (Liu 2003) showed no significant advantage in preventing second degree phlebitis (RR 0.68, 95% CI 0.21 to 2.23, $P = 0.53$, Analysis 5.2).

Incidence of third degree phlebitis

Comparing *Aloe vera* alone with no prophylactic intervention (14 studies) (Cao 2008; Dong 2008; Hu 2009; Ji 2007; Li 2011; Liu 2006; Liu 2012b; Pan 2008; Tan 2002; Wang 2006; Xiao 2008; Yao 2009; Yu 2006; Zheng 2010) we found a lower incidence of third degree phlebitis using *Aloe vera* alone, with a significant difference in the incidence of phlebitis (RR 0.06, 95% CI 0.03 to 0.11, $P < 0.00001$, $I^2 = 44\%$, Analysis 1.3). Two studies (Wang 2006; Wu 2009) compared *Aloe vera* with potato slice for preventing phlebitis and no significant difference was found in the incidence of third degree phlebitis (RR 0.45, 95% CI 0.04 to 4.94, $P = 0.52$, Analysis 2.3). In the two studies (Ren 2008; Zhang 2010) comparing *Aloe vera* with 50% MgSO₄ external compresses, a prophylactic effect on third degree phlebitis was not obvious (RR 0.28, 95% CI 0.07 to 1.02, $P = 0.05$, $I^2 = 0\%$, Analysis 4.3). One study reported the effect of *Aloe vera* combined with other interventions. Liu 2003 compared *Aloe vera* plus ice bag compresses with ice bag plus 75% MgSO₄. No significant difference between the comparison groups was found in the incidence of third degree phlebitis (RR 1.19, 95% CI 0.08 to 18.73, $P = 0.9$, Analysis 5.3).

Treatment of infusion phlebitis

The rate of resolution of phlebitis

Recovery rate of phlebitis

In the studies of *Aloe vera* alone versus other treatments, seven trials (Deng 2010; Deng 2012; Gao 2007; Li 2003; Liu 2012; Tang 2011; Yang 2008) compared *Aloe vera* with 50% MgSO₄. The treatment effect was statistically significant for the recovery rate of phlebitis (RR 1.42, 95% CI 1.24 to 1.61, $P < 0.0001$, $I^2 = 41\%$, Analysis 8.1). Compared with non-*Aloe vera* treatment, *Aloe vera* plus the same non-*Aloe vera* treatment (Chen 2009; Jin 2010; Zhang 2013; Zhong 2011) showed a significant difference for recovery rate of phlebitis (RR 1.75, 95% CI 1.24 to 2.46, $P = 0.001$, $I^2 = 57\%$, Analysis 9.1). One trial (Zhou 2006) compared *Aloe vera* with potato slice and the RR for the recovery rate of phlebitis was 2.77 (95% CI 1.52 to 5.04, $P = 0.0009$, Analysis 11.1). One trial (Wang 2010b) reported the result of application of *Aloe vera* versus hirudoid on the recovery rate of phlebitis and the RR value was 0.36 (95% CI 0.15 to 0.82, $P = 0.02$, Analysis 12.1). One trial compared *Aloe vera* plus routine treatment with the same routine treatment plus dexamethasone, the RR was 1.95 (95% CI 1.30 to 2.93, $P = 0.001$, Analysis 13.1).

Marked improvement rate of phlebitis

Two studies (Dong 2001; Li 2006) compared *Aloe vera* with 33% MgSO₄ for marked improvement of phlebitis, showing a statistically

significant difference (RR 1.97, 95% CI 1.44 to 2.70, $P < 0.001$, $I^2 = 33\%$, [Analysis 7.2](#)). Nine trials with 814 participants compared external application of *Aloe vera* versus 50% $MgSO_4$ and the pooled RR for marked improvement (including recovery) of phlebitis for treatment with *Aloe vera* compared to 50% $MgSO_4$ was 1.56 (95% CI 1.29 to 1.87, $P = 0.0002$, $I^2 = 73\%$, [Analysis 8.2](#)). In the studies of *Aloe vera* plus non-*Aloe vera* treatment versus the same non-*Aloe vera* treatment ([Chen 2009](#); [Jin 2010](#); [Zhong 2011](#)) the results showed that the application of *Aloe vera* combined with other treatments had a significant effect on the marked improvement rate of phlebitis (RR 1.26, 95% CI 1.09 to 1.47, $P = 0.003$, $I^2 = 0\%$, [Analysis 9.2](#)). One trial ([Lu 2004](#)) compared *Aloe vera* with 75% alcohol and the RR of marked improvement of phlebitis was 3.00 (95% CI 1.09 to 8.25, $P = 0.03$, [Analysis 10.1](#)). One trial ([Zhou 2006](#)) comparing *Aloe vera* with a potato slice in the treatment of phlebitis showed a statistically significant difference in the outcome of marked improvement (RR 1.89, 95% CI 1.36 to 2.62, $P = 0.0001$, [Analysis 11.2](#)). A single study ([Wang 2010b](#)) showed that *Aloe vera* was more effective at increasing the rate of marked improvement of phlebitis than hirudoid alone (RR 0.58, 95% CI 0.44 to 0.78, $P = 0.0002$, [Analysis 12.2](#)). One trial comparing *Aloe vera* plus routine treatment with the same routine treatment plus dexamethasone ([Wang 2008](#)) showed a statistically significant difference on the marked improvement rate of phlebitis (RR 1.95, 95% CI 1.30 to 2.93, $P = 0.0001$, [Analysis 13.2](#)).

Total improvement rate of phlebitis

Three trials ([Dong 2001](#); [Gao 2012](#); [Li 2006](#)) reported the effect of *Aloe vera* versus external application of 33% $MgSO_4$ in the treatment of phlebitis showing a statistically significant difference (RR 1.16, 95% CI 1.09 to 1.24, $P < 0.0001$, $I^2 = 26\%$, [Analysis 7.3](#)). Comparing external application of *Aloe vera* with external application of 50% $MgSO_4$, data for improvement (including recovery and marked improvement) of phlebitis were available in 10 studies ([Chen 2010](#); [Deng 2010](#); [Deng 2012](#); [Gao 2007](#); [Li 2003](#); [Li 2009](#); [Liu 2012](#); [Tang 2011](#); [Wang 2010](#); [Yang 2008](#)) and showed a significant difference in the total improvement of phlebitis (RR 1.22, 95% CI 1.16 to 1.28, $P < 0.0001$, $I^2 = 0\%$, [Analysis 8.3](#)). In studies of *Aloe vera* combined with non-*Aloe vera* treatment versus non-*Aloe vera* treatment, one trial ([Jin 2010](#)) compared *Aloe vera* plus hirudoid with hirudoid, one trial compared *Aloe vera* plus sulphonic acid mucopolysaccharide cream with sulphonic acid mucopolysaccharide cream ([Chen 2009](#)), and one compared *Aloe vera* plus sulphanilamide pyrimidine with sulphanilamide pyrimidine ([Zhong 2011](#)). A significant difference between the comparison groups was observed (RR 1.23, 95% CI 1.13 to 1.35, $P < 0.00001$, $I^2 = 37\%$, [Analysis 9.3](#)). One trial ([Lu 2004](#)) compared *Aloe vera* versus 75% alcohol, another ([Zhou 2006](#)) compared *Aloe vera* versus potato slice, with their results showing that application of *Aloe vera* had a significant effect on the improvement of phlebitis (RR 2.0, 95% CI 1.14 to 3.52, $P = 0.02$, [Analysis 10.2](#); RR 1.25, 95% CI 1.06 to 1.47, $P = 0.008$, [Analysis 11.3](#) respectively). However, one trial ([Wang 2010b](#)) showed no difference between *Aloe vera* and hirudoid alone, with the same rate of improvement of phlebitis (39/39, 100% in the *Aloe vera* group versus 30/30, 100% in the hirudoid group, [Analysis 12.3](#)). One trial ([Wang 2008](#)) compared *Aloe vera* plus routine treatment versus the same routine treatment plus dexamethasone; a significant difference between the comparison groups could be observed (RR 1.29, 95% CI 1.06 to 1.57, $P = 0.01$, [Analysis 13.3](#)).

Secondary outcomes

Prevention of infusion phlebitis

Duration of successful placement of a venous catheter

The duration of successful placement of a venous catheter is defined as the length of time which the venous catheter, such as the needle, is successfully retained in the vein after infusion.

Two trials ([Cao 2008](#); [Yao 2009](#)) compared *Aloe vera* with no treatment for the time the needle was successfully retained in the infused vein. The application of *Aloe vera* had a significant effect on the length of time the needle was successfully retained in the vein compared with no treatment. The MD was 0.79 days (95% CI 0.33 to 1.25) in [Cao 2008](#) and 3.40 days (95% CI 3.08 to 3.72) in [Yao 2009](#). A pooled analysis was not performed because of the heterogeneity between the two trials ($I^2 = 99\%$) ([Analysis 1.4](#)).

Other secondary outcomes

Other secondary outcomes such as health-related quality of life and adverse effects, predefined in the protocol, were not reported in the included studies on prevention of infusion phlebitis.

Treatment of infusion phlebitis

Symptom improvement of phlebitis

Time of elimination of red swelling symptoms in phlebitis

The time for elimination of red swelling symptoms in the infusion vein was measured in one trial ([Chen 2009](#)) comparing *Aloe vera* plus sulphonic acid mucopolysaccharide cream versus sulphonic acid mucopolysaccharide cream. The analysis showed that application of *Aloe vera* combined with sulphonic acid mucopolysaccharide cream was not significantly better than the application of sulphonic acid mucopolysaccharide cream alone in shortening the time of red swelling symptom elimination in the infusion vein (MD -2.93 hours, 95% CI -7.91 to 2.05, $P = 0.25$, [Analysis 9.4](#)).

Time of pain relief at the location of the infusion vein

Data for time of pain relief at the location of the infusion vein could be obtained from a single trial ([Chen 2009](#)). Compared with the application of sulphonic acid mucopolysaccharide cream alone, *Aloe vera* combined with sulphonic acid mucopolysaccharide cream shortened the time for pain relief at the location of the infusion vein (MD -0.97 hours, 95% CI -1.58 to -0.36, $P = 0.002$, [Analysis 9.5](#)).

Time of resolution of phlebitis

One trial ([Wang 2010](#)) of *Aloe vera* versus external application of 50% $MgSO_4$ reported the time of marked improvement and time of improvement of phlebitis symptoms. Compared with the external application of 50% $MgSO_4$, application of *Aloe vera* had a significant effect in shortening the time for marked improvement and improvement of phlebitis symptom (MD -20.0 hours, 95% CI -25.23 to -14.77, $P < 0.0001$, [Analysis 8.4](#); MD -13.0 hours, 95% CI -16.39 to -9.61, $P < 0.0001$, [Analysis 8.5](#) respectively).

Other secondary outcomes

Other secondary outcomes such as health-related quality of life and adverse effects, predefined in the protocol, were not reported in the included studies on treatment of infusion phlebitis.

Subgroup analysis

Analysis of data for 14 trials (Cao 2008; Dong 2008; Hu 2009; Ji 2007; Li 2011; Liu 2006; Liu 2012b; Pan 2008; Tan 2002; Wang 2006; Xiao 2008; Yao 2009; Yu 2006; Zheng 2010) with 4585 participants suggested that external application of fresh *Aloe vera* resulted in an overall benefit on prevention of third degree phlebitis compared with no treatment in the control group (RR 0.06, 95% CI 0.03 to 0.11, $I^2 = 44\%$, Analysis 1.3). We did not find definitive evidence that study duration explained the observed variation of effect. The test for subgroup differences by duration of treatment did not reach statistical significance overall ($P = 0.06$, Analysis 1.3).

Results of the subgroup analysis based on the incidence of second degree phlebitis were similar and an obvious advantage could be found comparing external application of *Aloe vera* for varied durations of treatment with no treatment (Analysis 1.2). The difference between the subgroups was significant ($\text{Chi}^2 = 29.81$, $\text{df} = 6$, $P < 0.0001$) and showed that the varied duration of treatment might explain some of the overall heterogeneity (Analysis 1.2). For the incidence of total phlebitis, the results of the subgroup analysis according to the varied durations showed that external application of *Aloe vera* was effective for prevention of phlebitis compared with no treatment but the overall heterogeneity was not substantially decreased between subgroups (Analysis 1.1).

Comparing *Aloe vera* and 50% MgSO_4 , nine trials (Chen 2010; Deng 2010; Deng 2012; Gao 2007; Li 2003; Li 2009; Liu 2012; Wang 2010; Yang 2008) with 814 participants reported marked improvement and total improvement outcomes; and seven trials (Deng 2010; Deng 2012; Gao 2007; Li 2003; Liu 2012; Tang 2011; Yang 2008) with 595 participants reported recovery as an outcome. All of the pooled results showed that external application of *Aloe vera* improved symptoms of phlebitis compared with the application of 50% MgSO_4 . Heterogeneity was observed among the included trials. We undertook subgroup analysis by duration of treatment (three, seven or 15 days). Based on the test for subgroup differences across the three outcomes, we did not have evidence of a statistically significant association between study duration and effect size (Analysis 8.1; Analysis 8.2; Analysis 8.3).

The pre-planned subgroup analysis for types of *Aloe vera* products (such as a thin slice or the juice of *Aloe vera* and *Aloe* derived products) was not conducted because of insufficient data.

Sensitivity analysis

When the meta-analysis for incidence of third degree phlebitis ($I^2 = 44\%$) with the comparison *Aloe vera* versus no treatment was based on a fixed-effect model (RR 0.06, 95% CI 0.03 to 0.11, $P < 0.00001$, Analysis 1.3) the RR was lower and the 95% CI was wider compared with when calculated with the random-effects model (RR 0.13, 95% CI 0.05 to 0.34, $P < 0.0001$, Analysis 14.1), but the selection of the statistical model did not have a substantial impact on the significance of effects.

Where possible, we performed sensitivity analyses by excluding qRCTs. The decrease in heterogeneity was very obvious in the analysis of external application of *Aloe vera* versus no treatment for incidence of third degree phlebitis and incidence of second degree phlebitis on excluding the four qRCTs (Hu 2009; Liu 2006; Wang 2006; Xiao 2008). The RR with the inclusion of qRCTs was 0.06 (95% CI 0.03 to 0.11, $P < 0.00001$, $I^2 = 44\%$, Analysis 1.3) and 0.18 (95% CI 0.10 to 0.31, $P < 0.00001$, $I^2 = 70\%$, Analysis 1.2) respectively. But the observed effect was RR 0.11 (95% CI 0.05 to 0.26, $P < 0.00001$, $I^2 = 0\%$, Analysis 14.2) and 0.16 (95% CI 0.11 to 0.24, $P < 0.00001$, $I^2 = 26\%$, Analysis 14.3) when qRCTs were excluded. However, qRCTs did not substantially reduce the overall heterogeneity for the total incidence of phlebitis in the comparison external application of *Aloe vera* versus no treatment (Analysis 14.4).

We did not perform the pre-planned sensitivity analyses for study quality and unpublished studies because the study quality of the included studies was similar and there were no unpublished trials included in the review.

Publication bias

We identified possible publication bias in the assessment of the total incidence of phlebitis, incidence of second degree phlebitis and the incidence of third degree phlebitis, with 10 or more trials available for meta-analysis. The funnel plots (Figure 4; Figure 5; Figure 6) showed obvious asymmetry suggesting evidence of publication bias.

Figure 4. Funnel plot of comparison: 1 *Aloe vera* versus no treatment for prevention of phlebitis, outcome: 1.1 Total incidence of phlebitis.

Figure 5. Funnel plot of comparison: 1 *Aloe vera* versus no treatment for prevention of phlebitis, outcome: 1.2 Incidence of second degree phlebitis.

Figure 6. Funnel plot of comparison: 1 *Aloe vera* versus no treatment for prevention of phlebitis, outcome: 1.3 Incidence of third degree phlebitis.

DISCUSSION

Summary of main results

In this review, external application of *Aloe vera* was associated with a statistically significant lower incidence of phlebitis compared with no prophylactic treatment; the RR was 0.28 (95% CI 0.11 to 0.68) for seven days of the intervention, and 0.29 (95% CI 0.11 to 0.74) for five days duration. In addition, *Aloe vera* reduced the degree of severity of phlebitis, with the RR for the incidence of third degree or second degree phlebitis significantly lower in participants receiving applications of *Aloe vera* than in participants with no prophylactic treatment (RR 0.06, 95% CI 0.03 to 0.11 and 0.18, 95% CI 0.10 to 0.31 respectively). When compared with external application of a potato slice, the incidence of phlebitis appeared lower with the application of *Aloe vera* (RR 0.90, 95% CI 0.58 to 1.40), but this difference did not reach statistical significance. Compared with external application of 75% alcohol, there was a statistically significant difference in the incidence of

phlebitis (RR 0.02, 95% CI 0.00 to 0.28). Compared with 50% MgSO₄, there was no statistically significant difference with the external application of *Aloe vera* in third degree phlebitis and all grades of phlebitis (RR 0.28, 95% CI 0.07 to 1.02; RR 0.41, 95% CI 0.16 to 1.07), but the second degree phlebitis did show a statistically significant improvement (RR 0.26, 95% CI 0.14 to 0.49). Compared with 33% MgSO₄, there was an obvious reduction in the risk of phlebitis (RR 0.43, 95% CI 0.24 to 0.78). In the comparison of *Aloe vera* combined with non-*Aloe vera* treatment versus the non-*Aloe vera* treatment, there was greater improvement in the prophylaxis of phlebitis with *Aloe vera* plus 0.9% NaCl₂ plus dexamethasone versus 0.9% NaCl₂ plus dexamethasone than with *Aloe vera* plus an ice bag versus an ice bag plus 75% MgSO₄.

Recovery, marked improvement and total improvement of phlebitis were significantly increased in trial participants treated with the external application of *Aloe vera* compared with the external application of 50% MgSO₄ (RR 1.42, 95% CI 1.24 to 1.61; RR 1.56,

95% CI 1.29 to 1.87; RR 1.22, 95% CI 1.16 to 1.28 respectively). Furthermore, the same effects were observed in comparisons with 33% MgSO₄ on marked improvement (RR 1.97 95% CI 1.44 to 2.70) and total improvement (RR 1.16 95% CI 1.09 to 1.24). Compared with external application of 75% alcohol or a potato slice, the treatment effects (including recovery, marked improvement and total improvement) of external application of *Aloe vera* for phlebitis were statistically significant. Compared with external application of hirudoid, the treatment effects, including recovery, marked improvement and total improvement, were less in trial participants treated with external application of *Aloe vera*. In the application of *Aloe vera* combined with non-*Aloe vera* treatment, the treatment effects including the recovery, marked improvement and total improvement outcomes were better in participants with *Aloe vera* plus routine treatment or hirudoid than the same routine treatment plus dexamethasone or hirudoid alone; but the same beneficial effect was not evident in the trial of *Aloe vera* plus sulphanilamide pyrimidine versus the application of sulphanilamide pyrimidine alone. In addition, compared with external application of 50% MgSO₄, the time to symptom improvement of phlebitis was obviously shortened in participants treated with *Aloe vera*. But compared with sulphonic acid mucopolysaccharide cream, application of *Aloe vera* plus sulphonic acid mucopolysaccharide cream did not obviously shorten the time for symptom improvement of phlebitis. When compared with no treatment, the time the infusion needle was retained in the vein was lengthened in participants receiving application of *Aloe vera*.

Overall completeness and applicability of evidence

The participants of the included studies were mainly the varied cancer patients who would be or had been part of a program of chemotherapy, and some of the participants were infused with 20% mannitol (Cao 2008; Jin 2010; Li 2006; Li 2009; Liang 2004; Tan 2002; Zheng 2010). Although some evidence indicated that the external application of *Aloe vera* was beneficial to treat or prevent phlebitis associated with the infusion of chemotherapy drugs or 20% mannitol, the included participants were not typical and showed a lack of clinical representation. The age of the included participants in all but one study ranged from 18 years to 75 years old. Only 90 participants in one study (Gao 2007) were children (aged from one month to three years old). The evaluated interventions in this review mainly involved fresh aloe leaf, usually cut into a thin slice (2 to 6 cm wide by 5 to 10 cm long) or squeezed into aloe juice. No other *Aloe vera*-derived products were used in the included studies. In the evaluation of the treatment effect, composite outcomes, for example marked improvement or improvement of phlebitis symptoms, were used in many of the included studies. The use of these composite outcomes can reduce the ability to understand the precise impact of *Aloe vera* use in improving the clinical symptoms of phlebitis. All included studies were performed in China, and no studies from other countries were identified. The use of the raw plant products of *Aloe vera* may be impossible to implement in countries other than China but the review's conclusion may be helpful for the development of research on *Aloe vera* products. Perhaps authorised products of aloe vera will be applied in countries other than China in the future.

Quality of the evidence

In general the included trials were small, except for one study (Hu 2009), and had diverse designs. Eight quasi-randomised controlled

trials (qRCTs) were included (Deng 2010; Gao 2007; Hou 2010; Hu 2009; Liu 2006; Wang 2006; Xiao 2008; Zhang 2010). The uncertain duration of treatment, for example two to three days and one to seven days, was noted in the included trials. It is important to note that the methodological shortcomings were obvious in the assessment of the studies. Firstly, only very few studies described detailed information on random sequence generation (Cao 2008; Jin 2010; Wang 2006), and almost all of the included studies did not mention the method of allocation concealment, which is considered to be one of the most important causes of bias in a randomised controlled trials (Altman 2001). Secondly, blinding was not used in all included trials. While it is impossible to blind the participants and personnel in the studies involved in the external application of therapies, and not blinding may not influence the judgement of outcomes, not blinding the outcome assessors may result in an overestimation of the intervention effect. Thirdly, the variation between the results of the studies was substantive and we were unable to explain this variation despite undertaking subgroup analyses by intervention duration. In addition, due to unavailable protocols for all included studies, selective reporting and attrition biases were unclear. We also identified possible publication bias in the assessment of the total incidence of phlebitis, incidence of second degree phlebitis and the incidence of third degree phlebitis, where funnel plots showed obvious asymmetry suggesting evidence of publication bias.

Potential biases in the review process

We attempted to minimise bias in the review process. Firstly, we performed a comprehensive literature search without language limits to identify all relevant studies. Secondly, two review authors independently assessed the studies for inclusion and carried out data extraction to ensure all relevant data were obtained. Two review authors independently assessed the risk of bias of the included studies according to the rules of the *Cochrane Handbook for Systematic Reviews of Interventions* (Higgins 2011), and disagreements were resolved by consensus. In addition, we strictly followed the protocol outline to perform the review. Nevertheless, potential biases still exist. For example, the process of assessing risk of bias involves some degree of subjective judgements from the assessors. The publication bias was not assessed using funnel plots for most comparisons in this review because the numbers of studies included in each comparison was less than 10. Publication bias is possible because we found that all included studies were published studies and the majority of their outcomes were positive. Many of the outcomes predefined in the protocol of this review (Zheng 2011), such as health-related quality of life, adverse effects etc, were not measured in the included studies, therefore we could not review their data to weigh up the effect. In addition, several comparisons, for example *Aloe vera* plus non-*Aloe vera* intervention versus non-*Aloe vera* intervention, only involved either a single study or a few studies and could cause spuriously significant evidence.

Agreements and disagreements with other studies or reviews

We did not identify any other systematic reviews comparing external application of *Aloe vera*, with or without another intervention, with no treatment or the other intervention in preventing or treating infusion phlebitis.

AUTHORS' CONCLUSIONS

Implications for practice

There is no strong evidence for the prevention or treatment of infusion phlebitis with external application of *Aloe vera*. The current available evidence is limited by the poor methodological quality and risk of selective outcome reporting of the included studies, and by variations in the direction and size of effect across the studies. The positive effects observed with external application of *Aloe vera* in preventing or treating infusion phlebitis compared with no intervention or external application of 33% or 50% MgSO₄ should therefore be viewed with caution.

Implications for research

Further research should consider the following points.

1. The methods of random sequence generation and allocation concealment should be adequately described.
2. Blinding of outcome assessors should be applied to reduce detection bias.
3. Clinical trial registers should be encouraged to provide the available protocols.
4. Participants who were withdrawals or dropouts during the trial should be clearly described.
5. Adverse events should be measured as a priority outcome.

ACKNOWLEDGEMENTS

We would like to thank Dr Marlene Stewart, Dr Karen Welch and the editors of the Cochrane Peripheral Vascular Disease Review Group.

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CHARACTERISTICS OF STUDIES

Characteristics of included studies [ordered by study ID]

Cao 2008

Methods	<p>Study design: Randomised controlled trial</p> <p>Method of randomisation: Computer program</p> <p>Concealment of allocation: Sealed envelope</p> <p>Exclusions post-randomisation: Treatment group: 3 subjects dropped out because of infusion drugs leakage; control group: 1 subject dropped out because of the infusion drug leakage</p> <p>Losses to follow up: None</p> <p>Intention-to-treat analysis: Yes</p>
Participants	<p>Country: China</p> <p>Setting: Hospital</p> <p>Number: 76 participants (38 treatment, 38 control)</p> <p>Age: Mean 60.23 years, range from 50 - 70 years</p> <p>Sex: Male/female 43/33</p> <p>Inclusion criteria: Conscious, cooperation, age (50 - 70 year), first undergo treatment with 20% mannitol (125 ml Q8h)</p> <p>Exclusion criteria: Confused state of mind, no cooperation, infusing other drugs which impair the vein (except for 20% mannitol), hypersensitive to aloe.</p>
Interventions	<p>Treatment: Fresh aloe slice (5 cm long, 3 cm wide) external application. Wet compress at punctured skin once a day</p> <p>Control: No treatment</p> <p>Duration: 5 days</p>
Outcomes	<p>Primary: The incidence of phlebitis</p> <p>(a) First degree: pain, red swelling appear on the punctured vein. Strip-shaped changes in veins are not observed, and no palpable venous callosity</p> <p>Treatment group: 26/38. Control group: 33/38</p> <p>(b) Second degree: pain, red swelling appear on the punctured vein. Strip-shaped changes in vein are observed, and no palpable venous callosity.</p> <p>Treatment group: 0/38. Control group: 1/38</p> <p>(c) Third degree: pain, red swelling appear on the punctured vein. Strip-shaped changes in vein are observed, with palpable venous callosity.</p> <p>Treatment group: 0/38. Control group: 0/38</p> <p>Secondary: The length of time the needle is detained in the vein</p>
Notes	
Risk of bias	

Cao 2008 (Continued)

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Random sequence was generated by using computer program
Allocation concealment (selection bias)	Low risk	Random sequence was concealed by using the sealed envelopes
Blinding of participants and personnel (performance bias) All outcomes	High risk	No blinding. The outcome assessment is likely to be influenced by the lack of blinding
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not reported.
Incomplete outcome data (attrition bias) All outcomes	Low risk	Treatment group: 3 subjects dropped out because of infusion drugs leakage Control group: 1 subject dropped out because of the infusion drug leakage ITT analysis was performed in this study
Selective reporting (reporting bias)	Low risk	The study protocol is not available, but it is clear that the published reports included all expected outcomes
Other bias	Low risk	There are no statistical differences in age, sex, illness, classification of phlebitis and nursing among the comparisons. The study appears to be free other sources of bias

Chen 2009

Methods	Study design: Randomised controlled trial Method of randomisation: Not described Concealment of allocation: Not reported Exclusions post-randomisation: Not reported Losses to follow up: None Intention-to-treat analysis: Not reported
Participants	Country: China Setting: Hospital Number: 60 participants (20 treatment, 20 control 1, 20 control 2) Age: Mean 48.2 years, range from 28 to 62 years Sex: Male/female 26/34 Inclusion criteria: Phlebitis met criteria of the Infusion Nursing Society of America Exclusion criteria: Not stated

Chen 2009 (Continued)

Interventions	Treatment: Sulphonic acid mucopolysaccharide cream smeared at punctured skin for 4 - 6 hours, once a day, then fresh aloe slice wet compress, at least twice a day	
	Control 1: Sulphonic acid mucopolysaccharide cream smeared at puncture skin for 4 - 6 hours, once a day	
	Control 2: 33% MgSO ₄ wet compress at punctured skin, change when dried	
	Duration: 14 days	
Outcomes	Primary: The rate of resolution of phlebitis	
	(a) Recovery: disappearance of swelling, callosity and strip-shaped change with index of effective 100% (index of effective = (scores before treatment - scores after treatment)/score before treatment	
	Treatment group: 0/20, Control group 1: 0/20, Control group 2: 0/20	
	(b) Marked improvement: regression of swelling, callosity and strip-shaped change with index of effective over 60%	
	Treatment group: 15/20, Control group 1: 12/20, Control group 2: 7/20	
	(c) Improvement: regression of swelling with index of effective over 20%, no obvious regression on callosity and strip-shaped change	
	Treatment group: 4/20, Control group 1: 6/20, Control group 2: 6/20	
	(d) Not effective: index of effective less than 20%, no change of symptoms of phlebitis	
	Treatment group: 1/20, Control group 1: 2/20, Control group 2: 7/20	
	Secondary: The time of red swelling eliminated, the time of relief of pain	
Notes		
Risk of bias		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomised, but the detailed information of randomisation method was not described
Allocation concealment (selection bias)	Unclear risk	Method of allocation concealment was not described
Blinding of participants and personnel (performance bias) All outcomes	High risk	No blinding. The outcome assessment is likely to be influenced by the lack of blinding
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not reported
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Number randomised not stated
Selective reporting (reporting bias)	Unclear risk	The study protocol is not available, and it is not clear if the published reports included all expected outcomes

Chen 2009 (Continued)

Other bias	Low risk	There are no statistical differences in age, sex, illness, classification of phlebitis and program of nursing among the comparisons. The study appears to be free other sources of bias
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Chen 2010

Methods	Study design: Randomised controlled trial Method of randomisation: Not described Concealment of allocation: Not reported Exclusions post-randomisation: Not reported Losses to follow up: None Intention-to-treat analysis: Not reported
Participants	Country: China Setting: Hospital Number: 100 participants (50 treatment, 50 control) Age: Mean 41.9 years, range from 18 to 76 years Sex: Male/female 64/36 Inclusion criteria: Phlebitis met criteria of the Infusion Nursing Society of America Exclusion criteria: Not stated
Interventions	Treatment: Aloe glue smeared at punctured skin, bid Control: 50% MgSO ₄ wet compress at punctured skin, bid Duration: 3 days
Outcomes	Primary: The rate of resolution of phlebitis (a) Marked improvement: no local red swelling, disappearance of pain Treatment group: 38/50. Control group: 3/50 (b) Improvement: regression of local red swelling, alleviation of pain Treatment group: 12/50. Control group: 33/50 (c) Not effective: no change of local red swelling and pain after treatment for 3 days Treatment group: 0/50. Control group: 14/50 Secondary: None
Notes	
Risk of bias	
Bias	Authors' judgement Support for judgement

Chen 2010 (Continued)

Random sequence generation (selection bias)	Unclear risk	Randomised, but the detailed information of randomisation method was not described
Allocation concealment (selection bias)	Unclear risk	Method of allocation concealment was not described
Blinding of participants and personnel (performance bias) All outcomes	High risk	No blinding. The outcome assessment is likely to be influenced by the lack of blinding
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not reported
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Number randomised not stated
Selective reporting (reporting bias)	Unclear risk	The study protocol is not available, and it is not clear if the published reports included all expected outcomes
Other bias	Low risk	There are no statistical differences in age, sex, illness, classification of phlebitis and program of nursing among the comparisons. The study appears to be free of other sources of bias

Chen 2012

Methods	Study design: Randomised controlled trial Method of randomisation: Not described Concealment of allocation: Not reported Exclusions post-randomisation: Not reported Losses to follow up: None Intention-to-treat analysis: Not reported
Participants	Country: China Setting: Hospital Number: 100 participants (50 treatment, 50 control) Age: Mean 42.26 years, range from 34 - 56 years Sex: Male/female 0/100 Inclusion criteria: Breast cancer patients with CMF (cyclophosphamide, methotrexate and 5-fluorouracil) chemotherapy Exclusion criteria: Not stated
Interventions	Treatment: Fresh aloe slice external application (wet compress at punctured skin), 3 - 4 times a day Control: 33% MgSO ₄ wet compress at punctured skin, 3 - 4 times a day

Chen 2012 (Continued)

Duration: 6 months

Outcomes

Primary: The incidence of phlebitis

Treatment group: 5/50, Control group: 10/50

Secondary: None

Notes

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomised, but the detailed information of randomisation method was not described
Allocation concealment (selection bias)	Unclear risk	Method of allocation concealment was not described
Blinding of participants and personnel (performance bias) All outcomes	High risk	No blinding. The outcome assessment is likely to be influenced by the lack of blinding
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not reported
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Flow of participants randomised was not available
Selective reporting (reporting bias)	Unclear risk	The study protocol is not available, and it is not clear if the published reports included all expected outcomes
Other bias	Unclear risk	The baseline information between comparison groups were not described

Deng 2010

Methods

Study design: Quasi-randomised controlled trial

Method of randomisation: Alternate allocation

Concealment of allocation: None

Exclusions post-randomisation: Not reported

Losses to follow up: None

Intention-to-treat analysis: Not reported

Participants

Country: China

Setting: Hospital

Number: 85 participants (43 treatment, 42 control)

Age: Mean 42.9 years, range from 21 to 75 years

Deng 2010 (Continued)

Sex: Male/female 46/39

Inclusion criteria: Phlebitis met the criteria of the Infusion Nursing Society of America

Exclusion criteria: Not stated

Interventions	<p>Treatment: The juice of fresh aloe leaf, rubbed on the punctured skin, once every 3 hours</p> <p>Control: 50% MgSO₄ rubbed on the punctured skin, 3 - 4 times per day</p> <p>Duration: 15 days</p>
Outcomes	<p>Primary: The rate of resolution of phlebitis</p> <p>(a) Recovery: disappearance of local pain, red swelling, scorching hot and strip-shaped change in veins within 4 days</p> <p>Treatment group: 36/43, Control group: 4/42</p> <p>(b) Improvement: disappearance degree of local pain, red swelling, scorching hot and strip-shaped change in veins within 7 days over 80%</p> <p>Treatment group: 7/43, Control group: 26/42</p> <p>(c) No improvement: no obvious improvement of symptoms within 15 days after treatment</p> <p>Treatment group: 0/43, Control group: 12/42</p> <p>Secondary: None</p>

Notes

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	Sequence generated by the admission sequence of participants
Allocation concealment (selection bias)	High risk	Alternate allocation according to admission sequence
Blinding of participants and personnel (performance bias) All outcomes	High risk	No blinding. The outcome assessment is likely to be influenced by the lack of blinding
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not reported
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Number randomised not stated
Selective reporting (reporting bias)	Unclear risk	The study protocol is not available, and it is not clear if the published reports included all expected outcomes
Other bias	Low risk	Sex, age, illness, the course of disease, program of chemotherapy and the severe degree of phlebitis between two groups are not statistically significant ($P > 0.05$). The study appears to be free other sources of bias

Deng 2012

Methods	<p>Study design: Randomised controlled trial</p> <p>Method of randomisation: Not described</p> <p>Concealment of allocation: Not reported</p> <p>Exclusions post-randomisation: Not reported</p> <p>Losses to follow up: None</p> <p>Intention-to-treat analysis: Not reported</p>
Participants	<p>Country: China</p> <p>Setting: Hospital</p> <p>Number: 116 participants (60 treatment, 56 control)</p> <p>Age: Mean $\pm$ SD: treatment 67.62 $\pm$ 12.96 years; control 71.10 $\pm$ 11.06 years</p> <p>Sex: Male/female: treatment 40/20; control 34/22</p> <p>Inclusion criteria: Phlebitis met the criteria of the Infusion Nursing Society of America</p> <p>Exclusion criteria: Complicated diabetes</p>
Interventions	<p>Treatment: Fresh aloe leaf wet compress, tid</p> <p>Control: 50% MgSO₄, tid</p> <p>Duration: 3 days</p>
Outcomes	<p>Primary: The rate of resolution of phlebitis</p> <p>(a) Recovery: disappearance of local pain, red swelling, scorching hot and strip-shaped change in veins</p> <p>Treatment group: 47/60, Control group: 30/56</p> <p>(b) Marked improvement: disappearance degree of local pain, red swelling, scorching hot and strip-shaped change in veins over 80%</p> <p>Treatment group: 11/60, Control group: 12/56</p> <p>(c) Improvement: disappearance of pain, scorching hot at local skin. the shortened area of red swelling was less than 80%</p> <p>Treatment group: 2/60, Control group: 7/56</p> <p>(c) No effect: no obvious change of symptoms after treatment</p> <p>Treatment group: 0/60, Control group: 7/56</p> <p>Secondary: None</p>
Notes	
Risk of bias	
Bias	<p>Authors' judgement</p> <p>Support for judgement</p>

Deng 2012 (Continued)

Random sequence generation (selection bias)	Unclear risk	Randomised, but the detailed information of randomisation method was not described
Allocation concealment (selection bias)	Unclear risk	Method of allocation concealment was not described
Blinding of participants and personnel (performance bias) All outcomes	High risk	No blinding. The outcome assessment is likely to be influenced by the lack of blinding
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not reported
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Flow of participants randomised was not available
Selective reporting (reporting bias)	Unclear risk	The study protocol is not available, and it is not clear if the published reports included all expected outcomes
Other bias	Unclear risk	The baseline information between comparison groups were not described

Dong 2001

Methods	Study design: Randomised controlled trial Method of randomisation: Not described Concealment of allocation: Not reported Exclusions post-randomisation: Not reported Losses to follow up: None Intention-to-treat analysis: Not reported
Participants	Country: China Setting: Hospital Number: 154 participants (80 treatment, 74 control) Age: mean 49.8 years, range from 23 to 76 years Sex: male/female 91/63 Inclusion criteria: Phlebitis met the criteria of the nursing conference in Hangzhou city 1990 Exclusion criteria: Not stated
Interventions	Treatment: Fresh aloe slice external application, once a day Control : 33% MgSO ₄ external application, tid Duration: 7 days
Outcomes	Primary: The rate of resolution of phlebitis

Dong 2001 (Continued)

(a) Marked improvement: disappearance of red swelling in the local vein, softening of callosity vein vessel, re-open the block vein vessel within one treatment course; disappearance of pain within two hours.

Treatment group: 26/80; Control group: 16/74

(b) Improvement: disappearance of phlebitis symptom over one treatment course and disappearance of pain over two hours

Treatment group: 49/80; Control group: 37/74

(c) No improvement: symptoms of phlebitis and pain were unchanged after treatment

Treatment group: 5/80; Control group: 21/74

Secondary: None

Notes

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomised, but the detailed information of randomisation method was not described
Allocation concealment (selection bias)	Unclear risk	Method of allocation concealment was not described
Blinding of participants and personnel (performance bias) All outcomes	High risk	No blinding. The outcome assessment is likely to be influenced by the lack of blinding
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not reported
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Flow of participants randomised was not available
Selective reporting (reporting bias)	Unclear risk	The study protocol is not available, and it is not clear if the published reports included all expected outcomes
Other bias	Unclear risk	The baseline information between comparison groups were not described

Dong 2008

Methods	Study design: Randomised controlled trial
	Method of randomisation: Not described
	Concealment of allocation: Not reported
	Exclusions post-randomisation: Not reported
	Losses to follow up: None
	Intention-to-treat analysis: Not reported

Dong 2008 (Continued)

Participants	Country: China Setting: Hospital Number: 57 participants (29 treatment, 28 control) Age: Mean 57.8 years Sex: Male/female 2/55 Inclusion criteria: Breast cancer patients due to receive chemotherapy Exclusion criteria: Not stated
Interventions	Treatment: 2 cm thick fresh aloe slice external application. Wet compress at punctured skin for 48 - 72h Control : No treatment Duration: 2 - 3 days
Outcomes	Primary: The incidence of phlebitis (a) First degree: local slight pain with red skin Treatment group 3/25, Control group: 4/28 (b) Second degree: local moderate pain with slight swelling, scorching hot Treatment group 1/25, Control group: 3/28 (c) Third degree: local moderate pain with moderate swelling and edema forming with diameter over 1 cm Treatment group 0/25, Control group: 2/28 Secondary: None
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomised, but the detailed information of randomisation method was not described
Allocation concealment (selection bias)	Unclear risk	Method of allocation concealment was not described
Blinding of participants and personnel (performance bias) All outcomes	High risk	No blinding. The outcome assessment is likely to be influenced by the lack of blinding
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not reported
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Number randomised not stated

Dong 2008 (Continued)

Selective reporting (reporting bias)	Unclear risk	The study protocol is not available, and it is not clear if the published reports included all expected outcomes
Other bias	Low risk	There are no statistical differences in age, sex, course of disease and drugs of chemotherapy between comparison groups. The study appears to be free of other sources of bias

Gao 2007

Methods	Study design: Quasi randomised controlled trial Method of randomisation: Alternate allocation according to admission sequence Concealment of allocation: None Exclusions post-randomisation: Not reported Losses to follow up: None Intention-to-treat analysis: Not reported
Participants	Country: China Setting: Hospital Number: 90 participants (48 treatment, 42 control) Age: Treatment: range from one month to 3 years; control: not described Sex: Treatment: male/female 23/25. control: male/female 22/20 Inclusion criteria: Not described Exclusion criteria: Not stated
Interventions	Treatment: Fresh aloe slice external application (wet compress), twice a day for phlebitis with red glow type, 4-5 times a day for phlebitis with sclerosis type Control: 50% MgSO ₄ external application (wet compress) Duration: 3 days
Outcomes	Primary: The rate of resolution of phlebitis (a) Recovery: disappearance of pain, red swelling and scorching hot at local skin Treatment group: 39 /48, Control group: 30 /42 (b) Marked improvement: disappearance of pain, scorching hot at local skin. the shortened area of red swelling exceeded 80% Treatment group: 6/48, Control group: 4/42 (c) Improvement: disappearance of pain, scorching hot at local skin. the shortened area of red swelling was less than 80% Treatment group: 3/48, Control group: 2/42 (d) Not effective: symptoms of phlebitis had not obviously changed after treatment. Treatment group: 0/48, Control group: 6/42

Gao 2007 (Continued)

Secondary: None

Notes

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	Sequence generated by the admission sequence of participants
Allocation concealment (selection bias)	High risk	Alternate allocation according to admission sequence
Blinding of participants and personnel (performance bias) All outcomes	High risk	No blinding. The outcome assessment is likely to be influenced by the lack of blinding
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not reported blinding for outcome assessors
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Number randomised not stated
Selective reporting (reporting bias)	Unclear risk	The study protocol is not available, and it is not clear if the published reports included all expected outcomes
Other bias	Unclear risk	The baseline information between comparison groups were not described

Gao 2012

Methods	Study design: Randomised controlled trial Method of randomisation: Not described Concealment of allocation: Not reported Exclusions post-randomisation: Not reported Losses to follow up: None Intention-to-treat analysis: Not reported
Participants	Country: China Setting: Hospital Number: 120 participants (60 treatment, 60 control) Age: Mean $\pm$ SD: Treatment 63 $\pm$ 11.2 years; control 65 $\pm$ 9.7 years Sex: Treatment: male/female 37/23. control: male/female 35/25 Inclusion criteria: Not described Exclusion criteria: Not stated

Gao 2012 (Continued)

Interventions	<p>Treatment: Aloe glue external application, bid</p> <p>Control: 33% MgSO₄ external application, bid</p> <p>Duration: 5 days</p>
Outcomes	<p>Primary: The rate of resolution of phlebitis</p> <p>(a) Recovery: disappearance of pain, red swelling and scorching hot at local skin</p> <p>Treatment group: 47 /60, Control group: 41 /60</p> <p>(b) Marked improvement: disappearance of pain, scorching hot at local skin. the shortened area of red swelling exceeded 80%</p> <p>Treatment group: 11/60, Control group: 10/60</p> <p>(c) Not effective: symptoms of phlebitis had not obviously changed after treatment</p> <p>Treatment group: 2/60, Control group: 9/60</p> <p>Secondary: None</p>

Notes

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomised, but the detailed information of randomisation method was not described
Allocation concealment (selection bias)	Unclear risk	Not reported
Blinding of participants and personnel (performance bias) All outcomes	High risk	No blinding. The outcome assessment is likely to be influenced by the lack of blinding
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not reported blinding for outcome assessors
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Number randomised not stated
Selective reporting (reporting bias)	Unclear risk	The study protocol is not available, and it is not clear if the published reports included all expected outcomes
Other bias	Unclear risk	The baseline information except for age, sex between comparison groups were not described

Hou 2010

Methods	Study design: Quasi-randomised controlled trial
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Hou 2010 (Continued)

Method of randomisation: Sequence generated by odd or even of the bed number

Concealment of allocation: None

Exclusions post-randomisation: Not reported

Losses to follow up: None

Intention-to-treat analysis: Not reported

Participants	Country: China Setting: Hospital Number: 100 participants (50 treatment, 50 control) Age: Mean 29 years, range from 21 to 42 years Sex: None reported Inclusion criteria: Invasive hydatidiform mole patients with treatment of chemotherapy Exclusion criteria: Not stated
Interventions	Treatment: Piece of fresh aloe leaf with about 10 cm long wet compress at punctured skin, 3 - 4 times per day Control: External application of 33% MgSO ₄ (wet compress) at punctured skin, 3 - 4 times per day Duration: one course of chemotherapy
Outcomes	Primary: The incidence of phlebitis Treatment group: 8/50, Control group: 20/50 Secondary: None

Notes

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	Sequence generated by odd or even bed number
Allocation concealment (selection bias)	High risk	No allocation concealment
Blinding of participants and personnel (performance bias) All outcomes	High risk	No blinding. The outcome assessment is likely to be influenced by the lack of blinding
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not reported
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Number randomised not stated

Hou 2010 (Continued)

Selective reporting (reporting bias)	Unclear risk	The study protocol is not available, and it is not clear if the published reports included all expected outcomes
Other bias	Low risk	Sex, age, illness, the course of disease, program of chemotherapy and the severe degree of phlebitis between two group are not statistically significant ($P > 0.05$). The study appears to be free other sources of bias

Hu 2009

Methods	<p>Study design: Quasi-randomised controlled trial</p> <p>Method of randomisation: Sequence generated by odd or even month of the participants' birthday</p> <p>Concealment of allocation: None</p> <p>Exclusions post-randomisation: Not reported</p> <p>Losses to follow up: None</p> <p>Intention-to-treat analysis: Not reported</p>
Participants	<p>Country: China</p> <p>Setting: Hospital</p> <p>Number: 3000 participants (2000 treatment, 1000 control)</p> <p>Age: Mean 55 years, range from 10 to 84 years</p> <p>Sex: Male/female 2044/956</p> <p>Inclusion criteria: Cancer patients with treatment of chemotherapy</p> <p>Exclusion criteria: Not stated</p>
Interventions	<p>Treatment: External application of a piece of fresh aloe leaf (15 cm long and 5 cm wide), wet compress at punctured skin, changes every two hours</p> <p>Control: No treatment</p> <p>Duration: One course of chemotherapy</p>
Outcomes	<p>Primary: The incidence of phlebitis</p> <p>(a) First degree: local pain, red swelling or edema, no strip-shaped changes in veins, no palpable venous cord</p> <p>Treatment group: 42/2000, Control group: 92/1000</p> <p>(b) Second degree: local pain, red swelling or edema, with strip-shaped changes in veins, no palpable venous cord</p> <p>Treatment group: 232/2000, Control group: 125/1000</p> <p>(c) Third degree: local pain, red swelling or edema, with strip-shaped changes in veins, palpable venous cord</p> <p>Treatment group: 0/2000, Control group: 68/1000</p> <p>Secondary: None</p>

Hu 2009 (Continued)

Notes

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	Sequence generated by odd or even month of the participant's birthday
Allocation concealment (selection bias)	High risk	No allocation concealment
Blinding of participants and personnel (performance bias) All outcomes	High risk	No blinding. The outcome assessment is likely to be influenced by the lack of blinding
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not reported
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Number randomised not stated
Selective reporting (reporting bias)	Unclear risk	The study protocol is not available, and it is not clear if the published reports included all expected outcomes
Other bias	Low risk	Sex, age, illness, the course of disease, program of chemotherapy and conditions of punctured veins between two group are not statistically significant ($P > 0.05$). The study appears to be free other sources of bias

Ji 2007

Methods	Study design: Randomised controlled trial Method of randomisation: Not described Concealment of allocation: Not reported Exclusions post-randomisation: Not reported Losses to follow up: None Intention-to-treat analysis: Not reported
Participants	Country: China Setting: Hospital Number: 42 participants Age: Mean 53 years, range from 36 - 74 years Sex: Male/female 24/18 Inclusion criteria: Cancer patients with vinorelbine tartrate injection

Ji 2007 (Continued)

Exclusion criteria: Not stated

Interventions	<p>Treatment : Fresh aloe slice external application (wet compress at punctured skin), bid</p> <p>Control: No treatment</p> <p>Duration: 3 days</p>
Outcomes	<p>Primary: The incidence of phlebitis</p> <p>(a) First degree: slightly pain, red swelling or hydrops were shown at the punctured vein. No change as trabs, no callosity was felt</p> <p>Treatment group: 4/70, Control group: 15/72</p> <p>(b) Second degree: pain, red swelling or hydrops become more severe at the punctured vein. No change as trabs, no callosity was felt</p> <p>Treatment group: 2/70, Control group: 13/72</p> <p>(c) Acute pain, severe red swelling and hydrops were shown at the punctured vein. Change as trabs appeared, callosity could be felt</p> <p>Treatment group: 0/70, Control group: 1/72</p> <p>Secondary: None</p>

Notes

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomised, but the detailed information of randomisation method was not described
Allocation concealment (selection bias)	Unclear risk	Not reported
Blinding of participants and personnel (performance bias) All outcomes	High risk	No blinding. The outcome assessment is likely to be influenced by the lack of blinding
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not reported
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Number randomised not stated
Selective reporting (reporting bias)	Unclear risk	The study protocol is not available, and it is not clear if the published reports included all expected outcomes
Other bias	Unclear risk	The baseline information between comparison groups were not described

Jin 2010

Methods	<p>Study design: Randomised controlled trial</p> <p>Method of randomisation: Random digits table</p> <p>Concealment of allocation: Not reported</p> <p>Exclusions post-randomisation: Not reported</p> <p>Losses to follow up: None</p> <p>Intention-to-treat analysis: Not reported</p>
Participants	<p>Country: China</p> <p>Setting: Hospital</p> <p>Number: 63 participants (32 treatment, 31 control)</p> <p>Age: Range from 19 to 88 years</p> <p>Sex: Male/female 35/28</p> <p>Inclusion criteria: Phlebitis met criteria of the Infusion Nursing Society of America</p> <p>Exclusion criteria: Not stated</p>
Interventions	<p>Treatment: Fresh aloe juice smeared at punctured skin, then Hirudoid with 3 cm thick smeared, tid</p> <p>Control : Hirudoid smeared at punctured skin. tid</p> <p>Duration: 3 - 7 days</p>
Outcomes	<p>Primary: The rate of resolution of phlebitis</p> <p>(a) Recovery: disappearance of red swelling, pain and scorching hot. elasticity of vein restored</p> <p>Treatment group: 25/32, Control group: 10/31</p> <p>(b) Marked improvement: the disappeared area of red swelling, pain and scorching hot with slight pressing pain on the punctured veins over 70%</p> <p>Treatment group: 3/32, Control group: 9/31</p> <p>(c) Improment: the disappeared area of red swelling, pain and scorching hot with obvious pressing pain on the punctured veins less than 70%</p> <p>Treatment group: 3/32, Control group: 4/31</p> <p>(d) Not effective: no changes of symptoms of phlebitis after treatment</p> <p>Treatment group: 1/32, Control group: 8/31</p> <p>Secondary: None</p>
Notes	
Risk of bias	
Bias	Authors' judgement Support for judgement
Random sequence genera- tion (selection bias)	<p>Low risk</p> <p>Random sequence was generated by using random digits table</p>

Jin 2010 (Continued)

Allocation concealment (selection bias)	Unclear risk	Not reported
Blinding of participants and personnel (performance bias) All outcomes	High risk	No blinding. The outcome assessment is likely to be influenced by the lack of blinding
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not reported
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Number randomised not stated
Selective reporting (reporting bias)	Unclear risk	The study protocol is not available, and it is not clear if the published reports included all expected outcomes
Other bias	Unclear risk	The baseline information between comparison groups were not described

Li 2003

Methods	Study design: Randomised controlled trial Method of randomisation: Not described Concealment of allocation: Not reported Exclusions post-randomisation: Not reported Losses to follow up: None Intention-to-treat analysis: Not reported
Participants	Country: China Setting: Hospital Number: 88 participants (46 treatment, 42 control) Age: Mean 56 years, range from 28 - 85 years Sex: Male/female 47/41 Inclusion criteria: Phlebitis met the criteria of the "Fundamentals of Nursing" (Yin L 2002) Exclusion criteria: Not stated
Interventions	Treatment: Fresh aloe slice external application, 3 - 4 times a day, for one hour Control: 50% MgSO ₄ external application, 3 - 4 times a day, for one hour Duration: 3 days
Outcomes	Primary: The rate of resolution of phlebitis (a) Recovery: disappearance of red swelling, scorching hot and pain along the punctured vein, and no pressing pain at the punctured vein

Li 2003 (Continued)

Treatment group: 28/46, Control group: 13/42

(b) Marked improvement: disappearance of red swelling, scorching hot. pain alleviated, slight pressing pain at the punctured vein

Treatment group: 13/46, Control group: 10/42

(c) Improvement: alleviation of red swelling, scorching hot and pain, pressing pain existing at the punctured vein

Treatment group: 4/46, Control group: 11/42

(d) Not effective: no change or more severe of phlebitis symptom after treatment

Treatment group: 1/46, Control group: 0/42

Secondary: None

Notes

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomised, but the detailed information of randomisation method was not described
Allocation concealment (selection bias)	Unclear risk	Not reported
Blinding of participants and personnel (performance bias) All outcomes	High risk	No blinding. The outcome assessment is likely to be influenced by the lack of blinding
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not reported
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Number randomised not stated
Selective reporting (reporting bias)	Unclear risk	The study protocol is not available, and it is not clear if the published reports included all expected outcomes
Other bias	Unclear risk	The baseline information between comparison groups were not described

Li 2006

Methods	Study design: Randomised controlled trial
	Method of randomisation: Not described
	Concealment of allocation: Not reported
	Exclusions post-randomisation: Not reported
	Losses to follow up: None

Li 2006 (Continued)

Intention-to-treat analysis: Not reported

Participants	Country: China Setting: Hospital Number: 148 participants (80 treatment, 68 control) Age: Mean 46.7 years, range from 17 - 72 years Sex: Male/female 98/50 Inclusion criteria: Phlebitis met criteria of the Infusion Nursing Society of America Exclusion criteria: Not stated
Interventions	Treatment: Fresh aloe slice external application (wet compress), tid, for one hour Control: 33% MgSO ₄ external application, tid Duration: 7 days
Outcomes	Primary: The rate of resolution of phlebitis (a) Marked improvement: disappearance of red swelling in the local vein, softening of callosity vein vessel, elasticity of vein vessel recover within one treatment course; disappearance of pain within two hour Treatment group: 56/80; Control group: 21/68 (b) Improvement: disappearance of phlebitis symptom over one treatment course and disappearance of pain over two hour Treatment group: 24/80; Control group: 39/68 (c) No improvement: symptoms of phlebitis and pain were unchanged after treatment Treatment group: 0/80; Control group: 8/68 Secondary: None

Notes

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomised, but the detailed information of randomisation method was not described
Allocation concealment (selection bias)	Unclear risk	Not reported
Blinding of participants and personnel (performance bias) All outcomes	High risk	No blinding. The outcome assessment is likely to be influenced by the lack of blinding
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not reported

Li 2006 (Continued)

Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Number randomised not stated. Flow of participants randomised was not available
Selective reporting (reporting bias)	Unclear risk	The study protocol is not available, and it is not clear if the published reports included all expected outcomes
Other bias	Unclear risk	The baseline information between comparison groups was not described

Li 2009

Methods	Study design: Randomised controlled trial Method of randomisation: Not described Concealment of allocation: Not reported Exclusions post-randomisation: Not reported Losses to follow up: None Intention-to-treat analysis: Not reported
Participants	Country: China Setting: Hospital Number: 180 participants (60 treatment 1, 60 treatment 2, 60 control) Age: Range from 16 to 82 years Sex: Male/female 98/82 Inclusion criteria: Phlebitis met criteria of the Infusion Nursing Society of America Exclusion criteria: Not stated
Interventions	Treatment 1: Fresh aloe slice wet compress at punctured skin for 20 minutes, twice a day Treatment 2: Fresh potato slice (0.1 - 0.2 cm thick) wet compress at punctured skin for 30 - 60 minutes, twice a day Control: 50% MgSO ₄ wet compress at punctured skin, changed every 4 - 6 hours Duration: 3 days
Outcomes	Primary: The rate of resolution of phlebitis (a) Marked improvement: disappearance of local pain and red swelling, no pressing pain, elasticity of vein restored Treatment group 1: 34/60. Treatment group 2: 36/60, Control group: 26/60 (b) Improvement: obvious alleviation of local pain and red swelling, no pressing pain, elasticity of vein partially restored Treatment group 1: 18/60. Treatment group 2: 20/60, Control group: 18/60 (c) Not effective: no obvious improvement of phlebitis symptom after treatment Treatment group 1: 6/60. Treatment group 2: 6/60, Control group: 16/60

Li 2009 (Continued)

Secondary: None

Notes

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomised, but the detailed information of randomisation method was not described
Allocation concealment (selection bias)	Unclear risk	Method of allocation concealment was not described
Blinding of participants and personnel (performance bias) All outcomes	High risk	No blinding. The outcome assessment is likely to be influenced by the lack of blinding
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not reported
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Number randomised not stated
Selective reporting (reporting bias)	Unclear risk	The study protocol is not available, and it is not clear if the published reports included all expected outcomes
Other bias	Low risk	There are no statistical differences in age, sex, the time and location of needles detained in the infused vein among the comparison groups. The study appears to be free other sources of bias

Li 2011

Methods	Study design: Randomised controlled trial Method of randomisation: Not described Concealment of allocation: Not reported Exclusions post-randomisation: Not reported Losses to follow up: None Intention-to-treat analysis: Not reported
Participants	Country: China Setting: Hospital Number: 80 participants (40 treatment, 40 control) Age: Treatment group: mean 60 years, range from 42 to 78 years; Control group: mean 61 years, range from 40 to 75 years Sex: Treatment group: male/female 32/8; Control group: male/ female 33/7

Li 2011 (Continued)

Inclusion criteria: Malignant tumour patients with chemotherapeutics

Exclusion criteria: Not stated

Interventions	Treatment: Aloe glue was smeared at punctured skin, tid Control: No treatment Duration: 7 days
Outcomes	Primary: The incidence of phlebitis (a) First degree: local slight pain, red, no strip-shaped changes in veins, no palpable venous cord Treatment group 3/40, Control group: 9/40 (b) Second degree: local severe pain, scorching hot, slight red swelling and edema, with strip-shaped changes in veins, palpable venous cord Treatment group 1/40, Control group: 7/40 (c) Third degree: local pain, red swelling and edema over 1 cm, with strip-shaped changes in veins, palpable venous cord Treatment group 1/40, Control group: 2/40 Secondary: None

Notes

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomised, but the detailed information of randomisation method was not described
Allocation concealment (selection bias)	Unclear risk	Method of allocation concealment was not described
Blinding of participants and personnel (performance bias) All outcomes	High risk	No blinding. The outcome assessment is likely to be influenced by the lack of blinding
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not reported
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Number randomised not stated
Selective reporting (reporting bias)	Unclear risk	The study protocol is not available, and it is not clear if the published reports included all expected outcomes
Other bias	Low risk	There are no statistical differences in age, sex, illness, chemotherapy drugs, veins between treatment and control groups. The study appears to be free other sources of bias

Liang 2004

Methods	Study design: Randomised controlled trial Method of randomisation: Not described Concealment of allocation: Not reported Exclusions post-randomisation: Not reported Losses to follow up: None Intention-to-treat analysis: Not reported
Participants	Country: China Setting: Hospital Number: 150 participants (75 treatment, 75 control) Age: Mean 58 years Sex: Male/ female 86/64 Inclusion criteria: Inpatients due to receive therapy of 20% mannitol Exclusion criteria: Not stated
Interventions	Treatment: Fresh aloe piece external application, consecutively rubbing 10 minutes at the punctured local skin after infusion Control: 75% alcohol rubbing 10 minutes at the punctured local skin after infusion Duration: 7 - 15 days
Outcomes	Primary: The incidence of phlebitis Treatment group: 0/75, Control group: 28/75 Secondary: None
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomised, but the detailed information of randomisation method was not described
Allocation concealment (selection bias)	Unclear risk	Method of allocation concealment was not described
Blinding of participants and personnel (performance bias) All outcomes	High risk	No blinding. The outcome assessment is likely to be influenced by the lack of blinding
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not reported

Liang 2004 (Continued)

Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Number randomised not stated
Selective reporting (reporting bias)	Unclear risk	The study protocol is not available, and it is not clear if the published reports included all expected outcomes
Other bias	Low risk	There are not the statistical difference on age, sex, illness, dose of the infused mannitol between treatment and control groups. The study appears to be free other sources of bias

Liu 2003

Methods	Study design: Randomised controlled trial Method of randomisation: Not described Concealment of allocation: Not reported Exclusions post-randomisation: Not reported Losses to follow up: None Intention-to-treat analysis: Not reported
Participants	Country: China Setting: Hospital Number: 147 participants (67 treatment, 80 control) Age: Mean 62.4 years, from 45 to 76 years Sex: Male/female 59/88 Inclusion criteria: Cancer patients due to be administered drugs of chemotherapy Exclusion criteria: Not stated
Interventions	Treatment: Fresh aloe slice plus ice bag external application (wet compress at punctured skin) Control: 75% MgSO ₄ external application (wet compress at punctured skin) Duration: One course of chemotherapy
Outcomes	Primary: The incidence of phlebitis (a) First degree phlebitis: pain, red swelling in local of punctured vein, vein has no the change as trabs and callosity Treatment group: 8/67; Control group: 6/80 (b) Second degree phlebitis: red swelling in local of vein, vein has changed as trabs and no callosity is touched Treatment group: 3/67; Control group: 6/80 (c) Third degree phlebitis: red swelling in local of vein, vein has changed as trabs and callosity is touched Treatment group: 1/67; Control group: 1/80

Liu 2003 (Continued)

Secondary: None

Notes

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomised, but the detailed information of randomisation method was not described
Allocation concealment (selection bias)	Unclear risk	Method of allocation concealment was not described
Blinding of participants and personnel (performance bias) All outcomes	High risk	No blinding. The outcome assessment is likely to be influenced by the lack of blinding
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not reported
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Flow of participants randomised was not available
Selective reporting (reporting bias)	Unclear risk	The study protocol is not available, and it is not clear if the published reports included all expected outcomes
Other bias	Unclear risk	The comparisons of baseline information between comparison groups were not described

Liu 2006

Methods	Study design: Quasi randomised controlled trial Method of randomisation: Random sequence was generated by admission of inpatient Concealment of allocation: None Exclusions post-randomisation: Not reported Losses to follow up: None Intention-to-treat analysis: Not reported
Participants	Country: China Setting: Hospital Number: 86 participants (43 treatment, 43 control) Age: Mean 56.3 years, range from 30 to 72 years Sex: Male/female 32/54 Inclusion criteria: Cancer patients due to receive treatment of vinorelbine chemotherapy

Liu 2006 (Continued)

Exclusion criteria: Not stated

Interventions	<p>Treatment: Fresh aloe slice external application, fresh aloe slice of 4 - 5 cm wide and 7 - 8 cm long compressed at punctured skin, 4-5 times per day</p> <p>Control: No treatment</p> <p>Duration: 3 days</p>
Outcomes	<p>Primary: The incidence of phlebitis</p> <p>(a) First degree: red swelling appear on the punctured vein, pressing pain is not obvious, elasticity of vein is moderate</p> <p>Treatment group: 10/43, Control group: 18/43</p> <p>(b) Second degree: red swelling appear on the punctured vein, pressing pain and chromatosis is obvious, elasticity of vein is badly. lumens of vein becomes narrow</p> <p>Treatment group: 6/43, Control group: 10/43</p> <p>(c) Third degree: above symptoms become severe, and the punctured vein appear the change as trabs</p> <p>Treatment group: 2/43, Control group: 7/43</p> <p>Secondary: None</p>

Notes

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	Sequence generated by odd or even of the bed number
Allocation concealment (selection bias)	High risk	No allocation concealment
Blinding of participants and personnel (performance bias) All outcomes	High risk	No blinding. The outcome assessment is likely to be influenced by the lack of blinding
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not reported
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Number randomised not stated
Selective reporting (reporting bias)	Unclear risk	The study protocol is not available, and it is not clear if the published reports included all expected outcomes
Other bias	Low risk	The baseline information sex, age, state of illness and dose of chemotherapy drug between comparison groups are not statistically significant ($P > 0.05$). The study appears to be free other sources of bias

Liu 2012

Methods	<p>Study design: Randomised controlled trial</p> <p>Method of randomisation: Not described</p> <p>Concealment of allocation: Not reported</p> <p>Exclusions post-randomisation: Not reported</p> <p>Losses to follow up: None</p> <p>Intention-to-treat analysis: Not reported</p>
Participants	<p>Country: China</p> <p>Setting: Hospital</p> <p>Number: 50 participants (25 treatment, 25 control)</p> <p>Age: Mean 48 years, range from 19 to 78 years</p> <p>Sex: Male/female 34/16</p> <p>Inclusion criteria: Phlebitis met criteria of the Infusion Nursing Society of America</p> <p>Exclusion criteria: Not stated</p>
Interventions	<p>Treatment : The fresh aloe slice of 4 - 5 cm wide and 7 - 8 cm long compressed at punctured skin, bid</p> <p>Control: 50% MgSO₄ wet compress at punctured skin, bid</p> <p>Duration: 7 days</p>
Outcomes	<p>Primary: The rate of resolution of phlebitis</p> <p>(a) Recovery: disappearance of red swelling, scorching hot and pain along the punctured vein, and no pressing pain at the punctured vein</p> <p>Treatment group: 14/25, Control group: 4/25</p> <p>(b) Marked improvement: disappearance of red swelling, pain, and changes like trabs in the local vein. no callosity on the vein is touched</p> <p>Treatment group one: 6/25; Treatment group two: 12/30, Control group: 5/25</p> <p>(c) Improvement: disappearance of red swelling, pain in the local vein; partial disappearance of vein changes like trabs; the callosity on the vein can be touched</p> <p>Treatment group one: 3/25; Treatment group two: 8/30, Control group: 6/25</p> <p>(d) No improvement: symptoms of phlebitis and pain were not obviously changed after treatment</p> <p>Treatment group one: 2/25; Treatment group two: 10/30, Control group: 10/25</p> <p>Secondary: None</p>
Notes	
Risk of bias	
Bias	<p>Authors' judgement</p> <p>Support for judgement</p>

Liu 2012 (Continued)

Random sequence generation (selection bias)	Unclear risk	Randomised, but the detailed information of randomisation method was not described
Allocation concealment (selection bias)	Unclear risk	Method of allocation concealment was not described
Blinding of participants and personnel (performance bias) All outcomes	High risk	No blinding. The outcome assessment is likely to be influenced by the lack of blinding
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not reported
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Flow of participants randomised was not available
Selective reporting (reporting bias)	Unclear risk	The study protocol is not available, and it is not clear if the published reports included all expected outcomes
Other bias	Unclear risk	The comparisons of baseline information between comparison groups were not described

Liu 2012b

Methods	Study design: Randomised controlled trial Method of randomisation: Not described Concealment of allocation: Not reported Exclusions post-randomisation: Not reported Losses to follow up: None Intention-to-treat analysis: Not reported
Participants	Country: China Setting: Hospital Number: 86 participants (43 treatment, 43 control) Age: From 25 to 75 years Sex: Male/female: treatment group 16/27; control group 23/20 Inclusion criteria: Patients with definite malignant tumour received treatment of chemotherapy; No drugs exosmose during treatment Exclusion criteria: Not stated
Interventions	Treatment: Fresh aloe leaf external application (wet compress at punctured skin after cleaned with distilled water) Control: No treatment

Liu 2012b (Continued)

Duration: One course of chemotherapy

Outcomes

Primary: The incidence of phlebitis.

(a) First degree: red swelling appear on the punctured vein, pressing pain is not obvious, elasticity of vein is moderate

Treatment group: 10/43, Control group: 18/43

(b) Second degree: red swelling appear on the punctured vein, pressing pain and chromatosis is obvious, elasticity of vein is badly. lumens of vein becomes narrow

Treatment group: 6/43, Control group: 10/43

(c) Third degree: above symptoms become severe, and the punctured vein appear the change as trabs

Treatment group: 2/43, Control group: 7/43

Secondary: None

Notes
Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomised, but the detailed information of randomisation method was not described
Allocation concealment (selection bias)	Unclear risk	Method of allocation concealment was not described
Blinding of participants and personnel (performance bias) All outcomes	High risk	No blinding. The outcome assessment is likely to be influenced by the lack of blinding
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not reported
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Flow of participants randomised was not available
Selective reporting (reporting bias)	Unclear risk	The study protocol is not available, and it is not clear if the published reports included all expected outcomes
Other bias	Unclear risk	The comparisons of baseline information between comparison groups were not described

Lu 2004
Methods

Study design: Randomised controlled trial

Method of randomisation: Not described

Concealment of allocation: Not reported

Lu 2004 (Continued)

Exclusions post-randomisation: Not reported

Losses to follow up: None

Intention-to-treat analysis: Not reported

Participants	Country: China Setting: Hospital Number: 90 participants (30 treatment 1, 30 treatment 2, 30 control) Age: From 26 to 86 years Sex: Male/female 90/56 Inclusion criteria: Phlebitis met criteria of the Infusion Nursing Society of America Exclusion criteria: Not stated
Interventions	Treatment 1: Dry aloe linimentum 30 ml, bid. The dry aloe linimentum (dry aloe 250 g plus 100 ml 75% alcohol soaked for 10 days, then filtered out the juice to use) Treatment 2: Fresh aloe linimentum 30 ml, bid. The fresh aloe linimentum (fresh aloe 250 g plus 100 ml 75% alcohol soaked for 10 days, then filtered out the juice to use) Control: 75% alcohol, bid Duration: 6 days
Outcomes	Primary: The rate of resolution of phlebitis (a) Marked improvement: disappearance of red swelling, pain, and changes like trabs in the local vein. no callosity on the vein is touched Treatment group one: 20/30; Treatment group two: 12/30, Control group: 4/30 (b) Improvement: disappearance of red swelling, pain in the local vein. partial disappearance of vein changes like trabs. the callosity on the vein can be touched Treatment group one: 9/30; Treatment group two: 8/30, Control group: 6/30 (c) No improvement: symptoms of phlebitis and pain were not obviously changed after treatment Treatment group one: 1/30; Treatment group two: 10/30, Control group: 20/30 Secondary: None

Notes

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomised, but the detailed information of randomisation method was not described
Allocation concealment (selection bias)	Unclear risk	Method of allocation concealment was not described
Blinding of participants and personnel (performance bias)	High risk	No blinding. The outcome assessment is likely to be influenced by the lack of blinding

Lu 2004 (Continued)

All outcomes

Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not reported
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Number randomised not stated
Selective reporting (reporting bias)	Unclear risk	The study protocol is not available, and it is not clear if the published reports included all expected outcomes
Other bias	Low risk	There were not statistical difference in age, sex, the severe degree of phlebitis among comparison groups. The study appears to be free other sources of bias

Pan 2008

Methods	Study design: Randomised controlled trial Method of randomisation: Not stated Concealment of allocation: Not reported Exclusions post-randomisation: Not reported Losses to follow up: None Intention-to-treat analysis: Not reported
Participants	Country: China Setting: Hospital Number: 132 participants (66 treatment, 66 control) Age: Range from 26 to 88 years Sex: Male/female 72/60 Inclusion criteria: Cancer patients due to receive chemotherapy medicine fluorouracil injection Exclusion criteria: Not stated
Interventions	Treatment: Fresh aloe slice (15 - 20 cm long, 6 - 8 cm wide) wet compresses at the punctured site. changed when dried Control: No treatment Duration: 3-5 days
Outcomes	Primary: The incidence of phlebitis (a) First degree: pain, red swelling appear on the punctured vein. Strip-shaped changes in veins are not observed, and no palpable venous callosity Treatment group: 4/66; Control group: 7/66 (b) Second degree: pain, red swelling appear on the punctured vein. Strip-shaped changes in vein are observed, and no palpable venous callosity

Pan 2008 (Continued)

Treatment group: 1/66. Control group: 31/66

(c) Third degree: pain, red swelling appear on the punctured vein. Strip-shaped changes in vein are observed, with palpable venous callosity

Treatment group: 0/66. Control group: 8/66

Secondary: None

Notes

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomised, but the detailed information of randomisation method was not described
Allocation concealment (selection bias)	Unclear risk	Method of allocation concealment was not described
Blinding of participants and personnel (performance bias) All outcomes	High risk	No blinding. The outcome assessment is likely to be influenced by the lack of blinding
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not reported
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Number randomised not stated
Selective reporting (reporting bias)	Unclear risk	The study protocol is not available, and it is not clear if the published reports included all expected outcomes
Other bias	Unclear risk	The baseline information between comparisons groups were not described

Peng 2009

Methods	<p>Study design: Randomised controlled trial</p> <p>Method of randomisation: Not described</p> <p>Concealment of allocation: Not reported</p> <p>Exclusions post-randomisation: Not reported</p> <p>Losses to follow up: None</p> <p>Intention-to-treat analysis: Not reported</p>
Participants	<p>Country: China</p> <p>Setting: Hospital</p> <p>Number: 50 participants (25 treatment, 25 control)</p>

Peng 2009 (Continued)

Age: Range from 32 to 76 years

Sex: Male/female 38/12

Inclusion criteria: Patients with chemotherapy medicine Chanchu injection

Exclusion criteria: Not stated

Interventions	Treatment: Fresh aloe slice compress at punctured skin, changed when dried Control: No treatment Duration: 3 - 5 days
Outcomes	Primary: The incidence of phlebitis Treatment group: 18/25, Control group: 15/25 Secondary: None

Notes

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomised, but the detailed information of randomisation method was not described
Allocation concealment (selection bias)	Unclear risk	Method of allocation concealment was not described
Blinding of participants and personnel (performance bias) All outcomes	High risk	No blinding. The outcome assessment is likely to be influenced by the lack of blinding
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not reported
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Number randomised not stated
Selective reporting (reporting bias)	Unclear risk	The study protocol is not available, and it is not clear if the published reports included all expected outcomes
Other bias	Low risk	There are not the statistical difference in age, sex, illness, the program of chemotherapy between treatment and control groups. The study appears to be free other sources of bias

Ren 2008

Methods	Study design: Randomised controlled trial Method of randomisation: Not described Concealment of allocation: Not reported
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Aloe vera for prevention and treatment of infusion phlebitis (Review)

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Ren 2008 (Continued)

Exclusions post-randomisation: Not reported

Losses to follow up: None

Intention-to-treat analysis: Not reported

Participants	Country: China Setting: Hospital Number: 66 participants Age: Range from 32 to 76 years Sex: Male/female 46/20 Inclusion criteria: Cancer patients due to receive chemotherapy drug fluorouracil injection Exclusion criteria: Not stated
Interventions	Treatment 1: Fresh aloe juice rubbed repeatedly at punctured skin. 30 - 60 min every time, once per 1 - 2 hours Treatment 2: 3 cm thick fresh potato slice external compress at punctured skin, changed once per 1 - 2 hours Control: 50% MgSO ₄ wet compress at punctured skin, changed once per 1 - 2 hours Duration: 7 days
Outcomes	Primary: The incidence of phlebitis (a) Grade I: no local pain with red skin Treatment group 1: 3/104, Treatment group 2: 1/62, Control group: 4/49 (b) Grade II: local slight pain with red skin less than 2 days Treatment group 1: 3/104, Treatment group 2: 2/62, Control group: 4/49 (c) Grade III: local pain with swelling, scorching hot over 2 days Treatment group 1: 2/104, Treatment group 2: 1/62, Control group: 4/49 Secondary: None

Notes

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomised, but the detailed information of randomisation method was not described
Allocation concealment (selection bias)	Unclear risk	Method of allocation concealment was not described
Blinding of participants and personnel (performance bias) All outcomes	High risk	No blinding. The outcome assessment is likely to be influenced by the lack of blinding

Ren 2008 (Continued)

Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not reported
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Number randomised not stated
Selective reporting (reporting bias)	Unclear risk	The study protocol is not available, and it is not clear if the published reports included all expected outcomes
Other bias	Low risk	There are not the statistical difference in age, sex, consist of diseases, condition of infusion vein among comparison groups. The study appears to be free other sources of bias

Tan 2002

Methods	Study design: Randomised controlled trial Method of randomisation: Not described Concealment of allocation: Not reported Exclusions post-randomisation: Not reported Losses to follow up: None Intention-to-treat analysis: Not reported
Participants	Country: China Setting: Hospital Number: 150 participants (76 treatment, 74 control) Age: Range from 17 to 78 years Sex: Male/female 99/51 Inclusion criteria: Patients with awake mind, first receiving a 20% mannitol injection, 250 ml per injection, 3 - 4 times per day Exclusion criteria: Not stated
Interventions	Treatment: Fresh aloe slice external application (wet compresses at punctured skin) Control: No treatment Duration: 7 - 15 days
Outcomes	Primary: The incidence of phlebitis (a) First degree phlebitis: pain, red swelling in local of punctured vein, vein has no the change as trabs and callosity Treatment group: 16/74; Control group: 20/76 (b) Second degree phlebitis: red swelling in local of vein, vein has changed as trabs and no callosity is touched Treatment group: 10/74; Control group: 32/76

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Tan 2002 (Continued)

(c) Third degree phlebitis: red swelling in local of vein, vein has changed as trabs and callosity is touched

Treatment group: 0/74; Control group: 24/76

Secondary: None

Notes

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomised, but the detailed information of randomisation method was not described
Allocation concealment (selection bias)	Unclear risk	Method of allocation concealment was not described
Blinding of participants and personnel (performance bias) All outcomes	High risk	No blinding. The outcome assessment is likely to be influenced by the lack of blinding
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not reported blinding for the outcome assessors
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Number randomised not stated
Selective reporting (reporting bias)	Unclear risk	The study protocol is not available, and it is not clear if the published reports included all expected outcomes
Other bias	Low risk	There are not the statistical difference in age, sex, consist of diseases, the dose of infused mannitol between comparison groups. The study appears to be free other sources of bias

Tang 2011

Methods	<p>Study design: Randomised controlled trial</p> <p>Method of randomisation: Random number table</p> <p>Concealment of allocation: Not reported</p> <p>Exclusions post-randomisation: Not reported</p> <p>Losses to follow up: None</p> <p>Intention-to-treat analysis: Not reported</p>
Participants	<p>Country: China</p> <p>Setting: Hospital</p> <p>Number: 66 participants (36 treatment, 30 control)</p>

Tang 2011 (Continued)

Age: treatment: Mean 6.03 years, range from 3 - 12 years. control: mean 6.11 years, range from 3 - 12 years

Sex: Male/female: treatment 23/13; control 18/12

Inclusion criteria: Not stated

Exclusion criteria: Not stated

Interventions	<p>Treatment: Fresh aloe vera juice external application, tid</p> <p>Control: 50% MgSO₄ wet compress, tid</p> <p>Duration: 15 days</p>
Outcomes	<p>Primary: The rate of resolution of phlebitis</p> <p>(a) Recovery: disappearance of symptoms of phlebitis. function of vein is restored</p> <p>Treatment group: 26/36, Control group: 13/30</p> <p>(b) Improvement: symptoms of phlebitis relieved obviously</p> <p>Treatment group: 8/36, Control group: 9/30</p> <p>(c) Not effective: no change of symptoms of phlebitis after treatment</p> <p>Treatment group: 2/36, Control group: 8/30</p> <p>Secondary: None</p>

Notes

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Randomised with random number table
Allocation concealment (selection bias)	Unclear risk	Method of allocation concealment was not described
Blinding of participants and personnel (performance bias) All outcomes	High risk	No blinding. The outcome assessment is likely to be influenced by the lack of blinding
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not reported blinding for the outcome assessors
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Number randomised not stated
Selective reporting (reporting bias)	Unclear risk	The study protocol is not available, and it is not clear if the published reports included all expected outcomes
Other bias	Unclear risk	The baseline information among comparison groups were not described

Wang 2006

Methods	<p>Study design: Quasi randomised controlled trial</p> <p>Method of randomisation: Random sequence was generated by admission number</p> <p>Concealment of allocation: None</p> <p>Exclusions post-randomisation: Not reported</p> <p>Losses to follow up: None</p> <p>Intention-to-treat analysis: Not reported</p>
Participants	<p>Country: China</p> <p>Setting: Hospital</p> <p>Number: 320 participants (110 treatment 1, 100 treatment 2, 110 control)</p> <p>Age: Treatment 1: mean 41.2 years, range from 19 to 83 years. Treatment 2: mean 47.7 years, range from 11 to 75 years. Control group: mean 45.3 years, range from 16 to 79 years</p> <p>Sex: Treatment 1: male/female 61/49. Treatment 2: male/female 57/43. Control: male/female 62/48</p> <p>Inclusion criteria: Cancer patients with treatment of chemotherapy</p> <p>Exclusion criteria: Not stated</p>
Interventions	<p>Treatment 1: Fresh aloe slice external application, about 10 cm long fresh aloe slice compressed at punctured skin, bid, for 4 - 5 hours</p> <p>Treatment 2: Fresh potato slice external application. fresh potato slice with 2 cm thick compressed at punctured skin, bid, for 4 - 5 hours</p> <p>Control: No treatment</p> <p>Duration: 1 - 7 days</p>
Outcomes	<p>Primary: The incidence of phlebitis</p> <p>(a) First degree: pain, red swelling appear on the punctured vein. Change of vein as trabs is not observed, and no callosity touched</p> <p>Treatment group 1: 12/110, Treatment group 2: 13/100. Control group: 22/110</p> <p>(b) Second degree: pain, red swelling appear on the punctured vein. Change of vein as trabs is observed, and no callosity touched</p> <p>Treatment group 1: 7/110, Treatment group 2: 4/100. Control group: 24/110</p> <p>(c) Third degree: pain, red swelling appear on the punctured vein. Change of vein as trabs is observed, and callosity is touched</p> <p>Treatment group 1: 1/110, Treatment group 2: 2/100. Control group: 8/110</p> <p>Secondary: None</p>
Notes	
Risk of bias	
Bias	Authors' judgement Support for judgement

Wang 2006 (Continued)

Random sequence generation (selection bias)	High risk	Random sequence was generated by admission number
Allocation concealment (selection bias)	High risk	Random sequence was generated by admission number
Blinding of participants and personnel (performance bias) All outcomes	High risk	No blinding. The outcome assessment is likely to be influenced by the lack of blinding
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not reported
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Number randomised not stated
Selective reporting (reporting bias)	Unclear risk	The study protocol is not available, and it is not clear if the published reports included all expected outcomes
Other bias	Low risk	There are not the statistical difference in age, sex, illness, course of disease chemotherapy time and program of chemotherapy among comparison groups. The study appears to be free other sources of bias

Wang 2008

Methods	Study design: Randomised controlled trial Method of randomisation: Not described Concealment of allocation: Not reported Exclusions post-randomisation: Not reported Losses to follow up: None Intention-to-treat analysis: Not reported
Participants	Country: China Setting: Hospital Number: 65 participants (34 treatment, 31 control) Age: treatment: Mean 46.5 years, range from 35 - 67 years; control: mean 45 years, range from 31 - 62 years Sex: Not described Inclusion criteria: Gynaecologic neoplasms patient due to receive chemotherapy Exclusion criteria: Not stated
Interventions	Treatment: Fresh aloe slice external application; fresh aloe slice with 3 - 4 cm wide and 7 - 8 cm long wet compress at punctured skin for 4 hours per day plus 100 ml NaCl ₂ and 10 mg dexamethasone infused, once a day

Wang 2008 (Continued)

Control: 100 ml NaCl₂ and 10 mg dexamethasone infused, once a day

Duration: 3 - 7 days

Outcomes	<p>Primary: The rate of resolution of phlebitis</p> <p>(a) Recovery: disappearance of symptoms of phlebitis. function of vein is restored</p> <p>Treatment group: 30/34, Control group: 14/31</p> <p>(b) Improvement: symptoms of phlebitis relieved obviously</p> <p>Treatment group: 4/34, Control group: 10/31</p> <p>(c) Not effective: no change of symptoms of phlebitis after treatment</p> <p>Treatment group: 0/34, Control group: 7/31</p> <p>Secondary: None</p>
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Notes

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomised, but the detailed information of randomisation method was not described
Allocation concealment (selection bias)	Unclear risk	Method of allocation concealment was not described
Blinding of participants and personnel (performance bias) All outcomes	High risk	No blinding. The outcome assessment is likely to be influenced by the lack of blinding
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not reported
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Number randomised not stated
Selective reporting (reporting bias)	Unclear risk	The study protocol is not available, and it is not clear if the published reports included all expected outcomes
Other bias	Low risk	There are not the statistical difference in age, sex, illness, course of disease and dose of chemotherapy between treatment and control groups The study appears to be free other sources of bias

Wang 2010

Methods	<p>Study design: Randomised controlled trial</p> <p>Method of randomisation: Not described</p> <p>Concealment of allocation: Not reported</p>
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Wang 2010 (Continued)

	Exclusions post-randomisation: Not reported
	Losses to follow up: None
	Intention-to-treat analysis: Not reported
Participants	Country: China Setting: Hospital Number: 65 participants (33 treatment, 32 control) Age: Mean 63.5 years, range from 43 to 82 years Sex: Male/female 40/25 Inclusion criteria: Phlebitis met criteria of the nursing conference in Hangzhou city, 1990 Exclusion criteria: Not stated
Interventions	Treatment: Fresh aloe slice wet compress at punctured skin. tid, for 4 hours Control: 50% MgSO ₄ wet compress at punctured skin. 4 times a day, for 2 hours Duration: 3 days
Outcomes	Primary: The rate of resolution of phlebitis (a) Marked improvement: appearance of red swelling, pain and scorching hot on the punctured veins, with softening vein Treatment group: 26/33, Control group: 9/32 (b) Impromtent: alleviation of red swelling, pain and scorching hot with obvious pressing pain on the punctured veins Treatment group: 7/33, Control group: 16/32 (c) No effective: no changes of symptoms of phlebitis after treatment Treatment group: 0/33, Control group: 7/32 Secondary: None

Notes

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomised, but the detailed information of randomisation method was not described
Allocation concealment (selection bias)	Unclear risk	Method of allocation concealment was not described
Blinding of participants and personnel (performance bias) All outcomes	High risk	No blinding. The outcome assessment is likely to be influenced by the lack of blinding
Blinding of outcome assessment (detection bias)	Unclear risk	Not reported blinding for the outcome assessors

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Wang 2010 (Continued)

All outcomes

Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Number randomised not stated
Selective reporting (reporting bias)	Unclear risk	The study protocol is not available, and it is not clear if the published reports included all expected outcomes
Other bias	Unclear risk	The baseline information among comparison groups were not described

Wang 2010b

Methods	Study design: Randomised controlled trial Method of randomisation: Using the random number table Concealment of allocation: Not reported Exclusions post-randomisation: Not reported Losses to follow up: None Intention-to-treat analysis: Not reported
Participants	Country: China Setting: Hospital Number: 84 participants Age: Mean 58.86 years, range from 46 to 72 years Sex: Male/female 63/21 Inclusion criteria: Phlebitis met criteria of the Infusion Nursing Society of America Exclusion criteria: Not stated
Interventions	Treatment: at day: Fresh aloe leaf with 15 - 20 cm long, 6 - 8 cm wide and 0.5 cm thick wet compress at punctured skin, changed every 1 - 2 hours; at night: Hirudoid painting, tid Control: Hirudoid painting, tid Duration: One course of treatment
Outcomes	Primary: The rate of resolution of phlebitis (a) Recovery: disappearance of local pain, red, swelling, scorching hot and strip-shaped change in vein, callosity softened Treatment group: 13/30, Control group: 6/39 (b) Marked improvement: obvious alleviation of local pain, red, swelling, scorching hot and strip-shaped change in vein, callosity softened Treatment group: 16/30, Control group: 16/39 (c) Improvement: slight alleviation of local pain, red, swelling and scorching hot. no regression of strip-shaped change in vein, no softened callosity

Wang 2010b (Continued)

Treatment group: 1/30, Control group: 17/39

Secondary: None

Notes

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Using the random number table
Allocation concealment (selection bias)	Unclear risk	Not reported
Blinding of participants and personnel (performance bias) All outcomes	High risk	No blinding. The outcome assessment is likely to be influenced by the lack of blinding
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not reported
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Number randomised not stated
Selective reporting (reporting bias)	Unclear risk	The study protocol is not available, and it is not clear if the published reports included all expected outcomes
Other bias	Low risk	There are no the statistical difference in age, sex, illness, the drugs, method and dose of chemotherapy, the condition of veins between treatment and control groups ($P > 0.05$). The study appears to be free other sources of bias

Wu 2009

Methods	Study design: Randomised controlled trial Method of randomisation: Not described Concealment of allocation: Not reported Exclusions post-randomisation: Not reported Losses to follow up: None Intention-to-treat analysis: Not reported
Participants	Country: China Setting: Hospital Number: 99 participants (33 treatment 1, 33 treatment 2, 33 treatment 3) Age: Mean 56 years, range from 23 - 76 years Sex: Male/female 51/48

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Wu 2009 (Continued)

Inclusion criteria: Patients with chemotherapy

Exclusion criteria: Not stated

Interventions	<p>Treatment 1: Fresh aloe slice external application, fresh aloe slice with 10 cm long compress at punctured skin, for 4 - 5 hours, tid</p> <p>Treatment 2: Fresh potato slice external application, fresh potato with 0.12 cm thick compress at punctured skin, for 4 - 5 hours, 1 - 2 times a day</p> <p>Treatment 3: Fresh aloe and potato alternating application</p> <p>Duration: 1 - 7 days</p>
Outcomes	<p>Primary: The incidence of phlebitis</p> <p>(a) First degree: local pain, red swelling or edema, no strip-shaped changes in veins, no palpable venous cord</p> <p>Treatment group 1: 7/33, Treatment group 2: 9/33, Treatment group 3: 1/33</p> <p>(b) Second degree: local pain, red swelling or edema, with strip-shaped changes in veins, no palpable venous cord</p> <p>Treatment group 1: 3/33, Treatment group 2: 3/33, Treatment group 3: 0/33</p> <p>(c) Third degree: local pain, red swelling or edema, with strip-shaped changes in veins, palpable venous cord</p> <p>Treatment group 1: 0/33, Treatment group 2: 0/33, Treatment group 3: 0/33</p> <p>Secondary: None</p>

Notes

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomised, but the detailed information of randomisation method was not described
Allocation concealment (selection bias)	Unclear risk	Method of allocation concealment was not described
Blinding of participants and personnel (performance bias) All outcomes	High risk	No blinding. The outcome assessment is likely to be influenced by the lack of blinding
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not reported
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Number randomised not stated
Selective reporting (reporting bias)	Unclear risk	The study protocol is not available, and it is not clear if the published reports included all expected outcomes

Wu 2009 (Continued)

Other bias	Unclear risk	The baseline information among comparison groups were not described
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Xiao 2008

Methods	Study design: Quasi-randomised controlled trial Method of randomisation: Sequence generated by odd or even of the bed number Concealment of allocation: None Exclusions post-randomisation: Not reported Losses to follow up: None Intention-to-treat analysis: Not reported
Participants	Country: China Setting: Hospital Number: 160 participants (80 treatment, 80 control) Age: Mean 41.3 years, range from 19 to 73 years Sex: Female 160 Inclusion criteria: Cancer patients due to receive treatment of chemotherapy Exclusion criteria: Not stated
Interventions	Treatment: Fresh aloe leaf piece sticking at punctured skin from 30 min before chemotherapy to 30 min after chemotherapy. Control: No treatment Duration: 5 days
Outcomes	Primary: The incidence of phlebitis (a) Grade 1. local pain, red swelling or edema, no strip-shaped changes in veins, no palpable venous cord Treatment group: 2/80, Control group: 12/80 (b) Grade 2: local pain, red swelling or edema, with strip-shaped changes in veins, no palpable venous cord Treatment group: 1/80, Control group: 4/80 (c) Grade 3. local pain, red swelling or edema, with strip-shaped changes in veins, palpable venous cord Treatment group: 0/80, Control group: 2/80 Secondary: None
Notes	
Risk of bias	
Bias	Authors' judgement Support for judgement

Xiao 2008 (Continued)

Random sequence generation (selection bias)	High risk	Sequence generated by odd or even of the bed number
Allocation concealment (selection bias)	High risk	No allocation concealment
Blinding of participants and personnel (performance bias) All outcomes	High risk	No blinding. The outcome assessment is likely to be influenced by the lack of blinding
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not reported
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Number randomised not stated
Selective reporting (reporting bias)	Unclear risk	The study protocol is not available, and it is not clear if the published reports included all expected outcomes
Other bias	Unclear risk	The baseline information between comparison groups were not described

Yang 2008

Methods	Study design: Randomised controlled trial Method of randomisation: Not described Concealment of allocation: Not reported Exclusions post-randomisation: Not reported Losses to follow up: None Intention-to-treat analysis: Not reported
Participants	Country: China Setting: Hospital Number: 100 participants (52 treatment, 48 control) Age: Mean 46 years, range from 18 to 69 years Sex: Male/female 46/54 Inclusion criteria: Phlebitis met criteria of the Infusion Nursing Society of America Exclusion criteria: Not stated
Interventions	Treatment: Fresh aloe slice external application, wet compress at punctured skin, changed every 30 min, for one hour, 3 - 4 times a day Control: 50% MgSO ₄ external application, wet compress at punctured skin, changed every 30 min, for one hour, 3 - 4 times a day Duration: 3 days

Yang 2008 (Continued)

Outcomes	<p>Primary: The rate of resolution of phlebitis</p> <p>(a) Recovery: disappearance of red swelling, pain and scorching hot</p> <p>Treatment group: 30/52, Control group: 15/48</p> <p>(b) Marked improvement: alleviation of red swelling, pain and scorching hot with slight pressing pain on the punctured veins</p> <p>Treatment group: 15/52, Control group: 11/48</p> <p>(c) Improvement: alleviation of red swelling, pain and scorching hot with obvious pressing pain on the punctured veins</p> <p>Treatment group: 5/52, Control group: 13/48</p> <p>(d) Not effective: no changes of symptoms of phlebitis after treatment</p> <p>Treatment group: 2/52, Control group: 9/48</p> <p>Secondary: None</p>
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Notes

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomised, but the detailed information of randomisation method was not described
Allocation concealment (selection bias)	Unclear risk	Method of allocation concealment was not described
Blinding of participants and personnel (performance bias) All outcomes	High risk	No blinding. The outcome assessment is likely to be influenced by the lack of blinding
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not reported
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Number randomised not stated
Selective reporting (reporting bias)	Unclear risk	The study protocol is not available, and it is not clear if the published reports included all expected outcomes
Other bias	Unclear risk	The baseline information between comparison groups were not described

Yao 2009

Methods	<p>Study design: Randomised controlled trial</p> <p>Method of randomisation: No described</p> <p>Concealment of allocation: Not reported</p>
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Yao 2009 (Continued)

Exclusions post-randomisation: Not reported

Losses to follow up: None

Intention-to-treat analysis: Not reported

Participants	Country: China Setting: Hospital Number: 196 participants (98 treatment, 98 control) Age: Treatment group: mean 51.01 years, range from 14 to 82 years, Control group: mean 48.51 years, range from 14 to 78 years Sex: Treatment group: male/female 60/38; Control group: male/ female 58/40 Inclusion criteria: Neurosurgery patients with the needle detained in the infused vein Exclusion criteria: Not stated
Interventions	Treatment: Fresh aloe slice wet compress at punctured skin, changed every 2 hours Control: No treatment Duration: 5 days
Outcomes	Primary: The incidence of phlebitis (a) First degree: local pain, red swelling or edema, no strip-shaped changes in veins, no palpable venous cord Treatment group: 2/98, Control group: 89/98 (b) Second degree: local pain, red swelling or edema, with strip-shaped changes in veins, no palpable venous cord Treatment group: 2/98, Control group: 9/98 (c) Third degree: local pain, red swelling or edema, with strip-shaped changes in veins, palpable venous cord Treatment group: 0/98, Control group: 0/98 Secondary: detain time of needle

Notes

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomised, but the detailed information of randomizations method was not described
Allocation concealment (selection bias)	Unclear risk	Method of allocation concealment was not described
Blinding of participants and personnel (performance bias) All outcomes	High risk	No blinding. The outcome assessment is likely to be influenced by the lack of blinding

Yao 2009 (Continued)

Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not reported
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Number randomised not stated
Selective reporting (reporting bias)	Unclear risk	The study protocol is not available, and it is not clear if the published reports included all expected outcomes
Other bias	Low risk	There are no the statistical difference in age, sex, illness, the infusion drugs between treatment and control groups. The study appears to be free other sources of bias

Yu 2006

Methods	Study design: Randomised controlled trial Method of randomisation: Not described Concealment of allocation: Not reported Exclusions post-randomisation: Not reported Losses to follow up: None Intention-to-treat analysis: Not reported
Participants	Country: China Setting: Hospital Number: 150 participants (75 treatment, 75 control) Age: Mean 57.6 years, range from 18 - 86 years Sex: Male/female 64/86 Inclusion criteria: Cancer patients due to receive the chemotherapy Exclusion criteria: Not stated
Interventions	Treatment : Fresh aloe slice external application, fresh aloe slice 4 - 6 cm long rubbed repeatedly near punctured skin for 6 - 7 min before chemotherapy, then fresh aloe slice compress at punctured skin for 60 min after chemotherapy Control: No treatment Duration: 1 - 7 days
Outcomes	Primary: The incidence of phlebitis (a) First degree: slightly discomfort at local vein. diameter range of pain, red swelling is less than 1 cm. elasticity of vein is normal Treatment group: 5/75, Control group: 16/75 (b) Second degree: diameter range of pain, red swelling exceed 5 cm. elasticity of vein become to weaken. speed of infusion become slowly

Yu 2006 (Continued)

Treatment group: 2/75, Control group: 11/75

(c) Third degree: diameter range of pain, red swelling exceed 10 cm. elasticity of vein disappear. speed of infusion become more slowly than second degree

Treatment group: 0/75, Control group: 6/75

Secondary: None

Notes

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomised, but the detailed information of randomisation method was not described
Allocation concealment (selection bias)	Unclear risk	Method of allocation concealment was not described
Blinding of participants and personnel (performance bias) All outcomes	High risk	No blinding. The outcome assessment is likely to be influenced by the lack of blinding
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not reported
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Number randomised not stated
Selective reporting (reporting bias)	Unclear risk	The study protocol is not available, and it is not clear if the published reports included all expected outcomes
Other bias	Low risk	There are no the statistical difference in age, sex, illness, the infusion drugs between treatment and control groups. The study appears to be free other sources of bias

Zhang 2010

Methods

Study design: Quasi randomised controlled trial

Method of randomisation: Random sequence was generated by the sequence of admission of inpatient

Concealment of allocation: None

Exclusions post-randomisation: Not reported

Losses to follow up: None

Intention-to-treat analysis: Not reported

Participants

Country: China

Setting: Hospital

Zhang 2010 (Continued)

Number: 116 participants (32 treatment 1, 31 treatment 2, 63 control)

Age: Range from 45 to 65 years

Sex: Not reported

Inclusion criteria: Cancer patients due to receive treatment of chemotherapy

Exclusion criteria: Not stated

Interventions	<p>Treatment 1: External application of piece of fresh aloe leaf, fresh aloe leaf with 10 cm long, 6 cm wide and 0.5 cm thick wet compress at punctured skin, changed every 2 hours</p> <p>Treatment 2: External application of sea tangle. sea tangle with 10 cm long, 6 cm wide and 0.5 cm thick wet compress at punctured skin, changed every 2 hours</p> <p>Control: 50% MgSO₄ wet compress at punctured skin</p> <p>Duration: 4 days</p>
Outcomes	<p>Primary: The incidence of phlebitis</p> <p>(a) First degree: local pain, red swelling or edema, no strip-shaped changes in veins, no palpable venous cord</p> <p>Treatment group1: 13/32, Treatment group 2: 12/31, Control group: 23/63</p> <p>(b) Second degree: local pain, red swelling or edema, with strip-shaped changes in veins, no palpable venous cord</p> <p>Treatment group1: 5/32, Treatment group 2: 7/31, Control group: 34/63</p> <p>(c) Third degree: local pain, red swelling or edema, with strip-shaped changes in veins, palpable venous cord</p> <p>Treatment group1: 1/32, Treatment group 2: 1/31, Control group: 6/63</p> <p>Secondary: None</p>

Notes

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	Random sequence was generated by the sequence of admission, and there was not parallel between treatment and control groups
Allocation concealment (selection bias)	High risk	Alternate allocation and not parallel
Blinding of participants and personnel (performance bias) All outcomes	High risk	No blinding. The outcome assessment is likely to be influenced by the lack of blinding
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not reported
Incomplete outcome data (attrition bias)	Unclear risk	Number randomised not stated

Zhang 2010 (Continued)

All outcomes

Selective reporting (reporting bias)	Unclear risk	The study protocol is not available, and it is not clear if the published reports included all expected outcomes
Other bias	Unclear risk	The baseline information among comparison groups was not described

Zhang 2013

Methods	Study design: Randomised controlled trial Method of randomisation: Not described Concealment of allocation: Not reported Exclusions post-randomisation: Not reported Losses to follow up: None Intention-to-treat analysis: Not reported
Participants	Country: China Setting: Hospital Number: 160 participants (80 treatment, 80 control) Age: Mean 45 years, range from 30 to 75 years Sex: Male/female 86/74 Inclusion criteria: Phlebitis met criteria of the Infusion Nursing Society of America Exclusion criteria: Not stated
Interventions	Treatment: Hirudoid plus fresh aloe vera slice smeared at punctured skin, once a day Control: Hirudoid smeared at punctured skin alone, once a day Duration: 7 days
Outcomes	Primary: The rate of resolution of phlebitis (a) Recovery: disappearance of local pain, red swelling Treatment group: 52/80, Control group: 27/80 (b) Improvement: alleviation of local pain, red swelling Treatment group: 25/80, Control group: 31/80 (c) No effective: no change of local symptom after treatment Treatment group: 3/80, Control group: 22/80 Secondary: None

Notes

Risk of bias

Zhang 2013 (Continued)

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomised, but randomisation method was not described
Allocation concealment (selection bias)	Unclear risk	Method of allocation concealment was not described
Blinding of participants and personnel (performance bias) All outcomes	High risk	No blinding. The outcome assessment is likely to be influenced by the lack of blinding
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not reported
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Number randomised not stated
Selective reporting (reporting bias)	Unclear risk	The study protocol is not available, and it is not clear if the published reports included all expected outcomes
Other bias	Unclear risk	The baseline information among comparison groups was not described

Zheng 2010

Methods	Study design: Randomised controlled trial Method of randomisation: Not described Concealment of allocation: Not reported Exclusions post-randomisation: Not reported Losses to follow up: None Intention-to-treat analysis: Not reported
Participants	Country: China Setting: Hospital Number: 50 participants (25 treatment, 25 control) Age: Mean 63.5 years, range from 35 to 78 years Sex: Male/female 31/19 Inclusion criteria: Cancer patients with treatment of chemotherapy Exclusion criteria: Not stated
Interventions	Treatment: Fresh aloe slice wet compress at punctured skin, changed every half hour Control: No treatment Duration: 5 days

Zheng 2010 (Continued)

Outcomes

Primary: The incidence of phlebitis

(a) First degree: local pain, red swelling or edema, no strip-shaped changes in veins, no palpable venous cord

Treatment group: 3/25, Control group: 12/25

(b) Second degree: local pain, red swelling or edema, with strip-shaped changes in veins, no palpable venous cord

Treatment group: 0/25, Control group: 4/25

(c) Third degree: local pain, red swelling or edema, with strip-shaped changes in veins, palpable venous cord

Treatment group: 0/25, Control group: 1/25

Secondary: None

Notes

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomised, but the detailed information of randomisation method was not described
Allocation concealment (selection bias)	Unclear risk	Method of allocation concealment was not described
Blinding of participants and personnel (performance bias) All outcomes	High risk	No blinding. The outcome assessment is likely to be influenced by the lack of blinding
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not reported
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Number randomised not stated
Selective reporting (reporting bias)	Unclear risk	The study protocol is not available, and it is not clear if the published reports included all expected outcomes
Other bias	Low risk	The baseline information such as age, sex, illness, amount of infused mannitol between treatment and control groups are not statistically significant ($P > 0.05$). The study appears to be free other sources of bias

Zhong 2011

Methods

Study design: Randomised controlled trial

Method of randomisation: Not described

Concealment of allocation: Not reported

Zhong 2011 (Continued)

	Exclusions post-randomisation: Not reported
	Losses to follow up: None
	Intention-to-treat analysis: Not reported
Participants	Country: China Setting: Hospital Number: 60 participants (30 treatment, 30 control) Age: Treatment group: mean 42 years, range from 18 to 72 years; Control group: mean 40 years, range from 17 to 70 years Sex: Treatment group: male/female 11/9; Control group: male/female 13/17 Inclusion criteria: Phlebitis met criteria of the Infusion Nursing Society of America Exclusion criteria: Not stated
Interventions	Treatment: Aloe plus sulphanilamide pyrimidine. Sulphanilamide pyrimidine was smeared at punctured skin, after one hour, flesh aloe leaf wet compressed at same site, once a day Control: Sulphanilamide pyrimidine was smeared at punctured skin, once a day Duration: 10 days
Outcomes	Primary: The rate of resolution of phlebitis (a) Recovery: disappearance of local pain, red swelling Treatment group: 25/30, Control group: 19/30 (b) Improvement: alleviation of local pain, red swelling Treatment group: 4/30, Control group: 5/30 (c) No effective: no change of local symptom after treatment Treatment group: 1/30, Control group: 6/30 Secondary: None
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomised, but the detailed information of randomisation method was not described
Allocation concealment (selection bias)	Unclear risk	Method of allocation concealment was not described
Blinding of participants and personnel (performance bias) All outcomes	High risk	No blinding. The outcome assessment is likely to be influenced by the lack of blinding
Blinding of outcome assessment (detection bias)	Unclear risk	Not reported

Zhong 2011 (Continued)

All outcomes

Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Number randomised not stated
Selective reporting (reporting bias)	Unclear risk	The study protocol is not available, and it is not clear if the published reports included all expected outcomes
Other bias	Low risk	The baseline information such as age, sex, illness, the grade of phlebitis between treatment and control groups are not statistically significant ($P > 0.05$). The study appears to be free other sources of bias

Zhou 2006

Methods	Study design: Randomised controlled trial Method of randomisation: Not described Concealment of allocation: Not reported Exclusions post-randomisation: Not reported Losses to follow up: None Intention-to-treat analysis: Not reported
Participants	Country: China Setting: Hospital Number: 100 participants (52 treatment, 48 control) Age: Mean 48 years, range from 20 - 76 years Sex: Male/female 58/42 Inclusion criteria: Phlebitis met the criteria of "Fundamentals of Nursing" (Yin L 2002) Exclusion criteria: Not stated
Interventions	Treatment: Fresh aloe slice external application, compressed at punctured skin for 10 hours a day, changed every 1 - 2 hours Control: Fresh potato slice external application, compressed at punctured skin for 10 hours a day, changed every 1 - 2 hours Duration: 3 days
Outcomes	Primary: The rate of resolution of phlebitis (a) Recovery: disappearance of red swelling, scorching hot and pain along the punctured vein, and no pressing pain at the punctured vein Treatment group: 30/52, Control group: 10/48 (b) Marked improvement: disappearance of red swelling, scorching hot, pain alleviated, slight pressing pain at the punctured vein Treatment group: 15/52, Control group: 12/48

Zhou 2006 (Continued)

(c) Improvement: alleviation of red swelling, scorching hot and pain, pressing pain existing at the punctured vein

Treatment group: 5/52, Control group: 16/48

(d) Not effective: no change or more severe of phlebitis symptom after treatment

Treatment group: 2/52, Control group: 10/48

Secondary: None

Notes

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Randomised, but the detailed information of randomisation method was not described
Allocation concealment (selection bias)	Unclear risk	Method of allocation concealment was not described
Blinding of participants and personnel (performance bias) All outcomes	High risk	No blinding. The outcome assessment is likely to be influenced by the lack of blinding
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not reported
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Number randomised not stated
Selective reporting (reporting bias)	Unclear risk	The study protocol is not available, and it is not clear if the published reports included all expected outcomes
Other bias	Low risk	The baseline information such as age, sex, illness, the program of chemotherapy, the severe degree of phlebitis between treatment and control groups ($P > 0.05$). The study appears to be free other sources of bias

bid: twice a day

callosity: also called callus. A localised thickening and enlargement of the horny layer of the skin

min: minutes

tid: three times a day

trabs: a thickening of the horny layer of the skin as a result of chronic pressure or friction

Characteristics of excluded studies [ordered by study ID]

Study	Reason for exclusion
Cao 2007	Fresh aloe slice plus anisodamine in treatment group versus fresh aloe slice in control group
Chen 2007	The duration of treatment was unclear in the study

Study	Reason for exclusion
Dai 2007	Health education about phlebitis plus 0.2% novocaine 10 ml injection plus fresh aloe slice plus 0.9% NaCl ₂ 100 ml once a day in treatment group versus no treatment in control group
Deng 2001	The intervention was the mixed liquor of fresh aloe juice, 40% MgSO ₄ and vitamin B12 in treatment group versus only 40% MgSO ₄ in control group
Deng 2009	Ice bag plus fresh <i>Aloe vera</i> plus bormeol flucinonide cream in treatment group versus 50% MgSO ₄ in control group
Gong 2004	Self-made compound aloe cream in treatment group, which included several Chinese medicines such as aloe, long gu, xue jie, huang bai, bormeol. Only 50% MgSO ₄ in control group
Gu 2013	Sanyrene combined with aloe in treatment group versus usual nursing in control group
Guo 2009	Fresh <i>Aloe vera</i> juice plus 40% MgSO ₄ plus glycerol plus vitamin B12 in treatment group versus 40% MgSO ₄ in control group
Hu 2011	Fresh <i>Aloe vera</i> slice combination with fresh potato slice in the treatment group versus 50% MgSO ₄ in the control group
Huang 2005	Crassulaceae power plus fresh aloe juice in treatment group versus 50% MgSO ₄ in control group
Huang 2009	The aloe safflower extraction liquor (dry aloe 500 g, dry safflower 500 g and 75% alcohol 10,000 ml soaked for three days, then filtered out aloe and safflower) in treatment group versus 75% alcohol in control group
Huang 2013	The duration of treatment was unclear in the study
Jiang 2007	Shi run shao shang cream plus ice compress plus fresh aloe slice in treatment group versus 0.9% NaCl ₂ 100 ml plus dexamethasone 5 - 10 mg in control group
Lei 2012	The duration of treatment was unclear in the study
Li 2003b	Self-made aloe pigmentum in treatment group which was mainly made of menthol, camphor and <i>Aloe vera</i> . Only 50% MgSO ₄ in control group
Li 2006b	Ice compress plus fresh aloe slices in treatment group versus no treatment in control group
Li 2010	The mixture of <i>Aloe vera</i> juice 5 ml and 40% MgSO ₄ 5 ml and Vitamin B12 500 µg in treatment group versus 40% MgSO ₄ 10 ml in control group
Li 2011b	Fresh <i>Aloe vera</i> slice plus hirudoid paste, once a day in treatment group. Mixed liquor of hypertonic glucose and vitamin B12 and dexamethasone in control group
Liang 2011	Fresh <i>Aloe vera</i> slice plus honey in treatment group versus 50% MgSO ₄ in control group
Lin 2009	Fresh <i>Aloe vera</i> slice plus Ruyijinhuang power in treatment group versus 50% MgSO ₄ in control group
Liu 2009	The duration of treatment was not described in the original study

Study	Reason for exclusion
Lu 2004b	Aloe safflower alcohol extraction solution (made of dry aloe 500 g, dry safflower 500 g, 75% alcohol 5000 ml soaking for three days, and filter out aloe and safflower) in treatment group. Only 50% MgSO ₄ in control group
Lu 2007	Self-made liniment including fresh aloe 500 g, safflower 500 g and 75% alcohol 1000 ml) compress in experimental group versus 75% alcohol in control group
Lu 2008	Aloe-carthamus alcohol hydropathic distilled liquid in treatment group versus no treatment in control group
Lu 2010	Moxibustion and compression of aloe-safflower-angelica alcohol hydropathical distilled liquid in treatment group versus 50% MgSO ₄ in control group
Lu 2010b	Treatment group 1: moxibustion, Treatment group 2: compress of aloe-safflower-angelica alcohol hydropathic distilled liquid. No control group
Lu 2011	Mixed extraction liquor of <i>Aloe vera</i> , safflower, Chinese angelica and alcohol external application in treatment group. Moxibustion in control group
Ma 2008	Yunnan white drug combination with fresh aloe slice in treatment group versus 33% MgSO ₄ in control group
Ma 2009	Garlic spread combination with fresh <i>Aloe vera</i> slice in treatment group versus fresh <i>Aloe vera</i> slice in control group
Mo 2008	Mixture of China wood oil and gypsum in treatment group versus fresh aloe slice in control group
Peng 2002	Fresh aloe slices combination with irradiation of Zhoulín spectrum apparatus in treatment group versus only 50% MgSO ₄ in control group
Shao 2008	Jinhuang power plus fresh aloe slice in treatment group versus fresh aloe slice in control group
Shen 2013	The compound aloe suckling containing aloe, magnesium sulfate, dexamethasone and pentamul in treatment group versus 50% manesium sulfate in control group
Shi 2013	The compound aloe suckling containing aloe, lidocaine, dexamethasone and vitamin B12 in treatment group versus usual nursing in control group
Su 2011	Fresh <i>Aloe vera</i> slice plus anisodamine in treatment group versus 50% MgSO ₄ in control group
Tang 2008	50% MgSO ₄ combination with fresh <i>Aloe vera</i> slice in treatment group versus NaCl ₂ 250 ml plus dexamethasone 5 mg injection in control group
Tang 2008b	POME irradiation plus fresh aloe slice in treatment group versus 50% MgSO ₄ in control group
Wang 2004	Fresh aloe slices in treatment group, no control group
Wang 2010c	Fresh <i>Aloe vera</i> slice combination with heparin sodium in treatment group versus 50% MgSO ₄ in control group
Wang 2011	Fresh aloe slice and hirudoid used alternately in treatment group versus 50% MgSO ₄ only in control group
Wang 2012	Aloe plus hirudoid paste in treatment group versus 50% MgSO ₄ in control group

Study	Reason for exclusion
Wang 2013	Aloe combined with honey dew in treatment group versus usual nursing in control group
Wei 2012	Moxibustion combined Chinese medicine containing the exacting solution of <i>Aloe vera</i> , <i>safflower</i> and <i>angelica</i> in treatment group versus 50% MgSO ₄ in control group
Wu 2010	Fresh <i>Aloe vera</i> slice plus irradiating with QK-medioapparatus in treatment group versus 50% MgSO ₄ in control group
Xu 2007	Fresh aloe slice plus potatoes slice in treatment group, and no treatment in control group
Xu 2008	Mixture of 10 ml fresh aloe juice and 10 ml glycerol in treatment group versus 50% MgSO ₄ in control group
Yan 2012	The duration of treatment was unclear in the study
Yang 2010	Liquid mixture of fresh <i>Aloe vera</i> , 25% magnesium sulphate, 50% glucose injection, vitamin B12 injection in treatment group versus 50% magnesium sulphate in control group
Ye 2008	Novocaine combination with fresh aloe slice in treatment group. The intervention method in control group was not described
Ye 2011	Fresh <i>Aloe vera</i> slice plus hirudoid in treatment group versus 50% MgSO ₄ in control group
Zhang 2003	The duration of treatment was unclear in the study
Zhang 2004	Fresh aloe slice plus 50% MgSO ₄ in treatment group versus 2% procaine plus dexamethasone plus NaCl ₂ plus 50% MgSO ₄ in control group
Zhang 2005	The duration of treatment was unclear in the study
Zhang 2006	The duration of treatment was unclear in the study
Zhang 2008	Fresh <i>Aloe vera</i> juice plus ultraviolet irradiation in treatment group versus 50% MgSO ₄ in control group
Zhang 2011	The duration of treatment was unclear in the study
Zhou 2001	The duration of treatment was unclear in the study
Zhu 2010	Bactroban in treatment group versus fresh <i>Aloe vera</i> in control group
Zhuang 2008	Dexamethasone 5 mg plus NaCl ₂ 10 ml plus fresh aloe slice in treatment group versus 50% MgSO ₄ in control group
Zou 2004	Self-controlled clinical trial

DATA AND ANALYSES

Comparison 1. Aloe vera versus no treatment for prevention of phlebitis

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Total incidence of phlebitis	15		Risk Ratio (IV, Random, 95% CI)	Subtotals only
1.1 duration: 7 days	1	80	Risk Ratio (IV, Random, 95% CI)	0.28 [0.11, 0.68]
1.2 duration: 5 days	5	532	Risk Ratio (IV, Random, 95% CI)	0.29 [0.11, 0.74]
1.3 duration: 1-7 days	2	370	Risk Ratio (IV, Random, 95% CI)	0.31 [0.18, 0.51]
1.4 duration: 3 days	3	312	Risk Ratio (IV, Random, 95% CI)	0.44 [0.29, 0.66]
1.5 duration: 2-3 days	2	189	Risk Ratio (IV, Random, 95% CI)	0.21 [0.05, 0.80]
1.6 duration: from the second day of treatment to one week after stopping treatment	1	150	Risk Ratio (IV, Random, 95% CI)	0.36 [0.26, 0.48]
1.7 duration: one course of treatment	1	3000	Risk Ratio (IV, Random, 95% CI)	0.11 [0.09, 0.15]
2 Incidence of second degree phlebitis	14	4585	Risk Ratio (IV, Random, 95% CI)	0.18 [0.10, 0.31]
2.1 duration: 7 days	1	80	Risk Ratio (IV, Random, 95% CI)	0.22 [0.05, 0.96]
2.2 duration: 5 days	4	482	Risk Ratio (IV, Random, 95% CI)	0.19 [0.07, 0.55]
2.3 duration: 1-7 days	2	370	Risk Ratio (IV, Random, 95% CI)	0.21 [0.11, 0.41]
2.4 duration: 3 days	3	314	Risk Ratio (IV, Random, 95% CI)	0.42 [0.22, 0.80]
2.5 duration: 2-3 days	2	189	Risk Ratio (IV, Random, 95% CI)	0.07 [0.01, 0.49]
2.6 duration: from the second day of treatment to one week after stopping treatment	1	150	Risk Ratio (IV, Random, 95% CI)	0.18 [0.10, 0.33]
2.7 duration: one course of treatment	1	3000	Risk Ratio (IV, Random, 95% CI)	0.06 [0.04, 0.09]
3 Incidence of third degree phlebitis	14	4585	Risk Ratio (M-H, Fixed, 95% CI)	0.06 [0.03, 0.11]
3.1 duration: 7 days	1	80	Risk Ratio (M-H, Fixed, 95% CI)	0.5 [0.05, 5.30]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
3.2 duration: 5 days	4	482	Risk Ratio (M-H, Fixed, 95% CI)	0.25 [0.03, 2.19]
3.3 duration: 1-7 days	2	370	Risk Ratio (M-H, Fixed, 95% CI)	0.10 [0.02, 0.55]
3.4 duration: 3 days	3	314	Risk Ratio (M-H, Fixed, 95% CI)	0.29 [0.11, 0.80]
3.5 duration: 2-3 days	2	189	Risk Ratio (M-H, Fixed, 95% CI)	0.09 [0.01, 0.69]
3.6 duration: from the second day of treatment to one week after stopping treatment	1	150	Risk Ratio (M-H, Fixed, 95% CI)	0.02 [0.00, 0.34]
3.7 duration: one course of treatment	1	3000	Risk Ratio (M-H, Fixed, 95% CI)	0.00 [0.00, 0.06]
4 Length of time needle is successfully detained in infused vein	2		Mean Difference (IV, Random, 95% CI)	Totals not selected

Analysis 1.1. Comparison 1 Aloe vera versus no treatment for prevention of phlebitis, Outcome 1 Total incidence of phlebitis.

Analysis 1.2. Comparison 1 Aloe vera versus no treatment for prevention of phlebitis, Outcome 2 Incidence of second degree phlebitis.

Analysis 1.3. Comparison 1 *Aloe vera* versus no treatment for prevention of phlebitis, Outcome 3 Incidence of third degree phlebitis.

Analysis 1.4. Comparison 1 Aloe vera versus no treatment for prevention of phlebitis, Outcome 4 Length of time needle is successfully detained in infused vein.

Comparison 2. Aloe vera versus potato for prevention of phlebitis

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Total incidence of phlebitis	2	276	Risk Ratio (IV, Fixed, 95% CI)	0.90 [0.58, 1.40]
2 Incidence of second degree phlebitis	2	276	Risk Ratio (IV, Fixed, 95% CI)	1.14 [0.49, 2.67]
3 Incidence of third degree phlebitis	2	276	Risk Ratio (IV, Fixed, 95% CI)	0.45 [0.04, 4.94]

Analysis 2.1. Comparison 2 Aloe vera versus potato for prevention of phlebitis, Outcome 1 Total incidence of phlebitis.

Analysis 2.2. Comparison 2 Aloe vera versus potato for prevention of phlebitis, Outcome 2 Incidence of second degree phlebitis.

Analysis 2.3. Comparison 2 Aloe vera versus potato for prevention of phlebitis, Outcome 3 Incidence of third degree phlebitis.

Comparison 3. Aloe vera versus 33% MgSO₄ for prevention of phlebitis

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Total incidence of phlebitis	2	200	Risk Ratio (M-H, Fixed, 95% CI)	0.43 [0.24, 0.78]

Analysis 3.1. Comparison 3 Aloe vera versus 33% MgSO₄ for prevention of phlebitis, Outcome 1 Total incidence of phlebitis.

Comparison 4. Aloe vera versus 50% MgSO₄ for prevention of phlebitis

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Total incidence of phlebitis	2	248	Risk Ratio (M-H, Random, 95% CI)	0.41 [0.16, 1.07]
2 Incidence of second degree phlebitis	2	248	Risk Ratio (M-H, Fixed, 95% CI)	0.26 [0.14, 0.50]
3 Incidence of third degree phlebitis	2	248	Risk Ratio (M-H, Fixed, 95% CI)	0.28 [0.07, 1.02]

Analysis 4.1. Comparison 4 Aloe vera versus 50% MgSO₄ for prevention of phlebitis, Outcome 1 Total incidence of phlebitis.

Analysis 4.2. Comparison 4 Aloe vera versus 50% MgSO₄ for prevention of phlebitis, Outcome 2 Incidence of second degree phlebitis.

Analysis 4.3. Comparison 4 Aloe vera versus 50% MgSO₄ for prevention of phlebitis, Outcome 3 Incidence of third degree phlebitis.

Comparison 5. Aloe vera plus ice bag versus ice bag plus 75% MgSO₄ for prevention of phlebitis

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Total incidence of phlebitis	1		Risk Ratio (IV, Fixed, 95% CI)	Totals not selected
2 Incidence of second degree phlebitis	1		Risk Ratio (IV, Fixed, 95% CI)	Totals not selected
3 Incidence of third degree phlebitis	1		Risk Ratio (M-H, Fixed, 95% CI)	Totals not selected

Analysis 5.1. Comparison 5 Aloe vera plus ice bag versus ice bag plus 75% MgSO₄ for prevention of phlebitis, Outcome 1 Total incidence of phlebitis.

Analysis 5.2. Comparison 5 Aloe vera plus ice bag versus ice bag plus 75% MgSO₄ for prevention of phlebitis, Outcome 2 Incidence of second degree phlebitis.

Study or subgroup	Aloe vera n/N	75% MgSO ₄ n/N	Risk Ratio IV, Fixed, 95% CI	Risk Ratio IV, Fixed, 95% CI
Liu 2003	4/67	7/80		0.68[0.21,2.23]

Analysis 5.3. Comparison 5 Aloe vera plus ice bag versus ice bag plus 75% MgSO₄ for prevention of phlebitis, Outcome 3 Incidence of third degree phlebitis.

Study or subgroup	Aloe vera n/N	75% MgSO ₄ n/N	Risk Ratio M-H, Fixed, 95% CI	Risk Ratio M-H, Fixed, 95% CI
Liu 2003	1/67	1/80		1.19[0.08,18.73]

Comparison 6. Aloe vera versus 75% alcohol for prevention of phlebitis

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Total incidence of phlebitis	1		Risk Ratio (IV, Fixed, 95% CI)	Totals not selected

Analysis 6.1. Comparison 6 Aloe vera versus 75% alcohol for prevention of phlebitis, Outcome 1 Total incidence of phlebitis.

Study or subgroup	Aloe vera n/N	75% alcohol n/N	Risk Ratio IV, Fixed, 95% CI	Risk Ratio IV, Fixed, 95% CI
Liang 2004	0/75	28/75		0.02[0.00,0.28]

Comparison 7. Aloe vera versus 33% MgSO₄ for treatment of phlebitis

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Rate of resolution phlebitis: recovery	1	120	Risk Ratio (M-H, Fixed, 95% CI)	1.15 [0.92, 1.43]
2 Rate of resolution phlebitis: marked improvement	2	302	Risk Ratio (IV, Fixed, 95% CI)	1.97 [1.44, 2.70]
3 Rate of resolution phlebitis: total improvement	3	422	Risk Ratio (IV, Fixed, 95% CI)	1.16 [1.09, 1.24]

Analysis 7.1. Comparison 7 Aloe vera versus 33% MgSO₄ for treatment of phlebitis, Outcome 1 Rate of resolution phlebitis: recovery.

Analysis 7.2. Comparison 7 Aloe vera versus 33% MgSO₄ for treatment of phlebitis, Outcome 2 Rate of resolution phlebitis: marked improvement.

Analysis 7.3. Comparison 7 Aloe vera versus 33% MgSO₄ for treatment of phlebitis, Outcome 3 Rate of resolution phlebitis: total improvement.

Comparison 8. *Aloe vera* versus 50% MgSO₄ for treatment of phlebitis

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Rate of resolution of phlebitis: recovery	7	595	Risk Ratio (IV, Fixed, 95% CI)	1.42 [1.24, 1.61]
1.1 duration: 3 days	4	394	Risk Ratio (IV, Fixed, 95% CI)	1.38 [1.17, 1.61]
1.2 duration: 7 days	1	50	Risk Ratio (IV, Fixed, 95% CI)	3.5 [1.34, 9.17]
1.3 duration: 15 days	2	151	Risk Ratio (IV, Fixed, 95% CI)	1.43 [1.13, 1.80]
2 Rate of resolution of phlebitis: marked improvement	9	814	Risk Ratio (IV, Random, 95% CI)	1.56 [1.29, 1.87]
2.1 duration: 3 days	7	679	Risk Ratio (IV, Random, 95% CI)	1.57 [1.25, 1.97]
2.2 duration: 7 days	1	50	Risk Ratio (IV, Random, 95% CI)	2.22 [1.27, 3.88]
2.3 duration: 15 days	1	85	Risk Ratio (IV, Random, 95% CI)	1.39 [1.15, 1.69]
3 Rate of resolution of phlebitis: total improvement	10	880	Risk Ratio (IV, Fixed, 95% CI)	1.22 [1.16, 1.28]
3.1 duration: 3 days	7	679	Risk Ratio (IV, Fixed, 95% CI)	1.20 [1.13, 1.26]
3.2 duration: 7 days	1	50	Risk Ratio (IV, Fixed, 95% CI)	1.53 [1.09, 2.15]
3.3 duration: 15 days	2	151	Risk Ratio (IV, Fixed, 95% CI)	1.35 [1.16, 1.56]
4 Time of marked improvement	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
5 Time of improvement	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected

Analysis 8.1. Comparison 8 *Aloe vera* versus 50% MgSO₄ for treatment of phlebitis, Outcome 1 Rate of resolution of phlebitis: recovery.

Analysis 8.2. Comparison 8 Aloe vera versus 50% MgSO₄ for treatment of phlebitis, Outcome 2 Rate of resolution of phlebitis: marked improvement.

Analysis 8.3. Comparison 8 Aloe vera versus 50% MgSO₄ for treatment of phlebitis, Outcome 3 Rate of resolution of phlebitis: total improvement.

Analysis 8.4. Comparison 8 Aloe vera versus 50% MgSO₄ for treatment of phlebitis, Outcome 4 Time of marked improvement.

Analysis 8.5. Comparison 8 Aloe vera versus 50% MgSO₄ for treatment of phlebitis, Outcome 5 Time of improvement.

Comparison 9. Aloe vera plus non-Aloe vera versus same non-Aloe vera for treatment of phlebitis

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Rate of resolution of phlebitis: recovery	3	283	Risk Ratio (IV, Random, 95% CI)	1.75 [1.24, 2.46]
2 Rate of resolution of phlebitis: marked improvement	3	163	Risk Ratio (IV, Fixed, 95% CI)	1.26 [1.09, 1.47]
3 Rate of resolution of phlebitis: total improvement	4	323	Risk Ratio (IV, Fixed, 95% CI)	1.23 [1.13, 1.35]
4 Time of red swelling symptom disappeared of phlebitis	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected
5 Time of relief of pain	1		Mean Difference (IV, Fixed, 95% CI)	Totals not selected

Analysis 9.1. Comparison 9 Aloe vera plus non-Aloe vera versus same non-Aloe vera for treatment of phlebitis, Outcome 1 Rate of resolution of phlebitis: recovery.

Analysis 9.2. Comparison 9 Aloe vera plus non-Aloe vera versus same non-Aloe vera for treatment of phlebitis, Outcome 2 Rate of resolution of phlebitis: marked improvement.

Analysis 9.3. Comparison 9 Aloe vera plus non-Aloe vera versus same non-Aloe vera for treatment of phlebitis, Outcome 3 Rate of resolution of phlebitis: total improvement.

Analysis 9.4. Comparison 9 Aloe vera plus non-Aloe vera versus same non-Aloe vera for treatment of phlebitis, Outcome 4 Time of red swelling symptom disappeared of phlebitis.

Study or subgroup	Aloe vera plus sulfonic acid mucopolysaccharide cremor		Sulfonic acid mucopolysaccharide cremor		Mean Difference	Mean Difference
	N	Mean(SD)	N	Mean(SD)	Fixed, 95% CI	Fixed, 95% CI
Chen 2009	20	15.3 (7.2)	20	18.2 (8.8)		-2.93[-7.91,2.05]
Favours aloe vera plus sulfonic acid mucopolysaccharide cremor						Favours sulfonic acid mucopolysaccharide cremor

Analysis 9.5. Comparison 9 Aloe vera plus non-Aloe vera versus same non-Aloe vera for treatment of phlebitis, Outcome 5 Time of relief of pain.

Study or subgroup	Aloe vera plus sulfonic acid mucopolysaccharide cremor		Sulfonic acid mucopolysaccharide cremor		Mean Difference	Mean Difference
	N	Mean(SD)	N	Mean(SD)	Fixed, 95% CI	Fixed, 95% CI
Chen 2009	20	1.2 (0.7)	20	2.1 (1.2)		-0.97[-1.58,-0.36]
Favours aloe vera plus sulfonic acid mucopolysaccharide cremor						Favours sulfonic acid mucopolysaccharide cremor

Comparison 10. Aloe vera versus 75% alcohol for treatment of phlebitis

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Rate of resolution of phlebitis: marked improvement	1		Risk Ratio (IV, Fixed, 95% CI)	Totals not selected
2 Rate of resolution of phlebitis: total improvement	1		Risk Ratio (IV, Fixed, 95% CI)	Totals not selected

Analysis 10.1. Comparison 10 Aloe vera versus 75% alcohol for treatment of phlebitis, Outcome 1 Rate of resolution of phlebitis: marked improvement.

Study or subgroup	Aloe vera n/N	75% alcohol n/N	Risk Ratio IV, Fixed, 95% CI	Risk Ratio IV, Fixed, 95% CI
Lu 2004	12/30	4/30		3[1.09,8.25]
Favours 75% alcohol				Favours aloe vera

Analysis 10.2. Comparison 10 Aloe vera versus 75% alcohol for treatment of phlebitis, Outcome 2 Rate of resolution of phlebitis: total improvement.

Study or subgroup	Aloe vera n/N	75% alcohol n/N	Risk Ratio IV, Fixed, 95% CI	Risk Ratio IV, Fixed, 95% CI
Lu 2004	20/30	10/30		2[1.14,3.52]
Favours 75% alcohol				Favours aloe vera

Comparison 11. Aloe vera versus potato for treatment of phlebitis

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Rate of resolution of phlebitis: recovery	1		Risk Ratio (IV, Fixed, 95% CI)	Totals not selected
2 Rate of resolution of phlebitis: marked improvement	1		Risk Ratio (IV, Fixed, 95% CI)	Totals not selected
3 Rate of resolution of phlebitis: total improvement	1		Risk Ratio (IV, Fixed, 95% CI)	Totals not selected

Analysis 11.1. Comparison 11 Aloe vera versus potato for treatment of phlebitis, Outcome 1 Rate of resolution of phlebitis: recovery.

Study or subgroup	Aloe vera n/N	Potato n/N	Risk Ratio IV, Fixed, 95% CI	Risk Ratio IV, Fixed, 95% CI
Zhou 2006	30/52	10/48		2.77[1.52,5.04]
Favours potato 0.01 0.1 1 10 100 Favours aloe vera				

Analysis 11.2. Comparison 11 Aloe vera versus potato for treatment of phlebitis, Outcome 2 Rate of resolution of phlebitis: marked improvement.

Study or subgroup	Aloe vera n/N	Potato n/N	Risk Ratio IV, Fixed, 95% CI	Risk Ratio IV, Fixed, 95% CI
Zhou 2006	45/52	22/48		1.89[1.36,2.62]
Favours potato 0.01 0.1 1 10 100 Favours aloe vera				

Analysis 11.3. Comparison 11 Aloe vera versus potato for treatment of phlebitis, Outcome 3 Rate of resolution of phlebitis: total improvement.

Study or subgroup	Aloe vera n/N	Potato n/N	Risk Ratio IV, Fixed, 95% CI	Risk Ratio IV, Fixed, 95% CI
Zhou 2006	50/52	37/48		1.25[1.06,1.47]
Favours potato 0.01 0.1 1 10 100 Favours aloe vera				

Comparison 12. *Aloe vera* versus hirudoid for treatment of phlebitis

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Rate of resolution of phlebitis: recovery	1		Risk Ratio (IV, Fixed, 95% CI)	Totals not selected
2 Rate of resolution of phlebitis: marked improvement	1		Risk Ratio (IV, Fixed, 95% CI)	Totals not selected
3 Rate of resolution of phlebitis: total improvement	1		Risk Ratio (IV, Fixed, 95% CI)	Totals not selected

Analysis 12.1. Comparison 12 *Aloe vera* versus hirudoid for treatment of phlebitis, Outcome 1 Rate of resolution of phlebitis: recovery.

Study or subgroup	<i>Aloe vera</i> n/N	Hirudoid n/N	Risk Ratio IV, Fixed, 95% CI	Risk Ratio IV, Fixed, 95% CI
Wang 2010b	6/39	13/30		0.36[0.15,0.82]

Analysis 12.2. Comparison 12 *Aloe vera* versus hirudoid for treatment of phlebitis, Outcome 2 Rate of resolution of phlebitis: marked improvement.

Study or subgroup	<i>Aloe vera</i> n/N	Hirudoid n/N	Risk Ratio IV, Fixed, 95% CI	Risk Ratio IV, Fixed, 95% CI
Wang 2010b	22/39	29/30		0.58[0.44,0.78]

Analysis 12.3. Comparison 12 *Aloe vera* versus hirudoid for treatment of phlebitis, Outcome 3 Rate of resolution of phlebitis: total improvement.

Study or subgroup	<i>Aloe vera</i> n/N	Hirudoid n/N	Risk Ratio IV, Fixed, 95% CI	Risk Ratio IV, Fixed, 95% CI
Wang 2010b	39/39	30/30		1[0.94,1.06]

Comparison 13. *Aloe vera* plus routine treatment versus routine treatment plus dexamethasone for treatment of phlebitis

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Rate of resolution of phlebitis: recovery	1		Risk Ratio (IV, Fixed, 95% CI)	Totals not selected

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
2 Rate of resolution of phlebitis: marked improvement	1		Risk Ratio (IV, Fixed, 95% CI)	Totals not selected
3 Rate of resolution of phlebitis: total improvement	1		Risk Ratio (IV, Fixed, 95% CI)	Totals not selected

Analysis 13.1. Comparison 13 *Aloe vera* plus routine treatment versus routine treatment plus dexamethasone for treatment of phlebitis, Outcome 1 Rate of resolution of phlebitis: recovery.

Study or subgroup	<i>Aloe vera</i> plus routine treatment n/N	Routine treatment plus dexamethasone n/N	Risk Ratio IV, Fixed, 95% CI	Risk Ratio IV, Fixed, 95% CI
Wang 2008	30/34	14/31		1.95[1.3,2.93]
Favours routine treatment plus dexamethasone 0.01 0.1 1 10 100 Favours <i>aloe vera</i> plus routine treatment				

Analysis 13.2. Comparison 13 *Aloe vera* plus routine treatment versus routine treatment plus dexamethasone for treatment of phlebitis, Outcome 2 Rate of resolution of phlebitis: marked improvement.

Study or subgroup	<i>Aloe vera</i> plus routine treatment n/N	Routine treatment plus dexamethasone n/N	Risk Ratio IV, Fixed, 95% CI	Risk Ratio IV, Fixed, 95% CI
Wang 2008	30/34	14/31		1.95[1.3,2.93]
Favours routine treatment plus dexamethasone 0.01 0.1 1 10 100 Favours <i>aloe vera</i> plus routine treatment				

Analysis 13.3. Comparison 13 *Aloe vera* plus routine treatment versus routine treatment plus dexamethasone for treatment of phlebitis, Outcome 3 Rate of resolution of phlebitis: total improvement.

Study or subgroup	<i>Aloe vera</i> plus routine treatment n/N	Routine treatment plus dexamethasone n/N	Risk Ratio IV, Fixed, 95% CI	Risk Ratio IV, Fixed, 95% CI
Wang 2008	34/34	24/31		1.29[1.06,1.57]
Favours routine treatment plus dexamethasone 0.01 0.1 1 10 100 Favours <i>aloe vera</i> plus routine treatment				

Comparison 14. *Aloe vera* versus no treatment for prevention of phlebitis (sensitivity analysis)

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Incidence of third degree phlebitis (random-effects model)	14	4585	Risk Ratio (M-H, Random, 95% CI)	0.13 [0.05, 0.34]
1.1 duration: 7 days	1	80	Risk Ratio (M-H, Random, 95% CI)	0.5 [0.05, 5.30]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1.2 duration: 5 days	4	482	Risk Ratio (M-H, Random, 95% CI)	0.26 [0.03, 2.26]
1.3 duration: 1-7 days	2	370	Risk Ratio (M-H, Random, 95% CI)	0.11 [0.02, 0.56]
1.4 duration: 3 days	3	314	Risk Ratio (M-H, Random, 95% CI)	0.29 [0.11, 0.80]
1.5 duration: 2-3 days	2	189	Risk Ratio (M-H, Random, 95% CI)	0.10 [0.01, 0.81]
1.6 duration: from the second day of treatment to one week after stopping treatment	1	150	Risk Ratio (M-H, Random, 95% CI)	0.02 [0.00, 0.34]
1.7 duration: one course of treatment	1	3000	Risk Ratio (M-H, Random, 95% CI)	0.00 [0.00, 0.06]
2 Incidence of third degree phlebitis (excluding qRCTs)	10	1119	Risk Ratio (M-H, Fixed, 95% CI)	0.11 [0.05, 0.26]
2.1 duration: 7 days	1	80	Risk Ratio (M-H, Fixed, 95% CI)	0.5 [0.05, 5.30]
2.2 duration: 5 days	3	322	Risk Ratio (M-H, Fixed, 95% CI)	0.33 [0.01, 7.81]
2.3 duration: 1-7 days	1	150	Risk Ratio (M-H, Fixed, 95% CI)	0.08 [0.00, 1.34]
2.4 duration: 3 days	2	228	Risk Ratio (M-H, Fixed, 95% CI)	0.30 [0.08, 1.16]
2.5 duration: 2-3 days	2	189	Risk Ratio (M-H, Fixed, 95% CI)	0.09 [0.01, 0.69]
2.6 duration: from the second day of treatment to one week after stopping treatment	1	150	Risk Ratio (M-H, Fixed, 95% CI)	0.02 [0.00, 0.34]
3 Incidence of second degree phlebitis (excluding qRCTs)	10	1119	Risk Ratio (M-H, Fixed, 95% CI)	0.16 [0.11, 0.24]
3.1 duration: 7 days	1	80	Risk Ratio (M-H, Fixed, 95% CI)	0.22 [0.05, 0.96]
3.2 duration: 5 days	3	322	Risk Ratio (M-H, Fixed, 95% CI)	0.19 [0.06, 0.63]
3.3 duration: 1-7 days	1	150	Risk Ratio (M-H, Fixed, 95% CI)	0.12 [0.03, 0.49]
3.4 duration: 3 days	2	228	Risk Ratio (M-H, Fixed, 95% CI)	0.34 [0.16, 0.72]
3.5 duration: 2-3 days	2	189	Risk Ratio (M-H, Fixed, 95% CI)	0.04 [0.01, 0.18]
3.6 duration: from the second day of treatment to one week after stopping treatment	1	150	Risk Ratio (M-H, Fixed, 95% CI)	0.18 [0.10, 0.33]
4 Total incidence of phlebitis (excluding qRCTs)	11		Risk Ratio (IV, Random, 95% CI)	Totals not selected

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
4.1 duration: 7 days	1		Risk Ratio (IV, Random, 95% CI)	0.0 [0.0, 0.0]
4.2 duration: 5 days	4		Risk Ratio (IV, Random, 95% CI)	0.0 [0.0, 0.0]
4.3 duration: 1-7 days	1		Risk Ratio (IV, Random, 95% CI)	0.0 [0.0, 0.0]
4.4 duration: 3 days	2		Risk Ratio (IV, Random, 95% CI)	0.0 [0.0, 0.0]
4.5 duration: 2-3 days	2		Risk Ratio (IV, Random, 95% CI)	0.0 [0.0, 0.0]
4.6 duration: from the second day of treatment to one week after stopping treatment	1		Risk Ratio (IV, Random, 95% CI)	0.0 [0.0, 0.0]

Analysis 14.1. Comparison 14 Aloe vera versus no treatment for prevention of phlebitis (sensitivity analysis), Outcome 1 Incidence of third degree phlebitis (random-effects model).

Analysis 14.2. Comparison 14 Aloe vera versus no treatment for prevention of phlebitis (sensitivity analysis), Outcome 2 Incidence of third degree phlebitis (excluding qRCTs).

Analysis 14.3. Comparison 14 *Aloe vera* versus no treatment for prevention of phlebitis (sensitivity analysis), Outcome 3 Incidence of second degree phlebitis (excluding qRCTs).

Analysis 14.4. Comparison 14 Aloe vera versus no treatment for prevention of phlebitis (sensitivity analysis), Outcome 4 Total incidence of phlebitis (excluding qRCTs).

APPENDICES

Appendix 1. CENTRAL search strategy

#1MeSH descriptor: [Aloe] explode all trees 51
 #2aloe*:ti,ab,kw 131
 #3#1 or #2 in Trials 117

Appendix 2. MEDLINE search strategy

Database: Ovid MEDLINE(R) <1946 to January Week 5 2014>

Search Strategy:

1 Aloe/ (873)

Aloe vera for prevention and treatment of infusion phlebitis (Review)

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2 aloe.ti,ab. (1235)

3 1 or 2 (1377)

4 Phlebitis/ (3177)

5 Infusions, Intravenous/ (46945)

6 phlebit\$.ti,ab. (3073)

7 (infus\$ or intravenous or catheter or cannul\$).ti,ab. (479891)

8 or/4-7 (495023)

9 3 and 8 (24)

Appendix 3. EMBASE search strategy

Database: Embase <1980 to 2014 Week 06>

Search Strategy:

1 exp Aloe vera extract/ (1048)

2 aloe.ti,ab. (2179)

3 1 or 2 (2718)

4 exp phlebitis/ (24578)

5 phlebit\$.ti,ab. (3751)

6 (infus\$ or intravenous or catheter or cannul\$).ti,ab. (621691)

7 intravenous drug administration/ (314008)

8 or/4-7 (853151)

9 3 and 8 (52)

Appendix 4. AMED search strategy

Database: AMED (Allied and Complementary Medicine) <1985 to February 2014>

Search Strategy:

1 exp Aloe/ (90)

2 aloe.ti,ab. (168)

3 1 or 2 (172)

4 Phlebit\$.ti,ab. (4)

5 injections/ (432)

6 (infus\$ or intravenous or catheter or cannul\$).ti,ab. (1379)

7 4 or 5 or 6 (1790)

8 3 and 7 (1)

Appendix 5. CBM search strategy

(from 1980 to 28 February 2014)

- 1# 主题词 芦荟 1666
2# 主题词 静脉炎 10779
3# 缺省 临床试验 217892
4# 缺省 临床疗效 257752
5# 缺省 临床观察 217678
6# 缺省 疗效观察 265887
7# 缺省 预防 548917
8# 缺省 预防效果 2623
9# 缺省 随机 632259
10# 缺省 对照 989828
11# 缺省 3# OR 4# OR 5# OR 6# OR 7# OR 8# 1261645
12# 缺省 1# AND 2# AND 9# AND 10# AND 11# 49

The English translation

- 1# subject Aloe vera 1666
2# subject phlebitis 10779
3# default clinical trial 217892
4# default clinical effect 257752
5# default clinical observation 217678
6# default effect observation 265887
7# default prophylaxis 548917
8# default prophylaxis effect 2623
9# default random 632259
10# default control 989828
11# default 3# OR 4# OR 5# OR 6# OR 7# OR 8# 1261645
12# default 1# AND 2# AND 9# AND 10# AND 11# 49

Appendix 6. Chinese VIP Information search strategy

(from 1989 to 28 February 2014)

- #1关键词：芦荟 n=3999
#2任意字段：静脉炎 n=12123
#3任意字段：随机 n=819209
#4任意字段：临床观察 n=218885
#5任意字段：疗效 n=1202848
#6任意字段：临床试验 n=27396
#7任意字段：预防 n=890314
#8任意字段：or #4-7 n=2155723

#9任意字段：#1 AND #2 AND #3 AND #8 n=52

The English translation

#1 key word: aloe n=3999

#2 all fields: phlebitis n=12123

#3 all fields: random n=819209

#4 all fields: clinical observation n=218885

#5 all fields: therapeutic effect n=1202848

6# all fields: clinical trial n=27396

7# all fields: prophylaxis n=890314

8# all fields: or #4-7 n=2155723

9# all fields: #1 AND #2 AND #3 AND #8 n=52

Appendix 7. Traditional Chinese Medical Database System search strategy

from 1984 to 28 February 2014

芦荟 AND 静脉炎 AND (临床试验 OR 疗效 OR 临床观察 OR 预防 OR 预防效果) AND 随机 AND 对照

n=16

The English translation

Aloe AND phlebitis AND (clinical trial OR therapeutic effect OR clinical observation OR prophylaxis OR prophylaxis effect) AND random AND control

n=16

Appendix 8. WangFang database search strategy

(from 1987 to February 2014)

(临床试验 + 疗效 + 临床观察 + 预防) * 芦荟 * 静脉炎 * 随机 n=63

The English translation

(clinical trial +therapeutic effect+clinical observation+prophylaxis) *aloe*phlebitis*random

n=63

Appendix 9. CMCC database search strategy

(from 1994 to 28 February 2014)

芦荟/fld=关键词 AND 静脉炎/fld=摘要 AND (临床试验/fld=摘要 OR 疗效/fld=摘要 OR 临床观察/fld=摘要 OR 预防/fld=摘要) AND (随机/fld=摘要) n=36

The English translation

Aloe/fld=key word AND phlebitis/fld=abstract AND (clinical trial/fld=abstract OR therapeutic effect/fld=abstract OR clinical observation/fld=abstract OR prophylaxis/fld=abstract) AND (random/fld=abstract)

n=36

Appendix 10. ChinaMedical Academic Conference search strategy

(from 1994 to February 2014)

((全文=临床试验) OR (全文=疗效) OR (全文=临床观察) OR (全文=预防)) AND (关键词=芦荟) AND (全文=静脉炎) AND (摘要=随机) n=5

The English translation

((full text=clinical trial) OR (full text=therapeutic effect) OR (full text=clinical observation) OR (full text=prophylaxis)) AND (key word=aloe) AND (full text=phlebitis) AND (abstract=random)

n=5

Appendix 11. Chinese Academic Conference Papers Database and Chinese Dissertation Database search strategy (from 1994 to 28 February 2014)

((全文=临床试验) OR (全文=疗效) OR (全文=临床观察) OR (全文=预防)) AND (关键词=芦荟) AND (全文=静脉炎) AND (摘要=随机)
n=0

The English translation

((full text=clinical trial) OR (full text=therapeutic effect) OR (full text=clinical observation) OR (full text=prophylaxis) AND (abstract=random)

n=0

Appendix 12. ChinaNational Knowledge Infrastructure (CNKI) search strategy (from 1994 to 28 February 2014)

((全文=临床试验) OR (全文=疗效) OR (全文=临床观察) OR (全文=预防)) AND (关键词=芦荟) AND (全文=静脉炎) AND (摘要=随机)
n=79

The English translation

((full text=clinical trial) OR (full text=therapeutic effect) OR (full text=clinical observation) OR (full text=prophylaxis)) AND (key word=aloe) AND (full text=phlebitis) AND (abstract=random)

n=79

WHAT'S NEW

Date	Event	Description
31 March 2017	Amended	Minor copyediting oversight amended in the 'Implications for re-search' section

CONTRIBUTIONS OF AUTHORS

Guo Hua Zheng: planning and writing the protocol; designing the search strategies; undertaking searches; screening search results; analysis of data; interpretation of data; providing a clinical perspective; writing the review.

Liu Yang: appraising quality of papers; extracting data from papers; analysis of data; providing a clinical perspective; writing the review.

Jian Feng Chu: undertaking searches; screening search results; appraising quality of papers; entering data into RevMan; analysis of data; writing the protocol background; appraising quality of papers.

Hai Ying Chen: undertaking searches; screening search results; extracting data from papers; data collection for the review; providing general advice on the review.

Li Juan Mei: undertaking searches; screening search results; extracting data from papers; data collection for the review; providing general advice on the review.

DECLARATIONS OF INTEREST

Guo Hua Zheng: none known

Liu Yang: none known

Hai Ying Chen: none known

Jian Feng Chu: none known

Lijuan Mei: none known

SOURCES OF SUPPORT

Internal sources

- No sources of support supplied

External sources

- Chief Scientist Office, Scottish Government Health Directorates, The Scottish Government, UK.

The PVD Group editorial base is supported by the Chief Scientist Office.

DIFFERENCES BETWEEN PROTOCOL AND REVIEW

We have removed the grade 1 to 3 criteria for diagnosis and classification of phlebitis listed in the protocol. This is because the criteria for diagnosis and classification of phlebitis in each of the included studies varied slightly. Therefore we have listed them in the 'Characteristics of studies' table of each included study.

We have added a new exclusion item in the review. We have excluded the trials without definite duration of treatment. We believe that the treatment duration of *Aloe vera* for phlebitis has a very strong association with the effect of therapy or prophylaxis. The trials without definite duration of treatment would cause obvious clinical heterogeneity and lower the quality of the evidence if they were included.

We changed the planned subgroup analyses 'Types of intervention (such as *Aloe vera* and *Aloe vera* plus routine treatment)', 'The different uses of interventions (such as prevention and treatment)' and 'Types of control (such as 75% alcohol, 50% to 75% magnesium sulphate and no treatment)' in the protocol to the corresponding comparisons. We have added a new item for subgroup analysis in the review: duration of treatment (such as *Aloe vera* used for three, five or seven days, etc) because we believe it was an important factor in the effect of treatment.

We have added the WangFang database (Chinese database) to search for published studies.

We did not calculate the risk difference (RD) or include the number needed to treat (NNT) in the analyses because these were not feasible with the data available. We did not perform the evaluation of adverse events because of the unavailable data in the included studies. If adverse events data are available in future updates we will calculate the number needed to harm (NNH).

INDEX TERMS

Medical Subject Headings (MeSH)

*Aloe; Administration, Topical; Central Venous Catheters [adverse effects]; Infusions, Intravenous [adverse effects]; Phlebitis [*drug therapy] [etiology] [*prevention & control]; Phytotherapy [*methods]; Randomized Controlled Trials as Topic

MeSH check words

Humans