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Routine prophylactic drugs in normal labour for reducing gastric aspiration and its effects (Review)

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[Intervention Review]

Routine prophylactic drugs in normal labour for reducing gastric aspiration and its effects

Gillian ML Gyte¹, Yana Richens²

¹Cochrane Pregnancy and Childbirth Group, School of Reproductive and Developmental Medicine, Division of Perinatal and Reproductive Medicine, The University of Liverpool, Liverpool, UK. ²Elizabeth Garrett Anderson and Obstetric Hospital, University College London Hospital Foundation Trust, London, UK

Contact: Gillian ML Gyte, Cochrane Pregnancy and Childbirth Group, School of Reproductive and Developmental Medicine, Division of Perinatal and Reproductive Medicine, The University of Liverpool, First Floor, Liverpool Women's NHS Foundation Trust, Crown Street, Liverpool, L8 7SS, UK. ggyte@cochrane.co.uk.

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ABSTRACT

Background

Women in normal labour may sometimes go on to have general anaesthesia if labour becomes abnormal, for example if a caesarean section is required. General anaesthesia carries a very small risk of regurgitation and inhalation of stomach contents into the lungs. This can cause inflammation, particularly if the fluid is acidic, and can lead to severe morbidity and very occasionally mortality. Labour hormones increase the risk of gastric aspiration or Mendelsohn's syndrome, though the exact incidence is unknown. The routine administration of acid prophylaxis drugs to all women in normal labour is commonly practiced worldwide, to reduce gastric aspiration by reducing the volume and acidity of stomach contents.

Objectives

To assess the effectiveness of routine prophylaxis drugs for women in normal labour to reduce gastric aspiration and its effects.

Search methods

We searched the Cochrane Pregnancy and Childbirth Group's Trials Register (December 2005), EMBASE (1974 to April 2005) and CINAHL (1982 to April 2005). We updated the search of the Cochrane Pregnancy and Childbirth Group's Trials Register on 1 October 2009 and added the results to the awaiting classification section.

Selection criteria

Randomised and quasi-randomised controlled trials of women in normal labour assessing the routine administration of drugs (antacids, H₂ receptor antagonists, dopamine antagonists and proton-pump inhibitors) compared with placebo/no treatment, and compared with other drugs for reducing gastric aspiration.

Data collection and analysis

Two review authors independently assessed eligibility, quality, extracted data and performed double-data entry.

Main results

Three trials were included, involving 2465 women, assessing the effects of antacids, H₂ receptor antagonists and dopamine antagonists. There were no trials on proton-pump inhibitors. None of the trials were of good quality, and none assessed the incidence of gastric aspiration, Mendelsohn's syndrome or their consequences. All the studies assessed vomiting, and there was limited evidence that vomiting

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may be reduced by antacids (relative risk (RR) 0.46, 95% confidence interval (CI) 0.27 to 0.77, n = 578, one trial) or by dopamine antagonists given alongside pethidine (RR 0.40, 95% CI 0.23 to 0.68, n = 584, one trial). Comparisons between different drugs showed no significant differences, though the number of participants was small. There was no evidence that H₂ receptor antagonists improved outcomes compared with antacids, though only one trial addressed this issue.

Authors' conclusions

There is no good evidence to support the routine administration of acid prophylaxis drugs in normal labour to prevent gastric aspiration and its consequences. Giving such drugs to women once a decision to give general anaesthesia is made, is assessed in another Cochrane review.

[Note: The four citations in the awaiting classification section of the review may alter the conclusions of the review once assessed.]

PLAIN LANGUAGE SUMMARY

Routine prophylactic drugs in normal labour for reducing gastric aspiration and its effects

No good evidence for drugs, like antacids, in normal labour to reduce the small chance of inhaling some stomach contents if general anaesthesia is required.

Caregivers are often concerned that some woman in normal labour may go on to have a general anaesthetic, either for a caesarean section in labour, or to remove the placenta after birth should it be retained. The concern arises because there is a very small risk that the woman might regurgitate and possibly inhale some of the stomach contents into the lungs (gastric aspiration or Mendelsohn's syndrome) during the general anaesthetic. This can cause severe lung and breathing problems, especially if the stomach contents are acid (low pH), and extremely rarely (one in a million) a woman may die from an anaesthetic problem. Giving drugs to reduce the volume of the stomach contents, or to make them less acid may help to reduce the problem. The review of trials looked to see whether giving such drugs routinely to all women in normal labour was effective. The review identified three trials involving 2465 women but none assessed gastric aspiration, probably because it is a very rare event. Instead the trials all assessed the incidence of vomiting, although there is no proven link between vomiting in labour and gastric aspiration during general anaesthesia. The review found some limited evidence that 1) drugs like antacids may reduce the chance of vomiting in labour, 2) H₂ receptor antagonist drugs (like ranitidine) appeared to have a similar impact on outcomes as antacids and 3) dopamine antagonists (like metoclopramide) may reduce the chance on vomiting in labour when given alongside pethidine. Overall, there was no evidence that any of these drugs reduced the incidence of gastric aspiration or Mendelsohn's syndrome.

BACKGROUND

Introduction

Many women have the ability to give birth without the need for medical interventions ([Gaskin 2003](#)). However, currently almost all women in income-rich countries are given medical interventions during labour with the aim of improving outcomes. There is concern that some interventions may undermine women's confidence in giving birth, so it is important to assess interventions to see if they achieve their clinical goals, but also to determine their impact on women's feelings and attitudes.

It is usual in some hospitals for women in normal labour to be given prophylactic drugs with the aim of preventing the inhalation of stomach (gastric) contents in labour or shortly afterwards, although this is an extremely rare occurrence and happens more often during general anaesthesia ([DH 2001](#); [DH 2004](#)). In other hospitals, these drugs are only given once the decision to administer anaesthesia has been made (either for caesarean section or manual removal of retained placenta) to minimise the risk of regurgitation of acidic stomach contents up the throat and back into the lungs. A Cochrane review is being undertaken to assess the effectiveness of giving drugs to prevent this problem (a practice known as acid prophylaxis) when caesarean section is undertaken ([Paranjothy 2004](#)). This review will look at the benefits and harms of giving these drugs routinely to all women in normal labour.

Variations in practice

There is considerable variation in practice around the use of these drugs in different hospitals and countries ([Power 1987](#)). The most recent data from an audit in UK hospitals in 2000, showed that in 34.5% of hospitals, acid prophylaxis (type of drug not specified) was used routinely for all women in labour, and 61% of hospitals gave it to women in labour only after a decision to perform a caesarean section ([Thomas 2001](#)). A German survey in 1999, reported 7% of hospitals gave routine acid aspiration prophylaxis in labour, and 68% gave it to women prior to emergency caesarean section ([Schneck 1999](#)). In 1989, 22% Australian hospitals used acid aspiration prophylaxis routinely for all women in labour, and the remaining 88% used it only for women requiring anaesthesia ([Burgess 1989](#)).

Gastric aspiration

Regurgitation and inhalation of stomach contents can cause inflammation of the lining of the lungs (pneumonitis), particularly if the fluid is acidic, and can lead to severe morbidity and occasionally death. Other adverse effects include narrowing of the airways in the lungs (bronchospasm), irregular breathing (dyspnoea), raised heart rate (tachycardia), increased fluid in the lung tissues (pulmonary oedema), lack of oxygen in the tissues (cyanosis), low blood pressure (hypotension) and an inability to breathe (asphyxia) ([Teabeaut 1952](#)). This condition is referred to as 'gastric aspiration syndrome', 'acid aspiration syndrome', 'aspiration pneumonia', 'aspiration pneumonitis' or Mendelsohn's syndrome, after Curtis Mendelsohn, the doctor who described the symptoms and investigated the problem in women in labour in the 1940s ([Mendelsohn 1946](#)). Mendelsohn reported the problem as an "asthmatic type syndrome" which had an acute duration of 24 to 36 hours following gastric aspiration.

Gastric aspiration can occur during general anaesthesia if the stomach is not empty because the anaesthetic drugs relax muscle tone, specifically the lower oesophageal sphincter. A 'cuffed oral endotracheal tube' is used during general anaesthesia, to fill the passage in the trachea (airway), thus preventing aspiration if regurgitation does occur. However, when the tube is inserted (intubation) and removed (extubation), there is a risk of aspiration and inhalation because the anaesthetic drugs suspend the protective laryngeal reflexes. Gastric aspiration has also been reported during regional anaesthesia (epidurals or spinals), although this is very rare ([Stonell 2000](#)). It may also occur with vomiting, even when an anaesthetic has not been administered, but again this is rare. However, vomiting in labour is quite common but there is no evidence that reducing the incidence of vomiting in labour will reduce the incidence of gastric aspiration during general anaesthesia should it be required.

Women in labour are thought to be at increased risk of gastric aspiration because progesterone (a hormone released in greater amounts during pregnancy and labour) causes relaxation of smooth muscle which slows down of fluid passing out of the stomach ([Carp 1992](#)). Other hormones and metabolic changes may also contribute to added risk ([Christofides 1982](#); [Smith 1995](#)). Furthermore, the use of opioid drugs for pain relief in labour, such as pethidine, further reduces gastric emptying time ([Anderson 1998](#); [Chern-Hughes 1999](#)).

Gastric acid is secreted in response to food and fluids entering the stomach, and withholding food and fluids are believed to reduce the volume and acidity of the stomach contents ([Power 1987](#)), although prolonged starvation stimulates acid secretion in the stomach. Hence, women in labour have increased gastric acid secretion and delayed gastric emptying, so both the volume and pH conditions predispose to increased risk of gastric aspiration. Routinely withholding food and fluids from women in labour has been standard practice in many hospitals in the UK ([DH 1989](#); [Hester 1977](#)), the USA ([Hawkins 1998](#)), and elsewhere ([Schneck 1999](#)), following the recommendation of Mendelsohn in 1946 ([Mendelsohn 1946](#)). The debate over the effectiveness of these measures continues ([Ludka 1993](#); [Pengelley 1998a](#); [Pengelley 1998b](#); [Pengelley 1998c](#); [Pengelley 1998d](#); [Pengelley 1998e](#); [Sharp 1997](#); [Sleuthal 1999](#)) and the discussion centres around two areas. Firstly, do these interventions reduce the incidence of gastric aspiration? Secondly, what are the adverse effects for women and their babies during labour? A Cochrane review has been undertaken to assess the effectiveness of preoperative fasting before general surgery ([Brady 2003](#)), and a review is being undertaken on restricting oral fluid and food intake in labour ([Singata 2002](#)).

Incidence

The incidence of gastric aspiration during anaesthesia in labour is not known, but the death of a mother from anaesthesia may happen about once every million maternities in well-resourced services. Maternal mortality from gastric aspiration has reduced dramatically in recent years in high-income countries and is now extremely low ([DH 1989](#); [DH 1991](#); [DH 1998](#); [DH 2001](#); [DH 2004](#); [Hawkins 1998](#)). In the UK, the number of maternal deaths directly associated with anaesthesia has fallen from six in three years (1985 to 1987), to one in three years (1994 to 1996; [DH 1998](#)) and three in three years (1997 to 1999), which is around one per million maternities ([DH 2001](#)). None of these latter deaths were due to gastric aspiration. The reduction in maternal deaths

from Mendelsohn's syndrome (Mendelsohn reported 66 cases of gastric aspiration in 44,016 pregnant women between 1932 and 1945 with two deaths: [Mendelsohn 1946](#)) is most likely due to improved anaesthetic techniques, better drugs, and the greater availability of experienced obstetric anaesthetists. Identifying women at increased risk of aspiration, e.g. women who are obese, smoke, have past obstetric history, past medical history, diabetes or hypertension, may also have helped ([Berg 1996](#); [DH 2001](#); [Hawkins 1997](#); [Roonnarinesingh 1998](#)).

Interventions

There are two basic interventions used to try to prevent gastric aspiration, or reduce its impact in normal labour. These interventions are based on those used in general surgery, namely: (1) not permitting the person to take food or fluids ('nil by mouth') for six hours prior to anaesthesia ([Brady 2003](#); [Hawkins 1997](#)) which means that food and fluids are withheld during labour ([Singata 2002](#)).

(2) acid prophylaxis, the administration of drugs to reduce the volume and/or acidity of the stomach contents. The four types of drugs used, and their potential adverse effects, are:

(a) antacids (e.g. magnesium trisilicate, sodium citrate)

Antacids are given orally. They are alkaline substances which reduce or neutralise the acidity of the stomach contents, thus reducing the adverse effects of acidity should aspiration occur. There are both particulate antacids (for example, magnesium trisilicate) and non-particulate or soluble antacids (for example, sodium citrate). Soluble drugs are thought likely to have fewer side-effects as particles in solution can cause added problems if aspiration occurs. The neutralising effect of antacids has been shown to last for about 15 to 20 minutes in women in labour ([Brock-Utne 1989](#)) and so repeated doses are used. Adverse effects of the drugs may include belching and diarrhoea ([BNF 1995](#)).

(b) H₂ receptor antagonists (e.g. cimetidine, ranitidine)

H₂ receptor antagonists are generally given orally. They inhibit the secretion of acid into the stomach which reduces the volume and acidity of the stomach contents ([Thwaites 1999](#)). This action is not immediate and so H₂ receptor antagonists are often used in combination with antacids. Adverse effects of the drugs may include dizziness, fatigue, rashes, headaches, digestive tract disturbances and also the drugs interact with warfarin (a drug given for blood clotting problems) ([BNF 1995](#)).

(c) dopamine antagonists as antiemetics (e.g. metoclopramide)

Dopamine antagonists are given intramuscularly. They inhibit vomiting and accelerate gastric emptying, and seem to be active from 20 minutes to about two hours after injection ([Rowe 1997](#)). Adverse effects of these drugs may include drowsiness, restlessness, diarrhoea and heart beat irregularities ([BNF 1995](#)).

(d) proton-pump inhibitors (e.g. omeprazole)

Proton-pump inhibitors are given orally and block the production of stomach acid by interfering with the pump which secretes protons (acid) into the stomach ([Browne 1993](#)). The most common adverse effects include rashes, diarrhoea, headaches, nausea, constipation, wind (flatulence), abdominal pain, dizziness, nausea, vomiting,

constipation and occasionally they can cause allergic reactions ([BNF 1995](#)).

Measuring outcomes

As maternal morbidity and mortality from gastric aspiration are rare, and individual trials are unlikely to have sufficient power to assess this outcome, studies in this area often use surrogate measures of effectiveness. Two measures generally used are 1) pH over 2.5 (i.e. less acidic), and 2) gastric volume less than 25 ml. These estimations are based on animals studies, e.g. in monkeys in the 1970s, and are extrapolated to humans ([Roberts 1976](#)). Later studies in rats suggested that problems are more likely to relate to acidity, and that raising the pH above 2.5 and thus decreasing acidity, was thought to be the more important surrogate measure ([James 1984](#); [Schwartz 1986](#)). However, it has since been recognised that the effectiveness of these agents in raising the stomach pH does not necessarily mean they will affect the incidence and severity of gastric aspiration ([Johnson 1989](#)). A literature search found no sound evidence that these measures are appropriate surrogates for morbidity from gastric aspiration in women, with the additional concern that both measurements require invasive tests. These data from trials will be reported in this review but with some qualification regarding interpretation.

Potential adverse effects

Apart from the potential of adverse effects from these drugs listed above, there are other possible effects that may arise from their use in normal labour. These potential adverse effects on women and babies may include stress, interfering with women's coping abilities, and some women may find taking these drugs unpleasant ([Simkin 1986](#)).

The aim of this review is to assess the effectiveness of routine prophylactic drugs given to all women during normal labour to reduce the adverse effects of gastric aspiration. Gastric aspiration is most likely to occur during general anaesthesia for caesarean section or for manual removal of retained placenta. Women being given these drugs specifically because they are to have an elective or emergency caesarean section will not be included in this current review, as this question is being addressed by another Cochrane review looking at drugs at caesarean section for preventing nausea, vomiting and aspiration pneumonitis ([Paranjothy 2004](#)).

OBJECTIVES

To assess the effectiveness and safety, for women and babies, of routine prophylactic drugs given to women during normal labour to reduce the incidence of gastric aspiration and the effects of inhaling stomach contents (gastric aspiration/Mendelsohn's syndrome). The review considered those interventions given routinely to all women in labour compared with no interventions/placebo, compared with other drugs for this purpose, and compared with combinations of drugs for this purpose. Subanalysis on women considered at high risk of needing anaesthesia would have been undertaken, but there were insufficient data available.

METHODS

Criteria for considering studies for this review

Types of studies

Randomised controlled trials and quasi-randomised controlled trials.

Types of participants

Women in normal labour who have a singleton full-term pregnancy with the baby in the vertex (head first) position (whether the woman is able to eat or not, whether she is given pethidine or other narcotic drugs for pain relief or not).

Types of interventions

Any drug, by any route of administration, with any dose, given with the aim of reducing the risk of inhaling stomach contents (gastric aspiration). Given prophylactically to:

1. women who are able to eat and drink at will;
2. women who were not permitted food and/or fluids during labour;
3. women who have had pethidine, or other narcotic drugs during labour;
4. women who have not had pethidine, or other narcotic drugs during labour.

The drug categories include:

- (i) antacids - a) particulate (e.g. magnesium hydroxide, magnesium trisilicate) and b) non-particulate (e.g. sodium citrate);
- (ii) H₂ receptor antagonists (e.g. cimetidine, ranitidine);
- (iii) dopamine antagonists (e.g. metoclopramide);
- (iv) proton-pump inhibitors (e.g. omeprazole).

These drugs were compared with placebo/no treatment and compared with each other, where the data permitted. Combinations of antacids with H₂ receptor antagonists or with dopamine antagonists or with proton-pump inhibitors, would also have been assessed, but the data were not available.

Types of outcome measures

The main primary outcome measure was the incidence of gastric aspiration in the mother. Other outcome measures were divided into maternal and fetal outcomes, and the definitions chosen by the trial authors and used by the group were used to categorise the outcomes.

Maternal

Gastric aspiration

Signs of gastric aspiration (e.g. tachycardia; dyspnoea; cyanosis; fever; cardiac failure; pulmonary oedema)

Pneumonitis/pneumonia

Adult respiratory distress syndrome

Ventilation

Admission to intensive care

Adverse effects of drugs (including belching, diarrhoea, dizziness, fatigue, rashes, headache, heart beat abnormalities, constipation, flatulence, abdominal pain, nausea, vomiting, allergic reactions)

Haemorrhage (blood loss over 1000 ml)

Morbidity

Mortality

Stomach acidity at time of anaesthesia

Volume of stomach contents at time of anaesthesia

Women's views of the interventions, outcomes and experience of birth

Caesarean section

General anaesthesia

Vomiting (post hoc)

Neonatal

Apgar score

Admission to special care

Adverse effects of drug

Morbidity

Mortality

Establishment of breastfeeding

Long-term effects

Search methods for identification of studies

Electronic searches

We searched the Cochrane Pregnancy and Childbirth Group Trials Register (December 2005). We updated this search on 1 October 2009 and added the results to [Studies awaiting classification](#).

The Cochrane Pregnancy and Childbirth Group's Trials Register is maintained by the Trials Search Co-ordinator and contains trials identified from:

1. quarterly searches of the Cochrane Central Register of Controlled Trials (CENTRAL);
2. weekly searches of MEDLINE;
3. handsearches of 30 journals and the proceedings of major conferences;
4. weekly current awareness alerts for a further 44 journals plus monthly BioMed Central email alerts.

Details of the search strategies for CENTRAL and MEDLINE, the list of handsearched journals and conference proceedings, and the list of journals reviewed via the current awareness service can be found in the 'Specialized Register' section within the editorial information about the [Cochrane Pregnancy and Childbirth Group](#).

Trials identified through the searching activities described above are each assigned to a review topic (or topics). The Trials Search Co-ordinator searches the register for each review using the topic list rather than keywords.

In addition, we searched the databases of EMBASE and CINAHL using the search strategies in [Appendix 1](#).

Searching other resources

Looking for ongoing trials in the papers reviewed provided no further information. Had there been any information about ongoing trials, we would have approached the authors or drug companies for relevant, unpublished data. The search attempted to identify all relevant studies irrespective of language. We would have assessed non-English papers if we had identified any and, if necessary, would have had them translated with the assistance of a native speaker.

Data collection and analysis

Selection of studies

The two review authors independently assessed each citation for inclusion in the review. Differences were resolved by discussion and the opinion of a third party was used to help resolve one issue about inclusion. Here, we decided to write to the study authors for clarification hence this study, with two publications, is in 'Studies awaiting assessment' ([Chesterfield 1978](#); [Chesterfield 1978b](#)).

Assessment of study quality

We independently assessed the validity of each included trial by using the criteria outlined in the Cochrane Handbook for Systematic Reviews of Interventions ([Higgins 2005](#)). We assessed each study for quality of randomisation plus concealment of allocation, blinding in the assessment of outcome and completeness of follow up.

Randomisation and allocation concealment

We both assigned a quality score for concealment of allocation to each trial, using the following criteria:

- (A) adequate concealment of allocation, such as telephone randomisation, consecutively numbered sealed opaque envelopes;
- (B) unclear whether adequate concealment of allocation;
- (C) inadequate concealment of allocation such as random number tables, sealed envelopes.

Where the method of allocation concealment was unclear, whenever possible we tried to make contact with the trial authors to provide further details.

Blinding

We both assessed blinding using the following criteria:

- 1. blinding of participants (yes/no/unclear);
- 2. blinding of caregiver (yes/no/unclear);
- 3. blinding of outcome assessment (yes/no/unclear).

Completeness of follow up

We both assessed completeness of follow up using the following criteria:

- (A) less than 5% of participants excluded;
- (B) 5% to 10% of participants excluded;
- (C) more than 10% and up to and including 20% of participants excluded.

We excluded studies if:

- 1. more than 20% of participants excluded;
- 2. more than 20% of analysis not in randomised groups and not possible to restore participants to correct group;
- 3. large difference (more than 10%) in withdrawal of participants between groups.

We analysed the data on an intention-to-treat basis. Where data were missing, we sought clarification from one trial author.

Data extraction

We both extracted data independently and any discrepancies were resolved through discussion. Further clarification from the trial

authors was required from one author. We undertook double-data entry onto the Review Manager software ([RevMan 2003](#)), and checked for accuracy.

Statistical analyses

We carried out the statistical analyses using Review Manager ([RevMan 2003](#)). For dichotomous data, we present results as summary relative risk with 95% confidence intervals. Had suitable data been available we would also have presented information as risk differences and numbers needed to treat. There were insufficient data to require tests of heterogeneity between trials to assess the significance of any differences between trials. In the absence of heterogeneity, we have pooled results using a fixed-effect model. If heterogeneity had been detected, we would have explored possible causes and would have performed subgroup analyses for the main outcomes. We did not require to model heterogeneity that was not explained by subgroup analyses using random-effects analysis as there were insufficient data.

Sensitivity analyses

There were insufficient data to carry out sensitivity analysis to explore the effect of trial quality on effect size. The predefined criteria for sensitivity analysis would have included all aspects of the quality assessments listed above. This would have involved analysis based on an A, B, or C rating of allocation concealment and completeness of follow up. The results of high-quality studies (rated A) would have been compared with those of poorer quality studies (rated B and C).

Subgroup analyses

The prespecified subgroup analysis would have been based on two groups, which would have been analysed separately.

- 1. Drugs given prophylactically to all women in normal labour.
- 2. Drugs given prophylactically to women considered at high risk of needing anaesthesia during or shortly after labour.
- 3. Drugs given prophylactically to women in normal labour where trials were undertaken in settings where acid prophylaxis is routinely given once the decision to induce anaesthesia is taken.

For each set of studies, the following comparisons would have been performed had there been sufficient data:

- 1. any group of drugs versus placebo or no treatment;
- 2. drugs from one group versus drugs from another group;
- 3. comparison of drugs within groups;
- 4. comparison of a combination of drug groups (e.g. antacids and H₂ receptor antagonists) versus placebo or no treatment, or against other drugs.

RESULTS

Description of studies

Our search of the Cochrane Pregnancy and Childbirth Group Trials Register identified nine studies for possible inclusion ([Belfast 1984](#); [Belfast 1985](#); [Cardiff 1971](#); [Chesterfield 1978](#); [Hull 2003](#); [London 1985](#); [Manchester 1973](#); [Manchester 1978](#); [Winston-Salem 1980](#)). Of these, four met the inclusion criteria initially, but one study ([London 1985](#)) reported results in a form which could not be used and so this study was subsequently excluded, leaving three included

studies (Belfast 1984; Cardiff 1971; Winston-Salem 1980). For one study (Chesterfield 1978), it was unclear if women having elective caesarean sections were included or not, so this study has been put in the [Studies awaiting classification](#) section whilst we contact the authors for clarification. Overall, therefore, there were five excluded studies (Belfast 1985; Hull 2003; London 1985; Manchester 1973; Manchester 1978). For reasons for exclusion see [Characteristics of excluded studies](#). The additional searches of EMBASE and CINAHL did not identify any further studies. (Two reports from an updated search in October 2009 have been added to [Studies awaiting classification](#).)

Of the included studies, one study with 578 participants compared three antacids with giving nothing and with each other (Winston-Salem 1980); there were no studies that compared H₂ receptor antagonists with placebo/no intervention; one study with 1287 participants compared an H₂ receptor antagonists with an antacid (Belfast 1984); one study with 600 women compared two dopamine antagonists with saline and with each other (Cardiff 1971); there were no studies identified that assessed proton-pump inhibitors.

Risk of bias in included studies

None of the studies were assessed as overall good quality using the criteria discussed in the methods section, mostly due to lack of information being available. In one study (Winston-Salem 1980), there is a considerable discrepancy in the numbers of women allocated to the three groups. It would be quite unlikely for differences this large to arise by chance, and hence there is concern that there may have been problems with randomisation process in this trial.

Randomisation and allocation

Two trials were unclear on their methods (Belfast 1984; Cardiff 1971) and one trial used an inadequate method (Winston-Salem 1980).

Blinding

One trial reported being double blind (Cardiff 1971) and the other two trials did not report on blinding (Belfast 1984; Winston-Salem 1980).

Attrition

In one trial, 16 out of 600 women (2.7%) were excluded from the analysis (this was similar across groups (grade A) (Cardiff 1971). In the other two studies, the attrition rate was unclear (Belfast 1984; Winston-Salem 1980).

Intention-to-treat analysis

None of the three studies mentioned intention-to-treat analysis, nor whether any participants received a different intervention from that to which they were allocated, it appeared that they did not.

Effects of interventions

Three trials were included, involving 2465 women. Each of the three trials assessed a different comparison and there were no trials involving proton-pump inhibitors. None of the trials assessed gastric aspiration as an outcome, nor any of the major consequences of gastric aspiration e.g. cyanosis, pneumonia, adult respiratory syndrome. All these outcomes are very rare and the included trials were really too small to consider them. The included

trials mainly assessed vomiting, clearly trialists thinking that reducing the incidence of vomiting would reduce the incidence of gastric aspiration. The validity of this assumption is unclear.

Antacids versus placebo/no treatment or compared with other antacids

Antacids appeared to reduce vomiting compared with no intervention (relative risk (RR) 0.46, 95% confidence interval (CI) 0.27 to 0.77, n = 578, one trial: graph 01.01).

There was no significant difference in the incidence of vomiting between three individual antacids tested in one study (Gelsuil, Maalox and Mylanta II), though the numbers in each group were small and the data came from just one trial (Winston-Salem 1980).

H₂ receptor antagonists versus antacids

There appeared to be no significant difference between H₂ receptor antagonists compared with antacids in terms of vomiting, caesarean section, emergency general anaesthetic, postpartum haemorrhage and stillbirth, identified in the one trial that addressed these issues, though the number of participants was insufficient to be able to comment with any degree of assurance (1287 women: graphs 11.01 to 11.07). The one study in this comparison (Belfast 1984) also assessed the pH and volume of the gastric contents but reported findings using mean values and ranges, and graphical representation. They reported that both drugs raised the gastric pH above 2.5 in most women, with the antacid showing a slightly better response, but also with a larger gastric volume compared with the H₂ receptor antagonist.

Dopamine antagonists versus placebo/no treatment and other dopamine antagonists

Dopamine antagonists appeared to reduced vomiting compared with placebo when given as an antiemetic alongside 100 mg pethidine (RR 0.40 95% CI 0.23 to 0.68, n = 584, one trial: graph 20.01). The trial showed no significant difference in Apgar scores less than seven at one minute, nor in perinatal death (graphs: 20.06; 20.07), though the number of participants was insufficient to be able to comment with any degree of assurance.

When metoclopramide was compared with perphenazine in the same trial, there was no significant difference in vomiting, Apgar scores less than seven at one minute, nor perinatal death, though the number of participants was insufficient to be able to comment with any degree of assurance (n = 393, graphs: 21.01 to 21.06).

DISCUSSION

There is surprisingly little data on the use of drugs given to women in normal labour to try to prevent gastric aspiration and Mendelsohn's syndrome, considering the wide spread use of these drugs routinely in labour in many countries worldwide. Also surprisingly, there is the lack of evidence of any impact of these drugs on the usual surrogate measures for gastric aspiration, namely, the pH and volume of stomach contents, with only one trial assessing these outcomes (Belfast 1984). The included studies in this review mostly assessed vomiting, but there is a lack of evidence linking this to gastric aspiration. Considering the rise in caesarean section rates worldwide over recent years (Thomas 2001), there seems to have been no reported corresponding rise in gastric aspiration or Mendelsohn's syndrome (DH 2004).

The studies identified were of questionable quality and only two trials were found which considered the placebo/no treatment comparisons that we wished to address ([Cardiff 1971](#); [Winston-Salem 1980](#)). One trial compared antacids with placebo/no treatment and found that the antacids seemed to reduce the incidence of vomiting ([Winston-Salem 1980](#)) though here are some concerns around the randomisation procedure used in this study; no trials compared H₂ receptor antagonists against placebo/no treatment; one trial compared dopamine antagonists given with pethidine compared with placebo given with pethidine and found the dopamine antagonist seemed to reduce the incidence of vomiting ([Cardiff 1971](#)); and there were no trials at all identified on proton-pump inhibitors. One trial compared H₂ receptor antagonists with antacids ([Belfast 1984](#)) and one trial compared two different dopamine antagonists ([Cardiff 1971](#)). As a result, there is insufficient evidence to be able to draw conclusions with any degree of assurance.

An alternative way of using these drugs to help to reduce gastric aspiration may be to give them to women once it has been agreed to give a general anaesthetic for either caesarean section or manual removal of placenta. Another Cochrane review is assessing the evidence on this alternative ([Paranjothy 2004](#)).

AUTHORS' CONCLUSIONS

Implications for practice

There is no evidence to support the routine administration of drugs to women in normal labour to reduce the incidence of gastric aspiration or Mendelsohn's syndrome.

Implications for research

In well-resourced settings, given that the incidence of gastric aspiration and Mendelsohn's syndrome is extremely low, together with the shift to regional anaesthesia in place of general anaesthesia for caesarean delivery, there seems little need to research this question further. The administration of these drugs to women once a decision to use general anaesthesia (for a caesarean or manual removal of placenta) is an alternative worth investigating, initially through a systematic review of trials already undertaken ([Paranjothy 2004](#)). It may be important to address these issues specifically in poorly-resourced settings.

[Note: The four citations in the awaiting classification section of the review may alter the conclusions of the review once assessed.]

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As part of the pre-publication editorial process, this review has been commented on by two peers (an editor and referee who are external to the editorial team), one or more members of the Pregnancy and Childbirth Group's international panel of consumers and the Group's Statistical Adviser.

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CHARACTERISTICS OF STUDIES

Characteristics of included studies [ordered by study ID]

Belfast 1984

Methods	Allocation: by random mix in ratio of approximately 3:1 in favour of ranitidine. Blinding: unclear. Attrition: unclear. ITT: unclear.
Participants	Women in active labour, more than 36 weeks' gestation without severe IUGR, diabetes or pre-eclampsia. 1287 women participated.
Interventions	Comparing an H2 receptor antagonist with an antacid. Intervention: ranitidine, 150 mg every 6 hours, N = 909. Control: magnesium trisilicate, 20 ml every 2 hours, N = 378. In both groups, if a GA was required a 30 ml dose of magnesium trisilicate was given.
Outcomes	Vomiting. CS.

Belfast 1984 (Continued)

PPH.
Emergency GA.
Stillbirth.
Volume.

Notes

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

Cardiff 1971

Methods Allocation: women were allocated to 1 of 3 in accordance with random sequence table.
Concealment was not clear.
Blinding: double blind.
Attrition: 2.7% excluded.
ITT: unclear.

Participants Women in labour being given 100 mg pethidine IM, expected to give birth vaginally.
600 women participated and 16 were excluded because they had a caesarean section.

Interventions Comparing two dopamine antagonists as antiemetics.
Intervention 1: metoclopramide, 10 mg IM, N = 196.
Intervention 2: perphenazine, 5 mg IM, N = 197.
Control: saline, 2 ml IM, N = 191.

Outcomes Vomiting.
Apgar < 7 at 1 minute.
Perinatal death.

Notes

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	B - Unclear

Winston-Salem 1980

Methods Allocation: drawn from a hat - open.
Blinding: unclear.
Attrition: unclear.

Winston-Salem 1980 (Continued)

ITT: unclear.

Participants	All women giving birth over a one month period. 578 women participated.
Interventions	Comparing 3 antacids with each other and with nothing. Every 3 hours: 1) gelusil, 30 ml every 3 hours, N = 170. 2) maalox, 30 ml every 3 hours, N = 130. 3) mylanta II, 30 ml every 3 hours, N = 155. Control: nothing, N = 123.
Outcomes	Vomiting.
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	High risk	C - Inadequate

CS: caesarean section

GA: general anaesthetic

IM: intramuscularly

ITT: 'intention-to-treat' analysis

IUGR: intrauterine growth restriction

PPH: postpartum haemorrhage

Characteristics of excluded studies [ordered by study ID]

Study	Reason for exclusion
Belfast 1985	Women included in this trials were at increased risk. It included women less than 36 weeks' gestation, with suspected IUGR, pre-eclampsia and diabetes.
Hull 2003	The intervention studied was P6 acupressure for nausea and vomiting in labour, not a drug intervention.
London 1985	Inclusion criteria were fine but the data were not in a form that could be used. Study reported percentages of women feeling and being sick, and with Apgar scores reported only means values with no information on SD or SE.
Manchester 1973	Inclusion criteria were fine but the study did not report any clinical outcomes.
Manchester 1978	The study population was pregnant women with heartburn.

IUGR: intrauterine growth restriction

SD: standard deviation

DE: standard error

DATA AND ANALYSES

Comparison 1. Antacids versus placebo or no treatment

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Vomiting	1	578	Risk Ratio (M-H, Fixed, 95% CI)	0.46 [0.27, 0.77]

Analysis 1.1. Comparison 1 Antacids versus placebo or no treatment, Outcome 1 Vomiting.

Comparison 2. Gelsuil versus Maalox

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Vomiting	1	300	Risk Ratio (M-H, Fixed, 95% CI)	0.83 [0.39, 1.75]

Analysis 2.1. Comparison 2 Gelsuil versus Maalox, Outcome 1 Vomiting.

Comparison 3. Gelsuil versus Mylanta II

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Vomiting	1	325	Risk Ratio (M-H, Fixed, 95% CI)	1.32 [0.58, 2.99]

Analysis 3.1. Comparison 3 Gelsuil versus Mylanta II, Outcome 1 Vomiting.

Comparison 4. Maalox versus Mylanta II

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Vomiting	1	285	Risk Ratio (M-H, Fixed, 95% CI)	1.59 [0.69, 3.65]

Analysis 4.1. Comparison 4 Maalox versus Mylanta II, Outcome 1 Vomiting.

Comparison 11. H2 receptor antagonists versus antacids

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Vomiting	1	1287	Risk Ratio (M-H, Fixed, 95% CI)	0.96 [0.73, 1.27]
3 Caesarean section	1	1287	Risk Ratio (M-H, Fixed, 95% CI)	0.93 [0.59, 1.47]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
4 Emergency general anaesthetic	1	1287	Risk Ratio (M-H, Fixed, 95% CI)	0.92 [0.62, 1.35]
5 Postpartum haemorrhage	1	1287	Risk Ratio (M-H, Fixed, 95% CI)	0.83 [0.08, 9.14]
7 Stillbirth	1	1287	Risk Ratio (M-H, Fixed, 95% CI)	0.69 [0.17, 2.89]

Analysis 11.1. Comparison 11 H2 receptor antagonists versus antacids, Outcome 1 Vomiting.

Analysis 11.3. Comparison 11 H2 receptor antagonists versus antacids, Outcome 3 Caesarean section.

Analysis 11.4. Comparison 11 H2 receptor antagonists versus antacids, Outcome 4 Emergency general anaesthetic.

Analysis 11.5. Comparison 11 H2 receptor antagonists versus antacids, Outcome 5 Postpartum haemorrhage.

Analysis 11.7. Comparison 11 H2 receptor antagonists versus antacids, Outcome 7 Stillbirth.

Comparison 20. Dopamine antagonists versus placebo or no treatment - given alongside pethidine

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Vomiting	1	584	Risk Ratio (M-H, Fixed, 95% CI)	0.40 [0.23, 0.68]
6 Apgar < 7 at 1 minute	1	584	Risk Ratio (M-H, Fixed, 95% CI)	1.02 [0.62, 1.69]
7 Perinatal death	1	584	Risk Ratio (M-H, Fixed, 95% CI)	1.22 [0.24, 6.21]

Analysis 20.1. Comparison 20 Dopamine antagonists versus placebo or no treatment - given alongside pethidine, Outcome 1 Vomiting.

Analysis 20.6. Comparison 20 Dopamine antagonists versus placebo or no treatment - given alongside pethidine, Outcome 6 Apgar < 7 at 1 minute.

Analysis 20.7. Comparison 20 Dopamine antagonists versus placebo or no treatment - given alongside pethidine, Outcome 7 Perinatal death.

Comparison 21. Metoclopramide versus Perphenazine - given alongside pethidine

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Vomiting	1	393	Risk Ratio (M-H, Fixed, 95% CI)	1.45 [0.64, 3.32]
3 Perinatal death	1	393	Risk Ratio (M-H, Fixed, 95% CI)	0.25 [0.03, 2.23]
6 Apgar < 7 at 1 minute	1	393	Risk Ratio (M-H, Fixed, 95% CI)	0.83 [0.47, 1.47]

Analysis 21.1. Comparison 21 Metoclopramide versus Perphenazine - given alongside pethidine, Outcome 1 Vomiting.

Analysis 21.3. Comparison 21 Metoclopramide versus Perphenazine - given alongside pethidine, Outcome 3 Perinatal death.

Analysis 21.6. Comparison 21 Metoclopramide versus Perphenazine - given alongside pethidine, Outcome 6 Apgar < 7 at 1 minute.

APPENDICES

Appendix 1. EMBASE and CINAHL search strategies

EMBASE (1974 to April 2005)

1. randomization/
2. double blind procedure/
3. crossover procedure/
4. intermethod comparison/
5. single blind procedure/

6. clinical study/
7. controlled study/
8. randomized controlled trial/
9. (clin\$ adj2 trial\$).tw.
- 10.((singl\$ or doubl\$ or trebl\$ or tripl\$) adj2 (blind\$ or mask\$)).tw.
- 11.exp clinical trial/
- 12.placebo/
- 13.placebo\$.tw.
- 14.random\$.tw.
- 15.comparison/
- 16.drug comparison/
- 17.follow up/
- 18.evaluation.mp. and follow up/
- 19."evaluation and follow up"/
- 20.exp "drug control"/
- 21.drug screening/
- 22.prospective study/
- 23.major clinical study/
- 24.(control\$ or prospectiv\$ or volunteer\$).tw.
- 25.or/1-17
- 26.or/18-24
- 27.25 or 26
- 28.exp Proton-Pump-Inhibitor/
- 29.exp Dopamine-Receptor-Blocking-Agent
- 30.exp Histamine-H2-Receptor-Antagonist
- 31.exp Antacid-Agent
- 32.exp Childbirth
- 33.labor or labour.tw.
- 34.Aspiration-Pneumonia-PC
- 35.28 or 29 or 30 or 31
- 36.32 or 33
- 37.35 and 36
- 38.34 and 36
- 39.37 or 38
- 40.39 and 27
- 41.limit 40 to human

CINAHL (1982 to April 2005)

1. exp Antacids/
2. exp Histamine H2 Antagonists/
3. exp Dopamine Antagonists/
4. exp Antiemetics/
5. 1 or 2 or 3 or 4
6. exp Childbirth/
7. (labour or labor).af.
8. 6 or 7
9. 5 and 8
- 10.exp Aspiration/dt, pc, th [Drug Therapy, Prevention and Control, Therapy]
- 11.10 and 8
- 12.9 or 11

WHAT'S NEW

Date	Event	Description
1 October 2009	Amended	Search updated. Two reports added to Studies awaiting classification (Frame 1984; Paech 2008).

HISTORY

Protocol first published: Issue 2, 2005

Review first published: Issue 3, 2006

Date	Event	Description
18 February 2008	Amended	Converted to new review format.
28 April 2006	New citation required and conclusions have changed	Substantive amendment

CONTRIBUTIONS OF AUTHORS

Gill Gyte wrote the first draft of the review, and Yana Richens made changes. Both authors assessed the trials and discussed the results and conclusions. The final version was agreed by both authors.

DECLARATIONS OF INTEREST

None known.

SOURCES OF SUPPORT

Internal sources

- University College Hospitals London, UK.

External sources

- No sources of support supplied

INDEX TERMS

Medical Subject Headings (MeSH)

*Labor, Obstetric; Antacids [therapeutic use]; Antiemetics [therapeutic use]; Histamine H2 Antagonists [therapeutic use]; Obstetric Labor Complications [*prevention & control]; Pneumonia, Aspiration [*prevention & control]; Randomized Controlled Trials as Topic; Vomiting [prevention & control]

MeSH check words

Female; Humans; Pregnancy