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[Intervention Review]

Levomepromazine for nausea and vomiting in palliative care

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ABSTRACT

Background

This is an updated version of the original Cochrane Review published in Issue 4, 2013, on Levomepromazine for nausea and vomiting in palliative care.

Nausea and vomiting are common, distressing symptoms for patients receiving palliative care. There are several drugs which can be used to treat these symptoms, known as antiemetics. Levomepromazine is an antipsychotic drug is commonly used as an antiemetic to alleviate nausea and vomiting in palliative care settings.

Objectives

To evaluate the efficacy of, and adverse events associated with, levomepromazine for the treatment of nausea and vomiting in palliative care patients.

Search methods

For this update we searched electronic databases, including those of Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE and EMBASE, up to February 2015. We searched clinical trial registers on 7 October 2015 for ongoing trials.

Selection criteria

Randomised controlled trials of levomepromazine for the treatment of nausea or vomiting, or both, in adults receiving palliative care. We excluded studies in which symptoms were thought to be due to pregnancy or surgery.

Data collection and analysis

We assessed the potential relevance of studies based on titles and abstracts. We obtained copies of any study reports that appeared to meet the inclusion criteria for further assessment. At least two review authors read each paper to determine suitability for inclusion and discussed discrepancies in order to achieve a consensus.

Main results

In the original review, we identified 421 abstracts using the search strategy. We considered eight studies for inclusion but ultimately excluded them all from the review. We updated the search in February 2015 and identified 35 abstracts, but again none met the inclusion criteria. We identified two trials from clinical trial registers, one of which is ongoing and one of which was closed due to poor recruitment.

Authors' conclusions

As in the initial review, we identified no published randomised controlled trials examining the use of levomepromazine for the management of nausea and vomiting in adults receiving palliative care, and our conclusion (that further studies of levomepromazine and other

antiemetic agents are needed to provide better evidence for their use in this setting) remains unchanged. We did, however, identify one ongoing study that we hope will contribute to the evidence base for this intervention in future updates of this review.

PLAIN LANGUAGE SUMMARY

Levomepromazine for the treatment of nausea and vomiting in people with advanced disease

This is an update of the review published in 2013. Nausea (feeling sick) and vomiting (being sick) are common and unpleasant symptoms that are often experienced by people with advanced disease. There are several different drug therapies which are available to treat these symptoms, known as antiemetics. Levomepromazine was originally used to treat schizophrenia but is also used to control nausea and vomiting. It can be given as a tablet or as an injection.

In February 2015, we were unable to identify any randomised controlled trials investigating whether levomepromazine is an effective treatment for nausea and vomiting in patients receiving palliative care.

There is a need for randomised studies to find out which drugs are the most effective treatments for nausea and vomiting in these patients. In the updated review we identified one ongoing study which aims to assess how well levomepromazine improves nausea and vomiting in patients with cancer.

BACKGROUND

This review is an update of a previously published review in the Cochrane Database of Systematic Reviews (Issue 4, 2013) (Darvill 2013).

Description of the condition

Nausea and vomiting are common, distressing symptoms often experienced by people with advanced disease. The European Association for Palliative Care defines palliative care as "the active, total care of the patients whose disease is not responsive to curative treatment. Control of pain, of other symptoms, and of social, psychological and spiritual problems is paramount" (EAPC 2010). Nausea and vomiting are thought to affect between 40% and 70% of patients with advanced cancer (Twycross 1998) and are also common in individuals with other terminal conditions (Edmonds 2001; Klinkenberg 2004). There are many causes of nausea and vomiting in patients receiving palliative care, including the underlying illness itself (for example cancer); biochemical disturbances (for example kidney failure or electrolyte disturbances); and other drugs given to the patient to control symptoms (for example morphine for the relief of pain).

Description of the intervention

Levomepromazine is a neuroleptic agent (an antipsychotic) which is commonly used to relieve nausea and vomiting in palliative care settings. Drugs used to treat nausea and vomiting are known as antiemetics. Levomepromazine is often used if first-line antiemetics do not provide adequate symptom control, but may be used first-line. In different medical settings, levomepromazine has a role as an antipsychotic in the treatment of individuals with schizophrenia.

How the intervention might work

Levomepromazine is a phenothiazine which has antagonist actions at multiple neurotransmitter receptor sites, including dopaminergic, cholinergic, serotonin and histamine receptors that are thought to mediate nausea and vomiting (Twycross 2014). Levomepromazine can be given orally or subcutaneously and can be used alone or in combination with other antiemetics. While it is often given as a continuous subcutaneous infusion, the long half-life of the drug (15 to 30 hours (Dahl 1977)) also enables levomepromazine to be administered once daily, which is potentially beneficial to the patient as the effects of the drug should last throughout the day. A typical starting dose would be 6 to 12.5 mg orally or subcutaneously in the evening. This can be increased up to 25 to 50 mg per 24 hours if necessary (Twycross 2014).

Why it is important to do this review

Careful assessment of each patient allows clinicians to choose an appropriate antiemetic based on what is thought to be the underlying cause of the symptoms (Bentley 2001). Although this is a widespread approach there is little evidence from randomised controlled trials (RCTs) for many of the drugs (for example cyclizine, haloperidol or levomepromazine) used to treat nausea and vomiting in this patient group (Glare 2004).

All patients with terminal illness should have access to palliative care, independent of their diagnosis, and we wanted to reflect this in our review. Defining this population has been identified as

a problem in previous reviews. We considered any adult patient in any setting who was receiving palliative care, as used in some previous reviews (Hirst 2001; Perkins 2009; Storrar 2014).

OBJECTIVES

To evaluate the efficacy of, and adverse events associated with, levomepromazine for the treatment of nausea and vomiting in palliative care patients.

METHODS

Criteria for considering studies for this review

Types of studies

Randomised controlled trials (RCTs) of levomepromazine for the treatment of nausea or vomiting, or both, in any setting.

Types of participants

Inclusion criteria

1. Adults (aged 18 years and over)
2. Receiving palliative care
3. Suffering from nausea or vomiting, or both

Exclusion criteria

1. Nausea or vomiting thought to be secondary to pregnancy or surgery
2. Studies of levomepromazine for the control of nausea or vomiting associated with chemotherapy were excluded unless all the participants (or a specified subgroup, analysed separately) were receiving palliative care

Types of interventions

Studies in which levomepromazine was used as an antiemetic (alone or in addition to other agents) at any dose, administered via any route and over any duration of follow up.

Acceptable comparators were placebo, other drugs or non-pharmacological interventions.

Types of outcome measures

Primary outcomes

1. Patient-reported nausea severity
2. Patient-reported vomiting severity
3. Patient-reported relief of symptoms of nausea and vomiting

Secondary outcomes

1. Quality-of-life assessed using any validated measure
2. Acceptability of treatment
3. Need for rescue antiemetic medication
4. Adverse events
5. Withdrawal from study because of side effects

Ideally, the studies would have used valid outcome measures but we did not exclude studies on the basis of their outcome measures.

Search methods for identification of studies

Electronic searches

We searched the following databases using relevant search terms and synonyms:

- MEDLINE - OVID (1950 to 10/2/15)
- Cochrane Central Register of Controlled Trials (CENTRAL), *The Cochrane Library* (Issue 1 of 12, 2015)
- EMBASE - OVID (1980 to 10/2/15).

We present the search strategies in [Appendix 1](#), [Appendix 2](#) and [Appendix 3](#). We imposed no any language restrictions on the searches.

Searching other resources

We searched the following electronic clinical trial registers on 7 October 2015:

- World Health Organization International Clinical Trials Registry Platform (<http://apps.who.int/trialsearch/>)
- ISRCTN registry (<http://www.isrctn.com/>)
- EU Clinical Trials Register (<https://www.clinicaltrialsregister.eu/>)
- ClinicalTrials.gov (<https://clinicaltrials.gov/>).

We handsearched the reference lists of included studies, relevant chapters and review articles in order to complement electronic searches.

Data collection and analysis

Selection of studies

We judged the potential relevance of studies based on their titles and abstracts, and obtained copies of studies that appeared to meet the inclusion criteria. At least two review authors read these papers to assess their suitability for inclusion and discussed discrepancies in order to achieve a consensus, so avoiding bias in our article selection.

Data extraction and management

We planned to extract data using a data extraction form and to enter data into Review Manager ([RevMan 2014](#)) independently to improve data input accuracy. If possible, we would have assessed studies for treatment effect (see '[Types of outcome measures](#)' above) specifying the number needed to treat for an additional beneficial outcome (NNTB) and the number needed to treat for an additional harmful outcome (NNTH).

Assessment of risk of bias in included studies

We planned to use the Cochrane 'Risk of bias' tool to assess sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, selective outcome reporting and other sources of bias ([Higgins 2011](#)).

We also planned to assess the methodological quality of studies using the Oxford Quality scale ([Jadad 1996](#)).

Measures of treatment effect

We planned to evaluate the treatment effect as measured in the primary studies.

Unit of analysis issues

We intended to evaluate data from RCTs.

Dealing with missing data

In the event of missing data, we would have made attempts to contact authors of the papers in question to acquire the data.

Assessment of heterogeneity

We planned to assess clinical heterogeneity by examining the types of participants, interventions and outcomes in each study.

If the heterogeneity of the studies allowed we would have performed a meta-analysis. If the I^2 statistic was less than 50% we would have used a fixed-effect model. If the I^2 statistic was more than 50% we would have used a random-effects model.

Assessment of reporting biases

We planned to assess publication bias using the method described by [Moore 2008](#) to calculate the amount of unpublished data which would be required to increase the NNTB beyond a clinically useful level.

Data synthesis

For dichotomous outcomes, we would have expressed the estimates of effect of an intervention as risk ratios (RRs) together with 95% confidence intervals (CIs). For continuous outcomes, we would have used mean differences (MDs) and standard deviations (SDs) to summarise the data for each group.

Subgroup analysis and investigation of heterogeneity

If there had been sufficient data we would have performed analyses for the following subgroups.

Population subgroups

1. Diagnoses of participants
2. Likely mechanism of nausea and vomiting (to include subgroups of nausea and vomiting related to opioid use, other drug use, bowel obstruction and metabolic disturbances)
3. Prognoses of participants
4. Age of participants
5. Gender of participants

Intervention subgroups

1. Route of administration
2. Drug dose (≤ 10 mg/24 hours; > 10 mg/24 hours)

Outcome subgroups

1. Nausea
2. Vomiting

Sensitivity analysis

We planned to use sensitivity analyses to examine the effects of randomisation, allocation concealment, blind outcome assessment (if appropriate) and the quality of the follow-up.

RESULTS

Description of studies

From the original searches run on 19 September 2011 and in March 2013 we identified 421 abstracts. Of these, we obtained copies of eight that potentially met the inclusion criteria, including two in German and one in Spanish. Translators enabled us to assess whether the three foreign language papers identified by the search met the inclusion criteria for the review.

At least two review authors independently assessed the studies in accordance with the inclusion criteria. There were no differences in opinion between the review authors with regard to the assessment of studies: none of the studies met the criteria for inclusion.

We identified 35 abstracts from the updated search carried out in February 2015, none of which met the inclusion criteria.

We identified two relevant trials from a search of clinical trial registers in October 2015, one of which is ongoing ([ACTRN12615000177550](#)), and one of which was closed due to poor recruitment ([ACTRN12610000482066](#)).

[Figure 1](#) illustrates the study selection process for this update.

Figure 1. Study flow diagram.

Results of the search

None of the studies we identified met the criteria for inclusion.

Included studies

We included no studies.

Excluded studies

We excluded eight studies from the original study and four from the update (see the '[Characteristics of excluded studies](#)' table). We were also able to identify several studies assessing the use of levomepromazine in the prophylaxis of chemotherapy-induced vomiting ([Ell 1983](#); [Higi 1980](#); [McCabe 2003](#)). Although these studies provide useful information the results are not directly applicable to a palliative care setting.

Uncontrolled studies

Although not suitable for inclusion in this review, we did identify two uncontrolled published studies which may be of interest to readers. An uncontrolled observational study with 70 people suffering from advanced cancer demonstrated that a subcutaneous bolus of levomepromazine decreased the intensity of nausea and vomiting. Their vomiting had been refractory to first-line agents. After administration of the drug 92% of the participants stopped vomiting ([Eisenclas 2005](#)). A similar observational study with 65 participants demonstrated the efficacy of low-dose levomepromazine for treatment of nausea and vomiting in people with advanced malignant disease ([Kennett 2004](#)). Unfortunately this was another uncontrolled trial and the attrition rate in this study was very high. The results should therefore be interpreted with caution.

[Twycross 1997](#) cites unpublished data from 23 patients which suggest that control of vomiting was achieved in 83%. Levomepromazine was stopped for three patients (13%) because of side effects (urticaria, akathisia, sedation).

Ongoing study

We identified one ongoing study: "A study for participants with cancer who experience ongoing nausea, not related to their treatment, despite taking standard and usual medications, that studies the effectiveness of oral methotrimeprazine [levomepromazine] versus oral haloperidol" ([ACTRN12615000177550](#)).

Risk of bias in included studies

As we included no studies in the review, this section is not applicable.

Allocation

As we included no studies in the review, this section is not applicable.

Blinding

As we included no studies in the review, this section is not applicable.

Incomplete outcome data

As we included no studies in the review, this section is not applicable.

Selective reporting

As we included no studies in the review, this section is not applicable.

Other potential sources of bias

As we included no studies in the review, this section is not applicable.

Effects of interventions

We were unable to draw definitive conclusions regarding the use of levomepromazine for the treatment of nausea and vomiting in adults receiving palliative care because we identified no RCTs for inclusion in this review.

DISCUSSION

Levomepromazine was originally licensed for the treatment of schizophrenia. In addition to its use as an antipsychotic, it has also been used in anaesthesia, as a sedative in terminal agitation, as an analgesic and now as a broad-spectrum antiemetic ([Skinner 1999](#)). Its actions at many of the receptors involved in vomiting, its stability with other drugs in a syringe driver, and its long duration of action that allows once-daily dosing make it a popular choice in palliative care ([Skinner 1999](#)).

Regarding tolerability, side effects other than mild sedation are uncommon with levomepromazine at the doses used in palliative care. Some patients may experience irritation at the site of the subcutaneous injection but this is fairly infrequent ([Eisenclas 2005](#)). The higher doses used to achieve antipsychotic activity with levomepromazine are more likely than lower doses to cause significant sedation or postural hypotension ([Skinner 1999](#)).

There has been much written previously about the lack of evidence from randomised controlled trials (RCTs) in palliative care ([Dietz 2013](#); [Wee 2008](#)), particularly because of the difficulty of conducting such studies in this setting ([Grande 2000](#)). Evidence for the use of many of the commonly used antiemetic drugs in palliative care is anecdotal or is derived from non-randomised studies ([Davis 2010](#); [Glare 2004](#); [Keeley 2009](#); [Perkins 2009](#)). Unfortunately this remains the case with regard to the use of levomepromazine as we were unable to find any published or unpublished evidence from RCTs on the use of levomepromazine in the palliative care setting.

We identified two published uncontrolled studies which assessed the use of levomepromazine for the treatment of nausea and vomiting in patients receiving palliative care ([Eisenclas 2005](#); [Kennett 2004](#)) and reference to unpublished data given in [Twycross 1997](#). Although these studies have limitations, and the evidence they provide is less robust than that of a RCT, they indicate that levomepromazine may be an effective antiemetic. The data obtained provide some support for the use of levomepromazine in this setting. Levomepromazine remains widely used by palliative care physicians despite the lack of data from RCTs.

Other phenothiazines such as chlorpromazine and prochlorperazine also suffer from a similar lack of evidence from RCTs but are widely used for nausea and vomiting as there is a consensus that they are likely to be beneficial ([Keeley 2009](#)).

Summary of main results

We identified no RCTs for inclusion in this review.

Overall completeness and applicability of evidence

We identified several studies examining the use of levomepromazine although none met the criteria for inclusion in this review. We provide details of the excluded studies in the 'Characteristics of excluded studies' table. As discussed above, some of these studies provide support for the use of levomepromazine as an antiemetic in patients with advanced cancer but they are not RCTs (Eisenclas 2005; Kennett 2004). We were also able to identify several studies assessing the use of levomepromazine in the prophylaxis of chemotherapy-induced vomiting (Ell 1983; Higi 1980; McCabe 2003). Although these studies provide useful information the results are not directly applicable to a palliative care setting.

Quality of the evidence

No RCTs were identified for inclusion in this review. The non-randomised studies mentioned above provide useful information, although the attrition rate in Kennett 2004 was high and there were some missing baseline data in Eisenclas 2005, so the results need to be interpreted with some caution.

Potential biases in the review process

All four review authors have prescribed levomepromazine for nausea and vomiting in patients under their care. None of the authors has received sponsorship from companies distributing levomepromazine.

Agreements and disagreements with other studies or reviews

Glare 2004 previously reported that there is little or no evidence from RCTs to support the use of most of the commonly used and seemingly effective antiemetics. Whereas the results of uncontrolled studies indicate a high response rate to standard regimens (75% to 93% for both nausea and vomiting), RCTs show much lower response rates to these agents (23% to 36% for nausea, 18% to 52% for vomiting) (Glare 2004). This large discrepancy between reported outcomes in uncontrolled studies and RCTs is significant and further highlights the need for well-designed randomised studies to be performed to provide evidence for the use of levomepromazine.

Keeley 2009 concluded that there is a consensus that phenothiazines (including levomepromazine) are effective in controlling nausea and vomiting in people with cancer, despite a lack of RCT evidence, citing the study by Eisenclas (Eisenclas 2005).

Davis and Hallerberg systematically reviewed the use of antiemetics for patients with cancer and nausea or vomiting not due to chemotherapy, radiotherapy or surgery (Davis 2010). They concluded that there is level B1 evidence (that is evidence from single-drug prospective studies or studies in which single-drug activity could be determined) that levomepromazine is an effective antiemetic based on the studies by Eisenclas 2005 and Kennett 2004. They also cited level C evidence (that is evidence from cohort studies, retrospective studies, case series and single-case

reports) for the effectiveness of levomepromazine (Amesbury 2004; Skinner 1999). Davis and Hallerberg also recommend the carrying out of prospective and randomised studies of the effectiveness of antiemetics to support their clinical use (Davis 2010).

Benze 2012 reviewed the treatment of nausea and vomiting with prokinetics and neuroleptics in palliative care patients (excluding those undergoing chemotherapy or radiotherapy). They concluded that there is poor quality (level C) evidence for the effectiveness of levomepromazine (Amesbury 2004; Baines 1985; Eisenclas 2005; Kennett 2004; Twycross 1997) and that RCTs are lacking.

Dietz 2013 looked at the evidence for the use of levomepromazine for symptom control in the palliative care setting. They concluded that there is low-grade evidence for levomepromazine as an antiemetic, citing the studies by Eisenclas 2005, Kennett 2004, Amesbury 2004 and Stephenson 2006, as well as reviews by Glare 2004, Davis 2010 and Douglas 2009. They also included studies of levomepromazine for chemotherapy induced nausea.

Gordon 2014 reviewed the aetiologies of nausea and vomiting in advanced cancer. They concluded that phenothiazines such as levomepromazine are effective antiemetics that have been used in malignancy, citing Skinner 1999.

AUTHORS' CONCLUSIONS

Implications for practice

There is currently insufficient evidence from randomised controlled trials to comment definitively on the effectiveness of levomepromazine for the management of nausea and vomiting in adults receiving palliative care, although uncontrolled studies suggest that it is effective.

Implications for research

There is a need for further research into the use of levomepromazine and other antiemetic agents in palliative care settings in order to identify which drugs are most effective with the fewest side effects. One ongoing study aims to improve the evidence base for this intervention: ACTRN12615000177550.

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CHARACTERISTICS OF STUDIES

Characteristics of excluded studies [ordered by study ID]

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Study	Reason for exclusion
Amesbury 2004	A case report only, not a randomised controlled trial.
Baines 1985	Open prospective case series, not a randomised controlled trial. Examined multiple medications & unclear which resulted in effect.
Benze 2012	Review article. Not a randomised controlled trial.
Dietz 2013	Review article. Not a randomised controlled trial.
Eisenchlas 2005	Not a randomised controlled trial. All participants given levomepromazine at different doses, no control group, no randomisation.
Ell 1983	Prophylaxis of chemotherapy-induced vomiting. Population not restricted to adults receiving palliative care.
Gordon 2014	Review article. Not a randomised controlled trial.
Higi 1980	Prophylaxis of chemotherapy-induced vomiting. Population not restricted to adults receiving palliative care.
Kennett 2004	Not a randomised controlled trial. All participants given levomepromazine at different doses, no control group, no randomisation.
McCabe 2003	Treatment of chemotherapy-induced vomiting. Population not restricted to adults receiving palliative care. Not a randomised controlled trial.
Sgouros 2003	Prophylaxis of chemotherapy-induced vomiting. Population not restricted to adults receiving palliative care. Abstract of poster presentation only.
Twycross 1997	Narrative review. Not a randomised controlled trial. Unpublished observational data included.

Characteristics of ongoing studies [ordered by study ID]

ACTRN12615000177550

Trial name or title	<p>A study in participants with cancer who experience ongoing nausea, not related to their treatment, despite taking standard and usual medications, that studies the effectiveness of oral methotrimeprazine versus oral haloperidol</p> <p>A randomised, controlled, double-blind study of oral methotrimeprazine versus oral haloperidol in patients with cancer and nausea not related to anticancer therapy (Nausea study 3), to compare the effectiveness of oral methotrimeprazine versus oral haloperidol in improving the management of nausea in participants with cancer and nausea not related to anticancer therapy</p>
Methods	Randomised, controlled, double blind study
Participants	Adults with cancer and nausea not related to anticancer therapy
Interventions	Either blinded encapsulated oral methotrimeprazine (levomepromazine) 6.25 mg or oral haloperidol 1.5 mg given once daily for three intervention days. If no response at 24 hours or 48 hours, dose can be increased to twice daily (12.5 mg methotrimeprazine or 3 mg haloperidol). Rescue medication of metoclopramide or domperidone is available

ACTRN12615000177550 (Continued)

Outcomes	<p>Primary outcome: response to treatment at 72 hours from time of first study drug administration, defined as more than a two-point improvement from baseline in average nausea over the preceding 24 hours on an 11-point numeric rating scale (0 no nausea to 10 worst possible nausea)</p> <p>Secondary outcomes: complete response (response as above, with a score less than 3); response assessed at 24 hours and 48 hours; best nausea score over the preceding 24 hours; number of rescue antiemetic doses; toxicity; episodes of vomiting; complete response at 24 hours and 48 hours</p>
Starting date	<p>Registered 23 February 2015</p> <p>Anticipated first enrolment 02 March 2015</p> <p>Anticipated last enrolment 05 March 2018</p>
Contact information	<p>Professor Janet R Hardy</p> <p>Director of Palliative Care, Mater Health Services, Raymond Terrace, South Brisbane QLD 4101</p> <p>Australia</p> <p>janet.hardy@mater.org.au</p>
Notes	ACTRN12615000177550

APPENDICES

Appendix 1. MEDLINE search strategy

1. exp Nausea/
2. exp Vomiting/
3. nause*.mp.
4. vomit*.mp.
5. emesis.mp.
6. (antiemetic* or anti-emetic*).mp.
7. 1 or 2 or 3 or 4 or 5 or 6
8. Methotrimeprazine/
9. levomepromazine.mp.
- 10.immobilon.mp.
- 11.levomeprazine.mp.
- 12.levoprome.mp.
- 13.methotrimeprazine.mp.
- 14.nozinan.mp.
- 15.tisercin.mp.
- 16.tizercine.mp.
- 17.tizertsin.mp.
- 18.8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17
- 19.7 and 18

Appendix 2. EMBASE search strategy

1. exp "nausea and vomiting"/
2. nause*.mp.
3. vomit*.mp.
4. emesis.mp.

5. (antiemetic* or anti-emetic*).mp.
6. 1 or 2 or 3 or 4 or 5
7. levomepromazine/
8. levomepromazine.mp.
9. methotrimeprazine.mp.
- 10.immobilon.mp
- 11.levomeprazine.mp.
- 12.levoprome.mp
- 13.nozinan.mp.
- 14.tisercin.mp.
- 15.tizercine.mp
- 16.tizertsin.mp.
- 17.7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16
- 18.6 and 17

Appendix 3. CENTRAL search strategy

1. MeSH descriptor **Nausea** explode all trees
2. MeSH descriptor **Vomiting** explode all trees
3. nause*
4. vomit*
5. emesis
6. antiemetic* or anti-emetic*
7. (1 or 2 or 3 or 4 or 5 or 6)
8. MeSH descriptor **Methotrimeprazine**, this term only
9. levomepromazine
- 10.immonilon
- 11.levomeprazine
- 12.levoprome
- 13.methotrimeprazine
- 14.nozinan
- 15.tisercin
- 16.tizercine
- 17.tizertsin
- 18.(8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17)
- 19.(7 and 18)

WHAT'S NEW

Date	Event	Description
5 May 2017	Review declared as stable	See Published notes .

HISTORY

Protocol first published: Issue 11, 2011
Review first published: Issue 4, 2013

Date	Event	Description
3 November 2015	Amended	Minor typo corrected.

Date	Event	Description
24 March 2015	New citation required but conclusions have not changed	We identified 35 new studies, none of which met the inclusion criteria. Two registered studies have been identified which aim to contribute to the evidence base for this intervention. The updated search has not altered the conclusions of the initial review.
6 March 2015	New search has been performed	Search updated February 2015. Change of authorship.
26 April 2013	Amended	Minor amendments to wording.

CONTRIBUTIONS OF AUTHORS

ED wrote the protocol and initial review with comments from SD and PP. For the original review, ED, SD and PP independently reviewed all titles and abstracts yielded by the search strategy and discussed any discrepancies to achieve a consensus. LC and SD independently reviewed all titles for the updated searches and wrote the updated review. SD will be responsible for further updates.

DECLARATIONS OF INTEREST

LC has no conflict of interest to declare. SD has no conflict of interest to declare. ED has no conflict of interest to declare.

SOURCES OF SUPPORT

Internal sources

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External sources

- No sources of support supplied

NOTES

A restricted search in May 2017 did not identify any potentially relevant studies likely to change the conclusions. Therefore, this review has now been stabilised following discussion with the authors and editors. We are aware of one relevant ongoing study, which we will assess when available. We will update the review if new evidence likely to change the conclusions is published, or if standards change substantially which necessitate major revisions.

INDEX TERMS

Medical Subject Headings (MeSH)

*Palliative Care; Antiemetics [adverse effects] [*therapeutic use]; Methotrimeprazine [adverse effects] [*therapeutic use]; Nausea [*drug therapy]; Vomiting [*drug therapy]

MeSH check words

Adult; Female; Humans; Pregnancy