Cochrane
Library

Cochrane Database of Systematic Reviews

Fasting for haemostasis in children with gastrointestinal bleeding (Review)

Luo SH, Guo Q, Liu GJ, Wan C

Luo S-H, Guo Q, Liu GJ, Wan C.

Fasting for haemostasis in children with gastrointestinal bleeding.

Cochrane Database of Systematic Reviews 2016, Issue 5. Art. No.: CD010714.

DOI: [10.1002/14651858.CD010714.pub2](https://doi.org/10.1002/14651858.CD010714.pub2).

www.cochranelibrary.com

Fasting for haemostasis in children with gastrointestinal bleeding (Review)

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

WILEY

TABLE OF CONTENTS

ABSTRACT	1
PLAIN LANGUAGE SUMMARY	2
SUMMARY OF FINDINGS	3
BACKGROUND	4
OBJECTIVES	5
METHODS	5
RESULTS	8
Figure 1.	9
DISCUSSION	10
AUTHORS' CONCLUSIONS	10
ACKNOWLEDGEMENTS	10
REFERENCES	11
APPENDICES	13
WHAT'S NEW	17
HISTORY	17
CONTRIBUTIONS OF AUTHORS	17
DECLARATIONS OF INTEREST	17
SOURCES OF SUPPORT	17
DIFFERENCES BETWEEN PROTOCOL AND REVIEW	17
NOTES	17
INDEX TERMS	17

[Intervention Review]

Fasting for haemostasis in children with gastrointestinal bleeding

Shuang-Hong Luo¹, Qin Guo^{2,3}, Guan J Liu⁴, Chaomin Wan¹

¹Department of Pediatrics, West China Second University Hospital, Sichuan University, Chengdu, China. ²Department of Pediatrics, West China Second University Hospital, West China Women's and Children's Hospital, Chengdu, China. ³Chinese Cochrane Centre, Chinese Evidence-Based Medicine Centre, West China Hospital, Sichuan University, Chengdu, China. ⁴Cochrane China, West China Hospital, Sichuan University, Chengdu, China

Contact: Chaomin Wan, wcm0220@sina.com.**Editorial group:** Cochrane Gut Group.**Publication status and date:** Edited (no change to conclusions), published in Issue 7, 2021.**Citation:** Luo S-H, Guo Q, Liu GJ, Wan C. Fasting for haemostasis in children with gastrointestinal bleeding. *Cochrane Database of Systematic Reviews* 2016, Issue 5. Art. No.: CD010714. DOI: [10.1002/14651858.CD010714.pub2](https://doi.org/10.1002/14651858.CD010714.pub2).

Copyright © 2016 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.

ABSTRACT

Background

Gastrointestinal bleeding refers to loss of blood from any site of the digestive tract. In paediatric clinical practice, it is usually a complaint of children attending the emergency department as a symptom of diseases such as ulcers, gastric or oesophageal varices, gastritis, Mallory-Weiss tears, anorectal fissures, allergic colitis, infectious colitis, intussusception, Henoch-Schonlein purpura, and Meckel's diverticulum; it also occurs with high incidence in critically ill children hospitalised in intensive care units and is caused by stress-induced gastropathy. No matter what the cause of gastrointestinal bleeding, fasting is believed to be necessary due to the fear that eating may affect haemostasis or aggravate bleeding.

Objectives

To assess the effects and safety of fasting for haemostasis in gastrointestinal bleeding in children.

Search methods

We searched EBM Reviews - the Cochrane Central Register of Controlled Trials (CENTRAL) (May 2016), Ovid MEDLINE(R) (1946 to 3 May 2016), EMBASE (1980 to 2016 Week 18), Chinese Biomedical Database (CBM) (1978 to 3 May 2016), China National Knowledge Infrastructure (CNKI) (1979 to 3 May 2016), VIP Database (1989 to 4 May 2016) and Wanfang Data (1990 to 4 May 2016). We used no restrictions on language or study setting and limited searches in CNKI and Wanfang Data to the medical field.

Selection criteria

Randomised controlled trials (RCTs) or quasi-RCTs in children with gastrointestinal bleeding that compared fasting with feeding.

Data collection and analysis

Two review authors independently screened the literature search results, and there were no disagreements.

Main results

We identified no RCTs or quasi-RCTs that compared the effects and safety of fasting with feeding for haemostasis in children with gastrointestinal bleeding. No study fulfilled the criteria for considering studies for our review.

Authors' conclusions

There is currently no information available from RCTs or quasi-RCTs to support or refute the use of fasting for haemostasis in children with gastrointestinal bleeding.

PLAIN LANGUAGE SUMMARY

Fasting for haemostasis in children with gastrointestinal bleeding

Review question

To determine the effects and safety of fasting for haemostasis in children with gastrointestinal bleeding.

Background

Gastrointestinal bleeding refers to loss of blood from any site of the digestive tract. If the bleeding site is near the ligament of Treitz (the muscle extending from the junction of the duodenum and jejunum to the diaphragm), it is described as upper gastrointestinal bleeding. If the bleeding site is away from the ligament of Treitz, it is described as lower gastrointestinal bleeding. People with a small amount of blood loss may have no symptoms, and have bloody vomiting or see blood in the stool with increased bleeding. Chronic mild gastrointestinal bleeding can lead to anaemia, causing fatigue or pallor; acute massive gastrointestinal bleeding can be life-threatening.

Gastrointestinal bleeding has two scenarios in children. The first is a complaint of attending the emergency department as a symptom of diseases such as ulcers, gastritis, Mallory-Weiss tears, anorectal fissures, allergic colitis, infectious colitis, intussusception, Henoch-Schonlein purpura, and Meckel's diverticulum. The second occurs in critically ill children hospitalised in intensive care units and is caused by stress-induced gastropathy. The incidence of the first scenario has not been well established, but there are substantial cases in paediatric intensive care units in the second scenario. Whatever the cause of gastrointestinal bleeding, fasting is believed to be necessary due to the fear that eating may affect haemostasis or aggravate bleeding.

Study characteristics

We searched EBM Reviews- Cochrane Central Register of Controlled Trials (CENTRAL) (May 2016), Ovid MEDLINE(R) (1946 to 3 May 2016), EMBASE (1980 to 2016 Week 18), Chinese Biomedical Database (CBM) (1978 to 3 May 2016), China National Knowledge Infrastructure (CNKI) (1979 to 3 May 2016), VIP Database (1989 to 4 May 2016) and Wanfang Data (1990 to 4 May 2016). We used no restrictions on language or study setting and limited searches in CNKI and Wanfang Data to medical field.

We did not find any randomised controlled trials or quasi-randomised controlled trials providing information about the effects and safety of fasting for haemostasis in children with gastrointestinal bleeding.

Key results

A randomised study is required to compare the effects and safety of fasting with feeding for haemostasis in children with gastrointestinal bleeding, especially for critically ill children, who are at high risk for gastrointestinal bleeding.

SUMMARY OF FINDINGS

Summary of findings 1. Fasting for haemostasis in children with gastrointestinal bleeding

Fasting for haemostasis in children with gastrointestinal bleeding

Patient or population: children with gastrointestinal bleeding

Settings: hospital

Intervention: fasting

Comparison: feeding

Outcomes	Comments
All-cause case fatality rate	No studies met the inclusion criteria for our review
Incidence of re-bleeding	
Incidence of continued bleeding	
Incidence of surgery for stopping bleeding	
Incidence of secondary infections	
Incidence of transfusion	
Adverse events	

BACKGROUND

Description of the condition

Gastrointestinal bleeding (GIB) refers to loss of blood from any site of the digestive tract, which can have many causes (Jensen 2011). GIB is divided into upper gastrointestinal bleeding (UGIB) and lower gastrointestinal bleeding (LGIB), according to the bleeding site. The former bleeding site arises proximal to the ligament of Treitz (Chawla 2007), and the latter is distal to this point (Leung 2002). The manifestations of GIB vary, ranging from no symptoms or unexplained fatigue or pallor to obvious symptoms such as seeing blood on paper after a bowel movement or mixed in stool, tarry black stools, and bloody diarrhoea and vomiting (Boyle 2008). Acute massive gastrointestinal bleeding often results in hypovolaemic shock and can be life-threatening (Cappell 2008; Marek 2011). Vomiting of bloody or brown material or tarry black stools usually indicate UGIB, and bloody diarrhoea or stool mixed or coated with blood often suggests LGIB (Boyle 2008).

GIB usually has two scenarios in paediatric clinical practice. It is one of the chief complaints of children attending the emergency department (Hébuterne 2011; McClave 2005), as a symptom of many diseases (Arora 2002; Leung 2002; Rayhorn 2001a; Rayhorn 2001b). Although the incidence of this scenario has not been well established because epidemiologic data are scarce, especially for LGIB (Fox 2000), the spectrum of diseases causing GIB is closely related to the age of children, and there is overlap among different age groups. For neonates, UGIB often occurs from vitamin K deficiency, congenital anomalies including intestinal duplication or vascular anomalies, coagulopathy, or milk protein intolerance; LGIB is usually caused by anorectal fissures, necrotising enterocolitis, malrotation with volvulus, Hirschsprung disease, or coagulopathy. The disease spectrum causing GIB in infants is similar to that of neonates. Infants can also experience UGIB due to Mallory-Weiss tear resulting from vomiting, ulcers, or gastritis after use of nonsteroidal anti-inflammatory drugs, oesophagitis of gastroesophageal reflux disease, recurrent emesis, caustic ingestion, gastric or oesophageal varices from cirrhosis or portal vein thrombosis, and ingestion of a foreign body. The most common causes of LGIB in infants are anorectal fissures, allergic colitis induced by milk or soy protein, infectious colitis, intussusception, Meckel's diverticulum, lymphonodular hyperplasia, or intestinal duplication. The causes of GIB in older children and adolescents are similar to those in adults. The most common causes of UGIB are Mallory-Weiss tears, peptic ulcers, gastritis, varices, foreign body, caustic ingestion, Henoch-Schonlein purpura, and Crohn's disease. Causes of LGIB in this age group are anorectal fissures, haemorrhoids, infectious colitis, polyp, Meckel's diverticulum, Henoch-Schonlein purpura, inflammatory bowel disease, and lymphonodular hyperplasia (Arora 2002; Leung 2002; Rayhorn 2001a; Rayhorn 2001b; Wyllie 2007). It worth noting that the causes of UGIB in children differ between high-income and low- and middle-income countries. It has been reported that peptic ulcers, oesophagitis, gastritis, or duodenitis are the most common causes of UGIB in children in the USA (Cox 1979), Japan (Kato 1991), and Israel (Zahavi 1994), but varices are the most common lesions in India (Mittal 1994; Yachha 1996). However, the spectrum of LGIB in India is similar to that of high-income countries (Yachha 1996).

The second scenario for GIB is in critically ill children usually from stress-induced gastropathy several days after their admission to hospital (Hébuterne 2011; McClave 2005). There have been

substantial cases in paediatric intensive care units (PICUs), especially in low- and middle-income countries (Chaïbou 1998; Cochran 1992; Deerojanawong 2009; Kuusela 2000; Lacroix 1992; Nithiwathanapong 2005). This can occur at any age. The incidence of GIB in PICUs has been reported as 25% in the USA (Cochran 1992), 6.4%, Lacroix 1992, to 15.3%, Chaïbou 1998, in Canada, 43.5%, Nithiwathanapong 2005, to 51.8%, Deerojanawong 2009, in Thailand, and for newborn infants 20% in Finland (Kuusela 2000). However, clinically significant bleeding was relatively rare (Chaïbou 1998; Deerojanawong 2009; Fox 2000; Lacroix 1992; Nithiwathanapong 2005), with the reported incidence being 0.4%, Lacroix 1992, to 1.6%, Chaïbou 1998, in Canada, and 3.6%, Deerojanawong 2009, to 5.3%, Nithiwathanapong 2005, in Thailand. While GIB can be severe, it rarely causes death (Wyllie 2007).

The basic pathogenesis of GIB in children is vascular injury of the gut induced by any underlying disease. In the first scenario described above, the differential diagnosis is wider, and the most likely causes of bleeding can be broadly divided into the following categories:

- Vascular anomalies (e.g. hemangiomas), collateral vessel formation (e.g. gastric or oesophageal varices from cirrhosis), and erosion of mucosa (e.g. inflammation, ulcer) bringing blood vessels close to the gastrointestinal lumen and susceptible to injury and rupture;
- Systematic vasculitis, which can involve gastrointestinal blood vessel or capillaries (e.g. Henoch-Schonlein purpura);
- Vascular congestion, thrombosis, or ischaemias (e.g. intussusception or malrotation with volvulus); coagulopathy (e.g. vitamin K deficiency or idiopathic thrombocytopenic purpura);
- Violent or frequent vomiting or retching, which can tear blood vessels or break capillaries directly (e.g. Mallory-Weiss tear or emetogenic gastropathy).

In this setting, the bleeding varies greatly by etiology, and the conditions can be very different. For example bleeding from peptic ulcers and rupture of gastric or oesophageal varices usually comes from only one site, but is an urgent problem that can quickly become life-threatening. In contrast, bleeding from milk protein intolerance usually comes from numerous sites, but causes only a small amount of blood loss. Necrotising enterocolitis or malrotation with volvulus require strict fasting, but Crohn's disease and haemorrhoid almost never affect eating. The treatment for GIB of Henoch-Schonlein purpura is very different from that of coagulopathy, although both conditions cause diffuse bleeding from small blood vessels or capillaries. UGIB is likely to be diagnosed and stopped by endoscopy more easily than LGIB in children.

In the second scenario, the pathophysiology of GIB in critically ill children is stress-induced gastropathy which involves mucosal ischaemias, mucosal integrity, gastrointestinal motility disturbance, secretion of gastric acid, and nutrition problems (Fennerty 2002). This bleeding comes from multiple diffuse erosions or very shallow ulcers which occur most commonly in the fundus of the stomach. The bleeding is usually low volume and does not need to be stopped by performing endoscopy or another haemostasis technique. Hence, a consideration of the underlying

diseases is crucial in determining the management of GIB caused by different etiology.

Description of the intervention

GIB in children requires combined treatments. Therapies directed to the underlying diseases causing GIB are key (Arora 2002; Leung 2002), but stabilising haemodynamics must be the immediate action (Arora 2002; Boyle 2008; Chawla 2007). Prompt and appropriate fluid resuscitation is essential (Boyle 2008; Colle 2011; Peters 2002). A series of measures should then be taken to arrest bleeding, including mainly endoscopic techniques, in Kay 2007, Peters 2002, and Sidhu 2007, and pharmacologic treatments, such as acid-suppressive agents (Barkun 2010; Leontiadis 2007; Sreedharan 2010), fibrinolysis inhibitors (Gluud 2012), and splanchnic vasoconstrictors (Boyle 2008; Peters 2002). Acid-suppressive agents and fibrinolysis inhibitors are used mainly to facilitate haemostasis in the gastrointestinal environment based on the evidence that haemostasis may be impaired by low pH value and pepsin (Green 1978; Low 1980; Patchett 1989). Splanchnic vasoconstrictors are safe and effective in stopping variceal bleeding by reducing portal pressure (D'Amico 2010; Villanueva 2008). At the same time, fasting will be prescribed for most children for fear that eating may affect haemostasis or aggravate bleeding (Hébuterne 2011; McClave 2005), although to our knowledge there is no clear statement about this in any guideline relevant to GIB. Almost all decisions about fasting for GIB were made based on paediatricians' education and clinical experience, and most paediatricians paid much more attention to GIB than to fasting and seldom considered the adverse effect of fasting.

How the intervention might work

Fasting is believed to be required in the treatment of GIB in children for the following reasons:

1. feeding stimulates further gastroduodenal secretion, which will interfere with the action of acid-suppressive agents and impair haemostasis by adversely affecting blood clotting over the lesions and fibrinolytic activity (Green 1978; Low 1980; Patchett 1989);
2. feeding increases blood flow to the gastrointestinal systemic circulation, and increased blood pressure (Braga 2001; Revelly 2001), which could lead to variceal re-bleeding (Hébuterne 2011);
3. feeding also initiates gastrointestinal motility to mix and empty food (Barrett 2009), which could impair stabilising of the clot.
4. feeding may interfere with endoscopy therapy.

In summary, fasting seems to be effective in eliminating the above risk factors contributing to failed haemostasis or re-bleeding, but the real effect of fasting in this context is unknown. In addition, the therapy mechanism of fasting may be different in different conditions, for example fasting may be more effective for necrotising enterocolitis than for peptic ulcer, and reducing gastric acid secretion by fasting may be effective in UGIB but not in LGIB.

Why it is important to do this review

Fasting is unpleasant and may not be safe. Firstly, parenteral nutrition following fasting, which appears to compensate for fasting, is invasive, expensive (Cangelosi 2011), and is associated with catheter-related infections (Beghetto 2005; Opilla 2008),

catheter-related thrombosis (Beck 1998; Kakzanov 2008), and other risks (Arenas-Marquez 2001; Sacks 2012). Secondly, fasting may bring potential disadvantages. Recent observations and prospective studies have shown that both short-term and prolonged fasting can induce insulin resistance and metabolic stress, which were found to increase postoperative infection, cause longer hospital stays, and result in mortality (Awad 2009; Awad 2010; Awad 2012; Hoeks 2010). Fasting can increase acute upper gastrointestinal haemorrhage by reactivating and aggravating pre-existing gastrointestinal disease (Ozkan 2009), and prolonged fasting can result in coagulation disorder (Moriwaki 2010). At present, there is no clear guideline about fasting for GIB caused by any condition. Strict or prolonged fasting is common, even though it may be unnecessary or even harmful in some conditions. Physicians are concerned about the adverse effects of feeding much more than those of fasting, although both lack systematically reviewed evidence for efficacy and safety. It is necessary to assess the effects and safety of fasting for children with GIB and explore the most appropriate length of fasting for different conditions.

OBJECTIVES

To assess the effects and safety of fasting for haemostasis in gastrointestinal bleeding in children.

METHODS

Criteria for considering studies for this review

Types of studies

Randomised controlled trials (RCTs) and quasi-RCTs of parallel design, irrespective of blinding, length of follow-up, language, or publication status. We planned to include quasi-RCTs because of the strong possibility of finding no RCTs.

Types of participants

Children aged 0 to 18 years, who had identified gastrointestinal bleeding (GIB) by any evidence of GIB.

Types of interventions

Fasting plus routine treatments versus feeding plus routine treatments.

We defined fasting as abstaining from all food including water.

We defined feeding as any feeding type and any food formula. Feeding type could be oral feeding, sip feeding, or tube feeding using nasogastric, gastrostomy, or jejunostomy tubes. Food formula could be ordinary diets, elemental diets, synthetic or semisynthetic diets, space diets, tube-feeding diets, complete liquid diets, supplemental liquid diets, or solid diets.

Types of outcome measures

We did not use outcome measures as criteria for including studies. We planned to measure each of the following outcomes at all time points within one month.

Primary outcomes

1. all-cause case fatality rate
2. incidence of re-bleeding
3. incidence of continued bleeding

Secondary outcomes

1. incidence of surgery for stopping bleeding
2. incidence of secondary infections
3. incidence of transfusion
4. any other adverse events

Search methods for identification of studies

Electronic searches

We searched the following databases:

- EBM Reviews - Cochrane Central Register of Controlled Trials (CENTRAL) (May 2016) ([Appendix 1](#))
- Ovid MEDLINE(R) (1946 to 3 May 2016) ([Appendix 2](#))
- EMBASE (1980 to 2016 Week 18) ([Appendix 3](#))
- Chinese Biomedical Database (CBM) (1978 to 3 May 2016) ([Appendix 4](#))
- China National Knowledge Infrastructure (CNKI) (1979 to 3 May 2016) ([Appendix 5](#))
- VIP Database (1989 to 4 May 2016) ([Appendix 6](#))
- Wanfang Data (1990 to 4 May 2016) ([Appendix 7](#))

We did not restrict searches by language or study setting. We limited searches in CNKI and Wanfang Data to the medical field.

Searching other resources

We planned to scrutinise all references of all included studies.

Data collection and analysis

Selection of studies

Two review authors (Luo SH, Guo Q) read titles and abstracts of all searched results independently to identify potentially relevant studies. We selected the citation of study to retrieve full text when its abstract provided the information that: it was a prospective study and it compared fasting with feeding. There was no disagreement between two authors regarding the selected result.

We planned to arrange two review authors (Luo SH, Guo Q) to examine full text of each selected study and use full text screening form to determine if it should be included or excluded, and resolve disagreements with the third author (Wan CM).

Data extraction and management

Two review authors (Luo SH, Guo Q) planned to independently extract the data of included studies using a data extraction form and resolve disagreements through discussion with a third review author (Wan CM). The data extraction form covered the following items:

- Study details: title, first author, publication type, publication information, country of publication, country of implementation, funding statement, and disclosure of potential conflicts of interest.
- Study methods: setting (multicentre or single centre), design (RCT or quasi-RCT or other), participants' information (inclusion criteria and exclusion criteria, number of participants randomised in intervention and comparison groups, baseline characteristics including sex, age, weight, diagnosis, bleeding site), interventions (fasting duration in intervention group,

feeding type and food formula in comparison groups), outcomes (all-cause case fatality rate, incidence of re-bleeding, continued bleeding, surgery for stopping bleeding, secondary infections, transfusion, and any other adverse events).

- 'Risk of bias' assessment: the judgement and basis for sequence generation, allocation concealment, blinding, incomplete outcome data, selective reporting bias, and other sources of bias.
- Study results: per-protocol analysis results (including number of participants randomised, excluded, withdrawn, lost to follow-up, and dropping out with reasons, and the last observed number in intervention and comparison groups) and intention-to-treat analysis results (including number of participants randomised, excluded, withdrawn, lost to follow-up, and dropping out with reasons and their last observations data, and the last-analysed number in intervention and comparison groups) at different time points of every outcome, and results of other outcomes of interest.

Assessment of risk of bias in included studies

Two review authors (Luo SH, Guo Q) planned to independently assess the risk of bias in sequence generation, allocation concealment, blinding, incomplete outcome data, selective reporting bias, and other sources of bias for each included study using the criteria outlined in the *Cochrane Handbook for Systematic Reviews of Interventions* ([Higgins 2011](#)), record their specific judgement and basis for every domain in the data extraction form, and resolve disagreements by discussion with the other two review authors (Wan CM, Liu Guan J). Our criteria for risk of bias is in [Appendix 8](#).

Measures of treatment effect

Dichotomous data

We planned to present all-cause case fatality rate, incidence of re-bleeding, incidence of continued bleeding, incidence of surgery for stopping bleeding, incidence of secondary infections, incidence of transfusion, and dichotomous data for any other adverse events (for example incidence of failure in endoscopic haemostasis) as summary risk ratios with corresponding 95% confidence intervals.

Continuous data

We planned to present continuous data for any other adverse events (for example duration of hospitalisation) as mean difference with corresponding 95% confidence intervals if outcomes were measured in the same way across all included trials or standardised mean difference with corresponding 95% confidence intervals if outcomes were measured in different ways.

Unit of analysis issues

'Multi-arm' trials

We planned to only include intervention groups relevant to our review in parallel-designed trials, and combine all relevant experimental intervention groups of a trial into a single experimental intervention group, and all relevant control intervention groups of a trial into a single control group. We planned to describe all intervention groups of all included trials in the 'Characteristics of included studies' table.

Time points of outcome measurement

GIB in children is generally an acute or recurrent condition, and all time points of outcome measurement may be similar, especially when GIB is caused by the same underlying disease, so we planned to measure only short-term outcomes within one month and include all related time points for each outcome measurement. If an outcome measure was reported at multiple time points in a study, we planned to analyse the time point closest to one month. If the time points were clearly different across all included trials, we planned to explore heterogeneity by sensitivity analysis ([Sensitivity analysis](#)) or subgroup analysis ([Assessment of heterogeneity](#)).

Dealing with missing data

We planned to contact the original authors to request missing data including missing outcomes, summary data, individual data, and study-level characteristics. If we could not obtain missing data, we planned to carry out intention-to-treat analysis by imputing data with an assumed best or worst outcome. The denominator for each outcome in each trial is the number randomised. We also planned to explore the impact of missing data on the overall assessment of intervention effect by performing sensitivity analysis (see [Sensitivity analysis](#)).

Assessment of heterogeneity

We planned to explore the suspected heterogeneity from clinical and methodologic characteristics of studies by prespecified subgroup or sensitivity analysis ([Subgroup analysis and investigation of heterogeneity](#) and [Sensitivity analysis](#)).

We also planned to use the I^2 statistic to measure heterogeneity among the trials in each analysis. If the I^2 was more than 50%, which suggests substantial heterogeneity, we planned to implement further investigation of heterogeneity.

Assessment of reporting biases

We planned to search clinical trial registration databases for protocols of included trials in order to verify whether all authors' prespecified outcomes had been reported in their articles. If this was not possible, and these data were thought to introduce serious bias, we planned to explore the impact of such studies on the results by a sensitivity analysis.

Data synthesis

Two review authors (Luo SH, Guo Q) planned to independently enter data into Review Manager software ([RevMan 2014](#)) and use a fixed-effect meta-analysis to combine data of trials sufficiently similar in their clinical and methodologic characteristics. If we identified heterogeneity in a fixed-effect meta-analysis, we planned to repeat the analysis using a random-effects method.

We planned to use random-effects meta-analysis to combine data where heterogeneity could not readily be explained after investigation by subgroup and sensitivity analysis ([Assessment of heterogeneity](#)).

If we could not combine data because of clinical and methodological heterogeneity, we planned to describe the results of individual studies narratively.

Subgroup analysis and investigation of heterogeneity

For all outcomes, taking into account the clinical characteristics of GIB, we planned to carry out the following subgroup analyses:

1. different bleeding site: UGIB and LGIB;
2. different disease causing GIB (If there were adequate studies): particularly necrotising enterocolitis, peptic ulcer, variceal bleeding, and stress-induced gastropathy in critically ill children.

If the data in the subgroups were independent, we planned to use an I^2 statistic across subgroup results to test subgroup differences. The I^2 statistic describes differences of typical effects across different subgroups in fixed-effect models and variation of the mean effects in the different subgroups in random-effects models.

In addition, we planned to inspect the confidence intervals of the summary estimates of subgroups. No overlap of the confidence intervals or overlap to a small degree may indicate a significant difference in treatment effect between the subgroups.

Sensitivity analysis

For all outcomes, we planned to use sensitivity analysis to:

1. explore the cause of clinical heterogeneity: characteristics of participants (bleeding site, primary disease), characteristics of intervention (different feeding type or food formula, different fasting duration), characteristics of outcome (time point of measurement, different definition of outcome);
2. explore the cause of methodologic heterogeneity: the impact of each level of bias on the results;
3. deal with missing data: compare the combined result by deselecting studies with low risk of incomplete outcome data, evaluate the influence of missing data on results (see [Dealing with missing data](#)): first, we planned to calculate the best or worst result. We would calculate the best results by assuming that all missing data in the fasting arm did have the outcome of interest and those in the feeding arm did not; we would calculate the worst results by assuming that missing data in the fasting arm did not have the outcome of interest and those in the feeding arm did. We planned to compare the best results to the worst results. Second, we planned to compare the results of intention-to-treat analysis to per-protocol analysis. If the different options for dealing with missing data can change the effect of the intervention, those missing data will have a significant impact on the result;
4. test the robustness of the evidence: compare the results of the fixed-effect model to the random-effects model meta-analysis.

We planned to use sensitivity analysis to explore the impact of any differences on the results.

Summary of findings and assessment of the certainty of the evidence

We planned to grade outcomes including all-cause case fatality rate, incidence of re-bleeding, incidence of continued bleeding, incidence of surgery, and incidence of secondary infections using GRADEprofiler software ([GRADE 2008](#)). Three review authors (Luo SH, Guo Q, Wan CM) planned to independently grade outcomes mentioned above using the criteria outlined

in the *GRADE Handbook for Grading Quality of Evidence and Strength of Recommendation* ([Schünemann 2009](#)), and resolve any disagreements by discussion. We planned to use GRADEprofiler software to create a 'Summary of findings' table for presenting all graded outcomes.

RESULTS

Description of studies

Results of the search

We retrieved 16,100 citations through searching electronic databases, including 9 citations from EBM Reviews - Cochrane

Central Register of Controlled Trials (CENTRAL), 20 citations from Ovid MEDLINE(R), 20 citations from EMBASE, 67 citations from CBM, 15,646 citations from CNKI, 0 citations from VIP, and 338 citations from Wanfang Data. The number of searched citations from CNKI was too large to fit in citation manager software.

Two review authors (Luo SH, Guo Q) independently screened searched results of CNKI online. We excluded 16,100 citations after reading the titles and abstracts. We found no potentially relevant studies. We have summarised the study screening and selection process in the PRISMA flow diagram ([Liberati 2009](#)) ([Figure 1](#)).

Figure 1. Study flow diagram.

Included studies

We identified no RCTs or quasi-RCTs that compared fasting with feeding. No study fulfilled the criteria for considering studies for our review.

Excluded studies

None.

Risk of bias in included studies

As no study met the inclusion criteria for our review, we did not perform a 'Risk of bias' assessment.

Effects of interventions

See: [Summary of findings 1 Fasting for haemostasis in children with gastrointestinal bleeding](#)

No study met the criteria for considering studies for our review, so we could not establish the effects and safety of fasting for haemostasis in gastrointestinal bleeding in children.

DISCUSSION

Summary of main results

For some time, paediatricians, based on their education and clinical experience, have usually used fasting for children with GIB. So the decision could be very different especially for critically ill children whose GIB resulted from stress-induced gastropathy, as there is no clear guideline about fasting for GIB especially resulted from stress-induced gastropathy. Some physicians may give strict and prolonged fasting until the defecate occult blood examination becomes negative, but others may give short-term fasting only when visible bloody vomiting or stool occur.

We found no RCT or quasi-RCT that compared the effects and safety of fasting with feeding for haemostasis in children with GIB. We therefore cannot draw any conclusions regarding fasting for haemostasis in children with GIB. After reviewing all searched citations, we did not even find a relevant prospective cohort study ([Summary of findings 1](#)).

Overall completeness and applicability of evidence

No study met the criteria for considering studies for our review, so we could not assess the overall completeness and applicability of evidence.

Quality of the evidence

No study met the criteria for considering studies for our review, so we could not grade the quality of evidence.

Potential biases in the review process

We could have missed a related study published in other language because we only searched English and Chinese databases.

Agreements and disagreements with other studies or reviews

We did not find a similar review relevant to fasting for haemostasis in GIB.

AUTHORS' CONCLUSIONS

Implications for practice

There is no evidence upon which to base the use of fasting for haemostasis in children with GIB.

Implications for research

A prospective study is required to compare the effects and safety of fasting with feeding for haemostasis in children with GIB, especially for critically ill children, who are at high risk for GIB from stress-induced gastropathy.

ACKNOWLEDGEMENTS

We thank the Cochrane Upper Gastrointestinal and Pancreatic Diseases Review Group for their support and advice throughout the development of this review. We thank Dr Efstratios Saliakellis, Stephenne Xavier, Statistical Editor Sarah Rhodes, and Consumer Representative Alfretta Vanderheyden for their advice on the protocol and the review.

REFERENCES

Additional references

Arenas-Marquez 2001

Arenas-Marquez H, Anaya-Prado R, Barrera-Zepeda LM, Gonzalez-Ojeda A. Complications of central venous catheters. *Current Opinion in Clinical Nutrition and Metabolic Care* 2001;**4**(3):207-10.

Arora 2002

Arora NK, Ganguly S, Mathur P, Ahuja A, Patwari A. Upper gastrointestinal bleeding: etiology and management. *Indian Journal of Pediatrics* 2002;**69**(2):155-68.

Awad 2009

Awad S, Constantin-Teodosiu D, Macdonald IA, Lobo DN. Short-term starvation and mitochondrial dysfunction - a possible mechanism leading to postoperative insulin resistance. *Clinical Nutrition* 2009;**28**(5):497-509. [DOI: [10.1016/j.clnu.2009.04.014](https://doi.org/10.1016/j.clnu.2009.04.014)]

Awad 2010

Awad S, Stephenson MC, Placidi E, Marciani L, Constantin-Teodosiu D, Gowland PA, et al. The effects of fasting and refeeding with a 'metabolic preconditioning' drink on substrate reserves and mononuclear cell mitochondrial function. *Clinical Nutrition* 2010;**29**(4):538-44. [DOI: [10.1016/j.clnu.2010.01.009](https://doi.org/10.1016/j.clnu.2010.01.009)]

Awad 2012

Awad S, Lobo DN. Metabolic conditioning to attenuate the adverse effects of perioperative fasting and improve patient outcomes. *Current Opinion in Clinical Nutrition and Metabolic Care* 2012;**15**(2):194-200. [DOI: [10.1097/MCO.0b013e32834f0078](https://doi.org/10.1097/MCO.0b013e32834f0078)]

Barkun 2010

Barkun AN, Bardou M, Kuipers EJ, Sung J, Hunt RH, Martel M, et al. International consensus recommendations on the management of patients with non variceal upper gastrointestinal bleeding. *Annals of Internal Medicine* 2010;**152**(2):101-13.

Barrett 2009

Barrett KE, Raybould HE. Gastrointestinal physiology. In: Koeppen BM, Stanton BA, editors(s). *Berne & Levy Physiology*. 6th edition. Philadelphia: Mosby, Elsevier, 2009:485-553.

Beck 1998

Beck C, Dubois J, Grignon A, Lacroix J, David M. Incidence and risk factors of catheter-related deep vein thrombosis in a pediatric intensive care unit: a prospective study. *Journal of Pediatrics* 1998;**133**(2):237-41.

Beghetto 2005

Beghetto MG, Victorino J, Teixeira L, de Azevedo MJ. Parenteral nutrition as a risk factor for central venous catheter-related infection. *Journal of Parenteral and Enteral Nutrition* 2005;**29**(5):367-73.

Boyle 2008

Boyle JT. Gastrointestinal bleeding in infants and children. *Pediatrics in Review* 2008;**29**(2):39-52. [DOI: [10.1542/pir.29-2-39](https://doi.org/10.1542/pir.29-2-39)]

Braga 2001

Braga M, Gianotti L, Gentilini O, Parisi V, Salis C, Di Carlo V. Early postoperative enteral nutrition improves gut oxygenation and reduces costs compared with total parenteral nutrition. *Critical Care Medicine* 2001;**29**(2):242-8.

Cangelosi 2011

Cangelosi MJ, Auerbach HR, Cohen JT. A clinical and economic evaluation of enteral nutrition. *Current Medical Research and Opinion* 2011;**27**(2):413-22. [DOI: [10.1185/03007995.2010.545816](https://doi.org/10.1185/03007995.2010.545816)]

Cappell 2008

Cappell MS. Common gastrointestinal emergencies. Preface. *Medical Clinics of North America* 2008;**92**(3):11-4. [DOI: [10.1016/j.mcna.2008.01.008](https://doi.org/10.1016/j.mcna.2008.01.008)]

Chaïbou 1998

Chaïbou M, Tucci M, Dugas MA, Farrell CA, Proulx F, Lacroix J. Clinically significant upper gastrointestinal bleeding acquired in a pediatric intensive care unit: a prospective study. *Pediatrics* 1998;**102**(4):933-8. [DOI: [10.1542/peds.102.4.933](https://doi.org/10.1542/peds.102.4.933)]

Chawla 2007

Chawla S, Seth D, Mahajan P, Kamat D. Upper gastrointestinal bleeding in children. *Clinical Pediatrics* 2007;**46**(1):16-21. [DOI: [10.1177/1084713806297151](https://doi.org/10.1177/1084713806297151)]

Cochran 1992

Cochran EB, Phelps SJ, Tolley EA, Stidham GL. Prevalence of, and risk factors for, upper gastrointestinal tract bleeding in critically ill paediatric patients. *Critical Care Medicine* 1992;**20**(11):1519-23.

Colle 2011

Colle I, Wilmer A, Moine OL, Debruyne R, Delwaide J, Dhondt E, et al. Upper gastrointestinal tract bleeding management: Belgian guidelines for a. *Acta Gastro-Enterologica Belgica* 2011;**74**:45-66.

Cox 1979

Cox K, Ament ME. Upper gastrointestinal bleeding in children and adolescents. *Pediatrics* 1979;**63**(3):408-13. [PMID: 312485]

D'Amico 2010

D'Amico G, Pagliaro L, Pietrosi G, Tarantino I. Emergency sclerotherapy versus vasoactive drugs for bleeding oesophageal varices in cirrhotic patients. *Cochrane Database of Systematic Reviews* 2010, Issue 3. Art. No: CD002233. [DOI: [10.1002/14651858.CD002233.pub2](https://doi.org/10.1002/14651858.CD002233.pub2)]

Deerojanawong 2009

Deerojanawong J, Peongsujarit D, Vivatvakin B, Prapphal N. Incidence and risk factors of upper gastrointestinal bleeding in mechanically ventilated children. *Pediatric*

Critical Care Medicine 2009;**10**(1):91-5. [DOI: [10.1097/PCC.0b013e3181936a37](https://doi.org/10.1097/PCC.0b013e3181936a37)]

Fennerty 2002

Fennerty MB. Pathophysiology of the upper gastrointestinal tract in the critically ill patient: rationale for the therapeutic benefits of acid suppression. *Critical Care Medicine* 2002;**30**(6 Suppl):S351-5.

Fox 2000

Fox VL. Gastrointestinal bleeding in infancy and childhood. *Gastroenterology Clinics of North America* 2000;**29**(1):37-66.

Glud 2012

Glud LL, Klingenberg SL, Langholz E. Tranexamic acid for upper gastrointestinal bleeding. *Cochrane Database of Systematic Reviews* 2012, Issue 1. Art. No: CD006640. [DOI: [10.1002/14651858.CD006640.pub2](https://doi.org/10.1002/14651858.CD006640.pub2)]

GRADE 2008 [Computer program]

GRADE Working Group GRADEprofiler (GRADEpro). Brozek J, Oxman A, Schunemann H, Version 3.6. GRADE Working Group, 2008.

Green 1978

Green FW Jr, Kaplan MM, Curtis LE, Levine PH. Effect of acid and pepsin on blood coagulation and platelet aggregation. A possible contributor prolonged gastroduodenal mucosal haemorrhage. *Gastroenterology* 1978;**74**(1):38-43.

Hébuterne 2011

Hébuterne X, Vanbiervliet G. Feeding the patients with upper gastrointestinal bleeding. *Current Opinion in Clinical Nutrition and Metabolic Care* 2011;**14**(2):197-201. [DOI: [10.1097/MCO.0b013e3283436dc5](https://doi.org/10.1097/MCO.0b013e3283436dc5)]

Higgins 2011

Higgins JPT, Green S (editors). *Cochrane Handbook for Systematic Reviews of Interventions* Version 5.1.0 [updated March 2011]. The Cochrane Collaboration, 2011. Available from www.cochrane-handbook.org.

Hoeks 2010

Hoeks J, van Herpen NA, Mensink M, Moonen-Kornips E, van Beurden D, Hesselink MK, et al. Prolonged fasting identifies skeletal muscle mitochondrial dysfunction as consequence rather than cause of human insulin resistance. *Diabetes* 2010;**59**(9):2117-25.

Jensen 2011

Jensen DM. Gastrointestinal haemorrhage and occult gastrointestinal bleeding. In: Goldman L, Schafer AI, editors(s). *Goldman's Cecil Medicine*. 24th edition. Philadelphia: Saunders, Elsevier Inc, 2011:857-62.

Kakzanov 2008

Kakzanov V, Monagle P, Chan AK. Thromboembolism in infants and children with gastrointestinal failure receiving long-term parenteral nutrition. *Journal of Parenteral and Enteral Nutrition* 2008;**32**(1):88-93.

Kato 1991

Kato S, Nakagawa H, Harada Y, Saito Y, Watanabe N, Abe J, et al. A clinical study of upper gastrointestinal endoscopy in Japanese children. *Acta Paediatric Japonica* 1991;**33**(1):36-42. [PMID: 1853712]

Kay 2007

Kay MH, Wyllie R. Therapeutic endoscopy for non variceal gastrointestinal bleeding. *Journal of Pediatric Gastroenterology and Nutrition* 2007;**45**(2):157-71.

Kuusela 2000

Kuusela AL, Mäki M, Ruuska T, Laippala P. Stress-induced gastric findings in critically ill newborn infants: frequency and risk factors. *Intensive Care Medicine* 2000;**26**:1501-6.

Lacroix 1992

Lacroix J, Nadeau D, Laberge S, Gauthier M, Lapierre G, Farrell CA. Frequency of upper gastrointestinal bleeding in a paediatric intensive care unit. *Critical Care Medicine* 1992;**20**(1):35-42.

Leontiadis 2007

Leontiadis GI, Sreedharan A, Dorward S, Barton P, Delaney B, Howden CW, et al. Systematic reviews of the clinical effectiveness and cost-effectiveness of proton pump inhibitors in acute upper gastrointestinal bleeding. *Health Technology Assessment* 2007;**11**(51):iii-iv, 1-164.

Leung 2002

Leung AK, Wong AL. Lower gastrointestinal bleeding in children. *Pediatric Emergency Care* 2002;**18**(4):319-23.

Liberati 2009

Liberati A, Altman DG, Tetzlaff J, Mulrow C, Gotzsche PC, Ioannidis JP, et al. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions: explanation and elaboration. *PLoS Medicine* 2009;**6**:e1000100.

Low 1980

Low J, Dodds AJ, Biggs JC. Fibrinolytic activity of gastroduodenal secretions - a possible role in upper gastrointestinal haemorrhage. *Thrombosis Research* 1980;**17**(6):819-30.

Marek 2011

Marek TA. Gastrointestinal bleeding. *Endoscopy* 2011;**43**(11):971-7. [DOI: <http://dx.doi.org/10.1055/s-0031-1291429>]

McClave 2005

McClave SA, Chang WK. When to feed the patient with gastrointestinal bleeding. *Nutrition in Clinical Practice* 2005;**20**(5):544-50. [DOI: [10.1177/0115426505020005544](https://doi.org/10.1177/0115426505020005544)]

Mittal 1994

Mittal SK, Kalra KK, Aggarwal V. Diagnostic upper GI endoscopy for hematemesis in children: experience from a pediatric gastroenterology centre in north India. *The Indian Journal of Pediatrics* 1994;**61**(6):651-4. [PMID: 7721369]

Moriwaki 2010

Moriwaki Y, Sugiyama M. Effect of fasting on coagulation factors in patients who undergo major abdominal surgery. *American Surgeon* 2010;**76**(2):168-71.

Nithiwathanapong 2005

Nithiwathanapong C, Reungrongrat S, Ukarapol N. Prevalence and risk factors of stress-induced gastrointestinal bleeding in critically ill children. *World Journal of Gastroenterology* 2005;**11**(43):6839-42.

Opilla 2008

Opilla M. Epidemiology of bloodstream infection associated with parenteral nutrition. *American Journal of Infection Control* 2008;**36**(10):S173.e5-8. [DOI: [10.1016/j.ajic.2008.10.007](https://doi.org/10.1016/j.ajic.2008.10.007)]

Ozkan 2009

Özkan S, Durukan P, Akdur O, Vardar A, Torun E, Ikizceli I. Does Ramadan fasting increase acute upper gastrointestinal haemorrhage? *Journal of International Medical Research* 2009;**37**(6):1988-93.

Patchett 1989

Patchett SE, Enright H, Afdhal N, O'Connell W, O'Donoghue DP. Clot lysis by gastric juice: an in vitro study. *Gut* 1989;**30**:1704-7. [DOI: [10.1136/gut.30.12.1704](https://doi.org/10.1136/gut.30.12.1704)]

Peters 2002

Peters JM. Management of gastrointestinal bleeding in children. *Current Treatment Options in Gastroenterology* 2002;**5**(5):399-413.

Rayhorn 2001a

Rayhorn N, Thrall C, Silber G. A review of the causes of upper gastrointestinal tract bleeding in children. *Gastroenterology Nursing* 2001;**24**(1):23-7.

Rayhorn 2001b

Rayhorn N, Thrall C, Silber G. A review of the causes of lower gastrointestinal tract bleeding in children. *Gastroenterology Nursing* 2001;**24**(2):77-83.

Revelly 2001

Revelly JP, Tappy L, Berger MM, Gersbach P, Cayeux C, Chiolero R. Early metabolic and splanchnic responses to enteral nutrition in postoperative cardiac surgery patients with circulatory compromise. *Intensive Care Medicine* 2001;**27**(3):540-7.

RevMan 2014 [Computer program]

The Nordic Cochrane Centre, The Cochrane Collaboration Review Manager (RevMan). Version 5.3. Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration, 2014.

Sacks 2012

Sacks GS. Safety surrounding parenteral nutrition systems. *Journal of Parenteral and Enteral Nutrition* 2012;**36**(2):Suppl:20S-22S. [DOI: [10.1177/0148607111434776](https://doi.org/10.1177/0148607111434776)]

Schünemann 2009

Schünemann H, Brożek J, Oxman A (editors). GRADE Handbook for Grading Quality of Evidence and Strength of Recommendation. Version 3.2 [updated March 2009]. The GRADE Working Group, 2009. Available from <http://www.ccs-ims.net/gradepro>.

Sidhu 2007

Sidhu R, McAlindon ME, Sanders DS, Thomson M. Capsule endoscopy in the evaluation of gastrointestinal disease. *Current Opinion in Pediatrics* 2007;**19**(5):586-90.

Sreedharan 2010

Sreedharan A, Martin J, Leontiadis GI, Dorward S, Howden CW, Forman D, et al. Proton pump inhibitor treatment initiated prior to endoscopic diagnosis in upper gastrointestinal bleeding. *Cochrane Database of Systematic Reviews* 2010, Issue 7. Art. No: CD005415. [DOI: [10.1002/14651858.CD005415.pub3](https://doi.org/10.1002/14651858.CD005415.pub3)]

Villanueva 2008

Villanueva C, Balanzo J. Variceal bleeding: pharmacological treatment and prophylactic strategies. *Drugs* 2008;**68**(16):2303-24.

Wyllie 2007

Wyllie R. Clinical manifestations of gastrointestinal disease. In: Kliegman RM, Behrman RE, Jenson H, Stanton BF, editors(s). *Nelson Textbook of Pediatrics*. 18th edition. Philadelphia: Saunders, Elsevier, 2007:1521-9.

Yachha 1996

Yachha SK, Khanduri A, Sharma BC, Kumar M. Gastrointestinal bleeding in children. *Journal of Gastroenterology and Hepatology* 1996;**11**(10):903-7. [PMID: 8912124]

Zahavi 1994

Zahavi I, Arnon R, Ovadia B, Rosenbach Y, Hirsch A, Dinari G. Upper gastrointestinal endoscopy in the paediatric patient. *Israel Journal of Medical Sciences* 1994;**30**(8):664-7. [PMID: 8045755]

APPENDICES

Appendix 1. Search strategy for EBM Reviews - Cochrane Central Register of Controlled Trials

1. exp Gastrointestinal Tract/ (9981)
2. (bleed\$ or re-bleed\$ or rebleed\$ or hemorrhag\$ or haemorrhag\$).tw. (24071)
3. 1 and 2 (447)
4. gastrointestinal hemorrhage/ (1219)
5. hematemesi\$ (13)

6. h*ematemesis.tw. (103)
7. melena/ (30)
8. (melena or melaena).tw. (84)
9. (coffee adj1 ground).tw. (7)
- 10.(haematochezia or hematochezia).tw. (40)
- 11.(blood* adj (stool or f*eces)).tw. (85)
- 12.or/4-11 (1455)
- 13.3 or 12 (1760)
- 14.Fasting/ (2468)
- 15.(food adj (abstinence or fast*)).tw. (31)
- 16.diet* restriction.tw. (212)
- 17.fasting.tw. (14391)
- 18.food restriction.tw. (31)
- 19.restricted diet.tw. (443)
- 20.or/14-19 (15645)
- 21.13 and 20 (11)

Appendix 2. Search strategy for Ovid MEDLINE(R)

Ovid MEDLINE(R) <1946 to April Week 3 2016>

RCT filter omitted

1. exp Gastrointestinal Tract/ (579461)
2. (bleed\$ or re-bleed\$ or rebleed\$ or hemorrhag\$ or haemorrhag\$).tw. (309702)
3. 1 and 2 (17861)
4. gastrointestinal hemorrhage/ (37729)
5. hematemesis/ (2227)
6. h*ematemesis.tw. (2713)
7. melena/ (2033)
8. (melena or melaena).tw. (2279)
9. (coffee adj1 ground).tw. (158)
- 10.(haematochezia or hematochezia).tw. (1127)
- 11.(blood* adj (stool or f*eces)).tw. (566)
- 12.or/4-11 (43588)
- 13.3 or 12 (53777)
- 14.Fasting/ (30934)
- 15.(food adj (abstinence or fast*)).tw. (61)
- 16.diet* restriction.tw. (3156)
- 17.fasting.tw. (77395)
- 18.food restriction.tw. (2591)
- 19.restricted diet.tw. (2280)
- 20.or/14-19 (96592)
- 21.13 and 20 (134)
- 22.limit 21 to ("all infant (birth to 23 months)" or "all child (0 to 18 years)") (21)

Appendix 3. Search strategy for EMBASE

Embase via OVID <1980 to 2016 Week 18>

RCT filter omitted

1. exp Gastrointestinal Tract/ (33849)
2. (bleed\$ or re-bleed\$ or rebleed\$ or hemorrhag\$ or haemorrhag\$).tw. (449051)
3. 1 and 2 (2013)
4. gastrointestinal hemorrhage/ (50030)

5. hematemesis/ (7250)
6. h*ematemesis.tw. (4495)
7. melena/ (7257)
8. (melena or melaena).tw. (4268)
9. (coffee adj1 ground).tw. (395)
- 10.hematochezia/ (5938)
- 11.(haematochezia or hematochezia).tw. (2573)
- 12.(blood* adj (stool or f*eces)).tw. (1000)
- 13.or/4-12 (67544)
- 14.3 or 13 (69021)
- 15.diet restriction/ (78817)
- 16.(food adj (abstinence or fast*)).tw. (82)
- 17.diet* restriction.tw. (4090)
- 18.fasting.tw. (117770)
- 19.food restriction.tw. (3183)
- 20.restricted diet.tw. (3140)
- 21.or/15-20 (149295)
- 22.14 and 21 (292)
- 23.limit 22 to (infant <to one year> or child <unspecified age> or preschool child <1 to 6 years> or school child <7 to 12 years> or adolescent <13 to 17 years>) (28)

Appendix 4. Search strategy for CBM

1. 全部字段=胃肠道出血 或 消化道出血 或 呕血 或 便血 或 血便 或 黑便 或 大便隐血(44588)
2. 全部字段=禁食 或 进食 或 限制饮食 或 饮食限制(30135)
3. 全部字段=新生儿 或 婴儿 或 幼儿 或 儿童 或 青少年(257713)
4. 1 and 2 and 3(57)

Appendix 5. Search strategy for CNKI

1. (胃肠道出血 或 消化道出血 或 呕血 或 便血 或 血便 或 黑便 或 大便隐血) .tw. (331364)
2. 在结果中检索：(禁食 或 进食 或 限制饮食 或 饮食限制) .tw. (76062)
3. 在结果中检索：(新生儿 或 婴儿 或 幼儿 或 儿童 或 青少年) .tw. (11988)

Appendix 6. Search strategy for VIP

1. 任意字段=胃肠道出血 或 消化道出血 或 呕血 或 便血 或 血便 或 黑便 或 大便隐血 (53873)
2. 任意字段=禁食 或 进食 或 限制饮食 或 饮食限制 (42586)
3. 任意字段=新生儿 或 婴儿 或 幼儿 或 儿童 或 青少年 (571982)
4. and/1-3 (132)

Appendix 7. Search strategy for Wanfang Data

1. (胃肠道出血 或 消化道出血 或 呕血 或 便血 或 血便 或 黑便 或 大便隐血) .tw. (272011)
2. (禁食 或 进食 或 限制饮食 或 饮食限制) .tw. (57345)
3. (新生儿 或 婴儿 或 幼儿 或 儿童 或 青少年) .tw. (954255)
4. and/1-3 (354)

Appendix 8. Criteria for 'risk of bias'

Sequence generation (checking for possible selection bias)

- Low risk of bias (sufficient information about adequate methods of sequence generation is available, e.g. referring to a random number table, using a computer random number generator, coin tossing, throwing dice);
- High risk of bias (sufficient information about inadequate methods of sequence generation is available, e.g. sequence generated by odd or even date of birth, admission, hospital, or clinic record number);
- Unclear risk of bias (insufficient information about sequence generation process makes judgement of 'low risk' or 'high risk' impossible).

Allocation concealment (checking for possible selection bias)

- Low risk of bias (adequate methods of allocation sequence concealment were described, e.g. central randomisation, sequentially numbered, sealed, opaque envelopes, sequentially numbered drug containers with same appearance);
- High risk of bias (inadequate methods of allocation sequence concealment were described or there was no use of allocation sequence concealment, e.g. random allocation schedule was open, assignment envelopes were unsealed or non-opaque, sequence generation was based on date of birth or case record number);
- Unclear risk of bias (insufficient information about implementation of allocation concealment makes judgement of 'low risk' or 'high risk' impossible).

Blinding (checking for possible performance bias and detection bias)

Blinding would seem to be impossible in studies comparing fasting versus feeding, but all of the outcomes above are not likely to be affected by lack of masking of participants, personnel, or outcome assessors. We generally planned to assess the blinding methods as having a low risk of bias.

However, for adverse events we planned to first consider whether the event is subjective or objective, such as patient-reported outcomes. For a subjective event, we planned to assess the methods as:

- Low risk of bias (any effective method was used to mask participants, personnel, and outcome assessors, or lack of blinding could not have affected the results);
- High risk of bias (lack of blinding could have affected the results, and no effective method was used to mask participants, personnel, and outcome assessors);
- Unclear risk of bias (lack of blinding could have affected the results, and insufficient information about blinding makes judgement of 'low risk' or 'high risk' impossible).

Incomplete outcome data (checking for possible attrition bias through withdrawals, dropouts, loss to follow-up, protocol deviations)

We planned to assess the completeness of outcome data for each outcome of each study, including attrition and exclusions from the analysis, and to investigate the following factors: whether attrition and exclusions were reported, whether reasons for attrition or exclusion were reported, whether the participant numbers were included in the analysis at each stage (compared with the total randomised participants), and whether missing data were balanced across groups or were related to outcomes. (If sufficient information could be supplied by the trial authors, we planned to re-include missing data in analyses.)

- Low risk of bias (no missing outcome data; reasons for missing outcome data unlikely to be related to true outcome; missing outcome data balanced in numbers and reasons for missing data across intervention groups; the proportion of missing outcomes compared with observed event risk is not enough to have a clinically relevant impact on the intervention effect estimate; missing data have been imputed using appropriate methods);
- High risk of bias (reason for missing outcome data likely to be related to true outcome; missing outcome data imbalanced in numbers or reasons for missing across intervention groups; the proportion of missing outcomes compared with observed event risk is enough to induce clinically relevant bias in intervention effect estimate; 'as-treated' analysis done with substantial departure of the intervention received from that assigned at randomisation, or analysis focuses only on children who complied with protocols; missing data have been imputed using inappropriate methods);
- Unclear risk of bias (reasons for missing outcome data were not reported, or the extent to which the proportion of missing outcomes compared with observed event risk had a clinically relevant impact on the intervention effect estimate is unknown).

Selective reporting bias

- Low risk of bias (the study protocol is available and all of the study's prespecified outcomes have been reported in the prespecified way; the study protocol is not available but all expected outcomes and those listed in the methods section in the article were reported with adequate detail);
- High risk of bias (the study protocol is available and not all of the study's prespecified outcomes have been reported, or some outcomes were not reported in the prespecified way, or non-prespecified outcomes were reported without clear justification for their reporting; expected outcomes or those listed in the methods section in the article were reported without adequate detail);
- Unclear risk of bias (insufficient information about selective reporting bias makes judgement of 'low risk' or 'high risk' impossible).

Other sources of bias

We planned to assess whether each study was free of other problems that could put it at risk of bias, and rate this as follows:

- Low risk of other bias;
- High risk of other bias;
- Unclear risk of other bias.

WHAT'S NEW

Date	Event	Description
5 July 2021	Amended	Editorial note added about updating status

HISTORY

Protocol first published: Issue 8, 2013

Review first published: Issue 5, 2016

CONTRIBUTIONS OF AUTHORS

Shuang-Hong Luo, Chaomin Wan, and Guan J Liu designed the protocol; Shuang-Hong Luo and Qin Guo developed the protocol; and Shuang-Hong Luo and Qin Guo searched the additional references.

DECLARATIONS OF INTEREST

S-HL: none known.

QG: none known.

GJL: none known.

CW: none known.

SOURCES OF SUPPORT

Internal sources

- West China Hospital, Sichuan University, Chengdu, China

External sources

- No sources of support provided

DIFFERENCES BETWEEN PROTOCOL AND REVIEW

As no study met the inclusion criteria for our review, we could not carry out the entire plan discussed in the protocol.

NOTES

No trials were identified when this Review was originally published (May 2016). No new evidence is available (as of July 2021); thus, there are no current plans to update it.

INDEX TERMS

Medical Subject Headings (MeSH)

*Fasting; Gastrointestinal Hemorrhage [etiology] [*therapy]; *Hemostasis

MeSH check words

Child; Humans