Fundoplication versus post-operative medication for gastro-oesophageal reflux in children with neurological impairment undergoing gastrostomy (Review)

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TABLE OF CONTENTS

[Intervention Review]

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ABSTRACT

Background

Children with neurological impairments (NI) frequently experience feeding difficulties which can lead to malnutrition and growth failure. Gastrostomy feeding is now the preferred method of providing nutritional support to children with NI who are unable to feed adequately by mouth. Complications may arise as a result of gastrostomy placement and the development or worsening of gastro-oesophageal reflux (GOR) has been widely reported. This has led to the frequent use of surgical anti-reflux treatment in the form of a fundoplication, or other Anti-Reflux Procedures. Fundoplication is associated with a high recurrence rate, surgical failure and significant morbidity and mortality.

Since Proton Pump Inhibitors (PPIs) were introduced in the 1990s they have come to play a larger part in the medical management of GOR in children with NI. Uncontrolled studies suggest that PPIs may be a safe, appropriate treatment for GOR. Other agents currently used include milk thickeners, acid suppression drugs, acid buffering agents, gut motility stimulants and sodium alginate preparations.

There are risks and benefits associated with both surgical and medical interventions and further comparison is necessary to determine the optimal treatment choice.

Objectives

To compare the effectiveness of anti-reflux surgery and anti-reflux medications for children with NI and GOR who are undergoing placement of a gastrostomy feeding tube.

Search strategy

We searched the Cochrane Central Register of Controlled Trials (CENTRAL) up to Issue 2, 2006, MEDLINE (1966 to June 2006), EMBASE (1980 to week 33, 2006), CINAHL (1982 -to May, week 4, 2006), LILACS (1982 to June 2006), ISI Web of Science (1970 to June 2006) and the Child Health Library (searched June 2006). We also performed online searches of trial registries, medical journals, conference proceedings, dissertations and theses. Specialists in the medical and industry setting were contacted for knowledge of completed or ongoing trials.

Selection criteria

We sought to include only randomised controlled trials that recruited children up to the age of 18 years with NI and GOR who were undergoing gastrostomy tube insertion.

Data collection and analysis

Review authors worked independently to select trials; none were identified.

Main results

No trials were identified that satisfied criteria for this review.

Authors' conclusions

There remains considerable uncertainty regarding the optimal treatment when faced with the decision of fundoplication surgery versus anti-reflux medications for gastro-oesophageal-reflux in the child with neurological impairment who is undergoing gastrostomy insertion. There is a need for robust scientific evidence in order to provide data on the comparable risks or benefits of the two interventions.

PLAIN LANGUAGE SUMMARY

Is surgery or medical treatment more effective in treating acid reflux in brain damaged children having a feeding tube inserted

Children with cerebral palsy often have oral motor impairment and need help with eating and drinking. Frequently this entails surgery to place a feeding tube (gastrostomy) directly into their stomach. They may also be found to have gastro-oesophageal reflux (where stomach acid flows back up into the oesophagus) which can be made worse by gastrostomy surgery. Reflux can be treated either with additional surgery at the same time as the gastrostomy (a fundoplication) or with anti-reflux medications. This review was carried out to determine which was the safest and most effective form of treatment. We found no randomised controlled trials that provided scientific evidence on which to base a conclusion, which highlighted the need for a trial comparing the two interventions.

BACKGROUND

Description of the condition

Children with neurological impairments (NI) frequently experience profound feeding difficulties which can lead to malnutrition and growth failure. These are often seen as inevitable consequences of many neurological disorders due to their associated physical abnormalities, communication difficulties and motor impairments (Samson-Fang 2003).

The causes of malnutrition in children with NI are multifactorial. Physiological abnormalities may manifest as oro-motor dysfunction and the associated incoordination of oropharyngeal reflexes (Puntis 2000) (Wadie 2002). Children may also be severely compromised in their inability to feed independently and subsequently experience frustration and behavioural problems (Puntis 2000). Many of the factors that lead to malnutrition and failure to thrive dictate a need to find alternate measures of providing adequate nutrition, such as an enteral feeding tube (Wadie 2002).

Enteral feeding is considered to be justified to prevent or reverse growth failure when other efforts to increase nutritional intake, such as dietary supplementation, have failed (Puntis 2000). The placement of a gastrostomy feeding tube is now the preferred method of providing long term nutritional support to children with neurological impairments. A gastrostomy is considered when enteral feeding is required beyond the short term period (greater than 6 weeks), when there are prolonged feeding times, inadequate weight gain and an unsafe swallow (Sullivan 1997) (Samson-Fang 2003). The use of gastrostomy tube feeding has previously been shown to increase weight, improve overall health and decrease feeding times for children with neurological impairment (Sullivan 2005). It has also demonstrated a significant, measurable improvement in the quality of life of carers (Sullivan 2004). The literature on prevalence of gastrostomy insertion in this population is limited but a study carried out in the UK by Sullivan in 2000 showed that 8% of children with neurological impairments were gastrostomy fed (Sullivan 2000).

Gastrostomy tube insertion can be performed by laparotomy, la-

parascopically or endoscopically and the most favoured procedure for tube placement has become the Percutaneous Endoscopic Gastrostomy (PEG) which was introduced by Gauderer in 1981 (Gauderer 1981). The PEG is associated with decreased morbidity in comparison to other techniques for gastrostomy insertion and has been assessed to be both efficient and cost-effective (Samuel 2002), (Byrne 1990). Complications may arise as a result of gastrostomy placement including infection, perforation, bleeding, tube migration/dislocation, intestinal fistulas and obstruction (Razeghi 2002). In addition the development or worsening of gastro-oesophageal reflux has been widely reported and is considered to be one of the long-term sequelae of gastrostomy placement (Razeghi 2002) (Mollitt 1985).

Gastro-oesophageal reflux (GOR) in children with neurological impairments is a well described phenomenon. It is attributed to a motility disturbance affecting the oesophagus and the lower oesophageal sphincter (LES) mechanism, and leads to retrograde, involuntary, effortless regurgitation of gastric contents into the oesophagus (Richards 2001) (Rosen 2000) (Vandenplas 2000). The prevalence of GOR among children with NI has been reported to range from 14-75% depending on the diagnostic criteria of GOR used, highlighting the fact that the role of reflux in this group is not well understood and may have a wide range of manifestations and symptoms (Sullivan 1992), (Gangil 2001), (Reyes 1993). The pathophysiological mechanisms of gastro-oesophageal reflux are multifarious. The underlying neurological damage may cause delayed gastric emptying and oesophageal dysmotility, while scoliosis, seizures, spasticity of abdominal musculature or constipation can all cause increased abdominal pressure. Due to their often profound physical disabilities, many children spend long periods in the supine position, thus minimising the effect of gravity to aid oesophageal clearance (Vandenplas 2000) (Halpern 1991) (Spitz 1993).

Description of the intervention

For the child with neurological impairments who has pre-existing gastro-oesophageal reflux and is referred for the insertion of a gastrostomy, the placement itself can lead to a worsening of symptoms with severe vomiting and aspiration (Wheatley 1991), (Mollitt 1985). Historically, medical management of GOR in the child with NI has had a high failure rate (Cheung 2001), (Gold 2002). This has led to the frequent use of surgical treatment in the form of an Anti-Reflux Procedure (ARP) such as a Nissens, Thal, Toupet or Belsey fundoplication (Ostlie 2002) (Hassall 2005). Fundoplication involves strengthening the barrier to acid reflux by wrapping the fundus of the stomach around the oesophagus at the gastro-oesophageal junction. Fundoplication procedures vary according to the degree of fundal wrap that is performed at the distal oesophagus and can range from a full 360° wrap to a partial 180° wrap depending on the operation performed (Hassall 2005). The fundoplication is designed to prevent gastro-oesophageal reflux by correcting hiatal herniation, lengthening the intra-abdominal portion of the oesophagus, tightening the crura and increasing the pressure of the lower-oesophageal sphincter (Di-Lorenzo 2002).

Despite its value in preventing gastro-oesophageal reflux, fundoplication has other consequences. It permanently alters the gastro-oesophageal anatomy and function and as has been shown in animal work, may lead to vagal nerve damage which sensitizes the emetic reflex (Richards 2000). Complications may ensue from these changes (Di-Lorenzo 2002). These may can be related to the underlying condition of the child; for example, seizure disorders or pulmonary disease may lead to increased abdominal pressure, or may arise from the effect of the surgery itself (Kimber 1998). Complications directly related to the surgery may include gas bloat syndrome, impaired gastric accommodation, gastric hypersensitivity, rapid gastric emptying (or 'dumping syndrome'), retching or dysphagia (Di-Lorenzo 2002),(Connor 2005). The challenging anatomy and physiology of this group of children mean they suffer from many conditions seemingly unrelated to GOR, such as scoliosis and epilepsy, which subsequently make it difficult for any anti-reflux intervention to be a guaranteed success. The anti-reflux procedure (fundoplication) is associated with a high recurrence rate and significant morbidity and mortality in this group of children, with a 40% surgical failure rate (Isch 1997), (Kimber 1998). Recurrent reflux post- fundoplication is experienced by 12 to 30% of children with NI, whilst 59% experience post-operative complications with a 1 to 3% mortality rate (Sullivan 1999), (Byrne 1990).

Traditional medical therapies for gastro-oesophageal reflux in this group of children include milk thickeners, acid suppression drugs (Histamine 2 Receptor Antagonists (H2RAs)), acid buffering agents (antacids), and gut motility stimulants (prokinetics). These therapies have poor response rates with studies showing that only 13% of neurologically impaired children respond completely to medical management, the remainder suffering persistence of symptoms (Cheung 2001), (Gold 2002), (Wilkinson 1981). The prokinetic drug Cisapride was withdrawn in many countries following concerns over safety and a lack of robust evidence of efficacy (Gold 2002) and there is now no effective prokinetic drug available.

Since the 1990s Proton Pump Inhibitors (PPIs) - e.g. omeprazole - have played a larger part with the medical management of GOR in children with NI. Uncontrolled studies of omeprazole have reported high levels of tolerability and efficacy suggesting high rates of healing, symptom relief and reduction of vomiting in up to 90% of participants (Hassall 2005), (Cheung 2001). PPIs are said to work by decreasing the acidity of the refluxate and decreasing gastric acid secretion volume, thereby improving gastric emptying (Hassall 2005). The long term effects of PPI use are not known at this point, but after a decade of use in the adult population, this group of medications have been found to have a good safety profile (Gold 2002).

Why it is important to do this review

This review aims to assess the efficacy of fundoplication for neurologically impaired children who are at a high risk of Anti Reflux Procedure failure compared with medical anti-reflux treatment. This is clinically important as there is some evidence of disappointing outcomes from surgery and the uncontrolled studies suggest that PPIs may be a safe, appropriate, cost-effective alternative (Heudebert 1997) (Hassall 2000), (Cheung 2001).

OBJECTIVES

To compare the effectiveness of anti-reflux surgery and anti-reflux medications for children with neurological impairment and gastro-oesophageal reflux who are undergoing placement of a gastrostomy feeding tube.

METHODS

Criteria for considering studies for this review

Types of studies

Randomised controlled trials.

Types of participants

Children up to the age of 18 years of age with neurological impairments (as defined by triallist) and gastro-oesophageal reflux who are undergoing insertion of a gastrostomy feeding tube.
Studies were excluded if there were neurologically normal children included in the trial (unless studied as a separate subgroup) or if the majority of children participating had neurological impairments that were caused by degenerative or metabolic conditions.

Types of interventions

Any type of surgical fundoplication anti-reflux procedure compared with the use of anti-reflux medications.

Types of outcome measures

Primary outcomes

Resolution of clinically measured, identifiable symptoms of GOR following gastrostomy surgery

Secondary outcomes

- Adverse events: morbidity - including wrap failure, retching, dumping, dysphagia, drug side effects and interactions
- Adverse events: mortality
- Pain: measured by parental reporting, behavioural observations
- Health related Quality of Life for child and/or carer: measured using validated scales

Search methods for identification of studies

Electronic searches

The following databases were searched:
CENTRAL (Cochrane Library), 2006 (Issue 2), Appendix 1; MEDLINE, searched through OVID, (1966 to June 2006), Appendix 2 ; EMBASE, searched through OVID, (1980 to week 33, 2006), Appendix 3; CINAHL ,searched through OVID, (1982 to May, week 4, 2006), Appendix 4; ISI Web of Science (1970 to June 2006), Appendix 5; the Child Health Library (searched June 2006), Appendix 6; the National Research Register, 2006 (Issue 2), Appendix 7; and LILACS (1982 to June 2006), Appendix 8. Please see each database's appendix for the relevant search strategy. Subject headings as well as free text terms were used where available.
Randomised controlled trials filters were used, where appropriate, with the search strategies. Bibliographies of identified articles were searched for additional studies when the original article was directly on the topic, even if not reporting a randomised controlled trial (RCT) itself. Neither language nor date restrictions were not applied.

Journals

The following journals were searched using their web-based search engines; *Journal of Paediatric Gastroenterology and Nutrition* (1982 to 2006), *Developmental Medicine and Child Neurology* (1960 to 2006), *Archives of Disease in Childhood* (1973 to 2006), *Journal of Pediatric Surgery* (1966 to 2006), *British Journal of Medicine* (1994 to 2006), *Gastroenterology* (1965-2006), *Pediatrics* (1948 to 2006), *Journal of Pediatrics* (1932 to 2006), *Surgery* (1995 to 2006), *Gastrointestinal Endoscopy* (1995 to 2006), *American Journal of Surgery* (1926 to 2006), *Child Care Health and Development* (1975 to 2006) and *Surgical Endoscopy* (1986 to 2006).

Trial registries

The following trial registries were searched online with no language or date restrictions; National Research Register (Issue 2, 2006) (see Table 7), ClinicalTrials.gov (searched June 2006), ClinicalStudyResults.org (searched June 2006), TrialsCentral (searched

June 2006), Current Controlled Trials (searched June 2006) CenterWatch (searched June 2006), Pharmaceutical Industry Clinical Trials Database (searched June 2006) and the International Federation of Pharmaceutical Manufacturers and Associations (searched June 2006).

Searching other resources

Pharmaceutical companies and equipment manufacturers

Manufacturers of relevant equipment (gastrostomy tubes) and pharmaceutical companies that produce the anti-reflux medication were contacted. These included: Wyeth UK; Altana Pharma (Kapoor 2006); Merck Pharmaceuticals (Armstrong 2006); Vygon (Edwards 2006); AstraZeneca (MacDonald 2006) and Fresenius Kabi.

The following pharmaceutical websites were also searched in June 2006:

Pharmaceutical Industry Clinical Trials Database (https://www.cmrinteract.com/clintrial/)

International Federation of Pharmaceutical Manufacturers and Associations (http://www.ifpma.org/)

GlaxoSmithKline (http://ctr.gsk.co.uk/welcome.asp)

AstraZeneca (http://www.astrazenecaclinicaltrials.com/)

Roche Pharmaceuticals (http://www.roche-trials.com/)

Grey Literature

The following databases/websites were searched in an attempt to identify grey literature in the form of theses, abstracts or conference proceedings: Index to Theses (searched June 2006), ProQuest Digital Dissertations (searched June 2006), ISI Proceedings (1990 to 2006), Cambridge Scientific Abstracts (CSA) Illumina (searched June 2006) and the System for Information on Grey Literature in Europe (SIGLE) (searched June 2006).

The review team wrote to leading experts in the field, either known to them or identified as authors of studies specific to the review topic, to ask whether they were aware of any studies not identified by the searches described above (Gottrand 2006; Spitz 2006; Lloyd 2006; Di-Lorenzo 2006; Esposito 2006; Gold 2006; Kawahara 2006; Vandenplas 2006; Gremse 2006; Hassall 2006; Orenstein 2006, Tolia 2006; Langer 2006; Heine 2006). None of these colleagues were able to report randomised controlled trials undertaken in the past or in progress.

No trials meeting the inclusion criteria were identified from this search.

Data collection and analysis

As previously stated, no trials meeting the inclusion criteria were identified from this search.

The protocol for this review was published in the Cochrane Library in Issue 3, 2006. The Methods section of the original protocol has been reorganised and some parts of it re-labelled to meet the standards of the latest version of the Cochrane Handbook (Higgins 2008). It is now reproduced within the Additional methods for future updates table (Table 1) to inform readers of how review updates will be handled if relevant studies are identified in the future.

Table 1. Additional methods for future updates

Issue	Method
Selection of studies	Titles and abstracts of studies will be identified from the search and read independently by two authors (AVR and PBS). Those that do not meet the inclusion criteria will be discarded and any disagreements over suitability for inclusion will be resolved by discussion and/or adjudication by editors of the Cochrane Developmental, Psychosocial and Learning Problems Group. If further information is sought from trial authors the study will be categorised as awaiting assessment.
Data extraction and management	Data collection forms will be designed to include study methods, participant characteristics, intervention type and outcomes. Data will be extracted independently by two authors (AVR and PBS) and disagreements will be resolved through discussion or by contacting the study author for further information. Data will be organised using Review Manager 4.2.

Table 1. Additional methods for future updates (*Continued*)

Assessment of methodological quality	Selected studies will be independently evaluated by two authors (AVR and PBS) and assigned to a quality category based on allocation concealment as set out in the Cochrane Collaboration Handbook (Higgins 2005). Categories are (A) adequate, (B) unclear and (C) inadequate and can be categorised as follows: (A) indicates that adequate methods of concealment were used for random allocation. This would include centralised or pharmacy-controlled randomisation, telephone randomisation or the use of sequentially numbered, sealed, opaque envelopes. (B) indicates uncertainty as to whether allocation was adequately concealed from triallist or participant. This would include methodology where the method of concealment is not known. If the method of concealment and allocation is unclear the study authors will be contacted to obtain precise information. (C) indicates that although the methods of randomisation were described, the method was inadequate to guarantee allocation concealment. This would include alternation, dates of birth or any procedure that is transparent before allocation such as an open list of random numbers. Studies in categories A, B and C will be included in this review, with data pooled from those only in categories A and B. *Randomisation* Randomisation will be judged as 'adequate' when computer-generated random numbers, a random numbers table, or coin-tossing were used to allocate participants to treatment conditions. *Blinding of assessors* Blinding to the study intervention following allocation would not be possible either for triallists or participants in these studies. The intervention compares a surgical procedure to a medication regime following insertion of a gastrostomy feeding tube. This means it would be very difficult to eliminate detection and performance bias. *Loss to follow up* Adequate = losses to follow up were equally distributed between treatment and comparison groups; Unclear = information about losses to follow up unavailable; and Inadequate = losses to follow up in excess of 30% or unevenly (more than 10% difference) distributed between treatment and comparison groups. Studies will also be assessed as to their capacity to support intention-to-treat analysis. In the event a study may not have performed ITT, we will make assessments as follow: Adequate = intention-to-treat analyses performed or could be performed using available data; Unclear = information about whether intention-to-treat analyses were performed was not available and could not be acquired by contacting the researchers of the study; and Inadequate = intention-to-treat analyses were not performed and could not be done using available data.

Table 1. Additional methods for future updates (*Continued*)

Measures of treatment effect	*Binary data* For dichotomous data the relative risk and its 95% confidence interval will be calculated. *Continuous data* For studies using standardised assessment tools that have generated a scored outcome measure we will calculate a weighted mean difference. For studies using different scales we will calculate the standardised difference in means with a 95% confidence interval.
Dealing with missing data	In the event that data are missing or unclear in any aspect of the trial (from methodological aspects to trial results) primary investigators will be contacted. Data will, if possible, be analysed on an intention to treat basis.
Assessment of heterogeneity	Result consistency will be examined graphically to determine overlap of confidence intervals, poor overlap signifying heterogeneity. We will also consider the I^2 descriptive statistic available in RevMan 4.2 to calculate the proportion of variation that is due to heterogeneity rather than chance. Both fixed-effect and random-effects analysis will be performed.
Assessment of reporting biases	We will attempt to avoid publication bias by seeking data from all sources including conference proceedings and unpublished data from pharmaceutical companies (see search strategy). Should sufficient data be identified, funnel plots will be drawn to investigate any relationship between effect size and study precision (closely related to sample size). Such a relationship could be due to publication or related biases, systematic differences between small and large studies, or poor methodology. If a relationship is found, clinical diversity of the studies will be further examined as a possible explanation.
Data synthesis	Where meta-analysis is feasible (i.e. if two or more included studies are identified that are considered sufficiently homogeneous) we will perform a meta-analysis.
Subgroup analysis and investigation of heterogeneity	If sufficient data are identified we anticipate undertaking sub-group analyses as follows: 1. degree of clinically measured symptomatic GOR prior to GT surgery 2. level of disability 3. presence of underlying seizure disorders or pulmonary disease
Sensitivity analysis	Sensitivity analysis will be conducted to assess the impact of study quality on the outcome of the meta-analysis. This will determine whether, for example, studies with unclear allocation concealment or high rates of loss to follow up are more likely to show positive outcomes.

RESULTS

Description of studies

Results of the search

1,033 reports were identified from electronic searches, recognised across databases from their keywords. Those papers identified varied from reviews and editorials, to different study designs, both retrospective and prospective.

Included studies

No trials meeting the inclusion criteria were identified from this search; however, as a result of our search of the online trial registries we identified an ongoing study that matched the inclusion criteria (Lloyd 2000). The lead investigator was contacted and subsequently explained that the trial had been registered but not started due to methodological problems with the randomisation of children following previous failed medical management. Through our search of the grey literature we identified a thesis which was a design of a randomised clinical trial of surgical versus medical management for clinically significant gastro-oesophageal reflux in adults (Whelan 1979).

Excluded studies

The papers included, for example, alternative options for reflux treatment, effectiveness studies of different surgical anti-reflux techniques, and risk and benefit studies of gastrostomy surgery with fundoplication. The studies identified either met the exclusion criteria in that they included children who were neurologically normal, or they failed to meet the inclusion criteria as they were not randomised controlled trials, or did not feature the comparison of medical versus surgical treatments.

Risk of bias in included studies

No trials meeting the inclusion criteria were identified from this search.

Effects of interventions

No trials meeting the inclusion criteria were identified from this search.

DISCUSSION

The objectives of this review were to compare the effectiveness of anti-reflux fundoplication surgery with the use of anti-reflux medications in those children with neurological impairments who are undergoing gastrostomy feeding tube insertion. No trials meeting the inclusion criteria were identified from this search. This review has shown us that there is no evidence available from reliable sources on which to make a conclusion. We cannot provide data on the comparable risks or benefits of either treatment and are subsequently unable to provide recommendations for the best approach in this group of children.

AUTHORS' CONCLUSIONS

Implications for practice

There continues to be considerable uncertainty regarding the optimal treatment option when faced with the decision of performing surgery or prescribing medications for gastro-oesphageal reflux in the child with neurological impairment who is undergoing a gastrostomy. In order for surgeons and physicians to ensure that parents are fully informed as to the risks and benefits of both treatment options it is important for the lack of evidence highlighted in this review to be considered and the information shared with families.

It is important to highlight the fact that although this review deals specifically with the comparison of fundoplication versus medication, other surgical and endoscopic treatment options are becoming available for managing gastro-oesophageal reflux in this group of children. The durability and long term outcomes are not yet known within the paediatric population and further research is required before they are included as part of clinical practice.

Implications for research

A randomised controlled trial of fundoplication versus post-operative medication for children with neurological impairment and severe gastro-oesophageal reflux undergoing gastrostomy should be undertaken to resolve the current uncertainties about the optimal management strategy, for preference, a large multi-centre trial. Due to the nature of the two treatment options it would not be possible to blind the trial to triallists or participants, but blinding to the assessor may be possible when measuring pre and post-operative gastro-oesophageal reflux. The trial would have to be analysed on an intention to treat basis as those randomised to the medication arm of the trial could subsequently suffer worsening reflux and require fundoplication, but those having surgery could not revert to the medication arm post procedure. There would need to be strict inclusion and exclusion criteria to identify those children with very severe gastro-oesophageal reflux, such as those experiencing life-threatening events as a result, in whom a fundoplication is strongly indicated.

Through personal communication with Professor David Lloyd (Lloyd 2006) and Professor Jacob Langer (Langer 2006), an ethical consideration was brought to the reviewers attention with regards to the process of randomisation. Children with neurological impairments who are referred for gastrostomy insertion and have pre-existing reflux may have previously been treated with medications that have not resolved their symptoms. It would not be ethical in this instance to randomly allocate them to a treatment group knowing that one of the two options had previously failed to alleviate symptoms. This would not provide a fair chance of symptom relief from either therapy. In order to avoid this issue when performing a trial, children would need to be randomised to a treatment arm as soon as the diagnosis of GOR was made, and the gastrostomy surgery, with or without fundoplication, should

proceed as soon as possible.

While it is important to acknowledge that any research performed with this group of children will be difficult due to their anatomical and physiological problems, this is a population with ever increasing health needs and in particular this critically needed area for research.

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* *Indicates the major publication for the study*

DATA AND ANALYSES

This review has no analyses.

APPENDICES

Appendix 1. CENTRAL search strategy

Issue 2, 2006 of Cochrane Central Register of Controlled Trials (CENTRAL) was searched via the Cochrane Library
#1 MeSH descriptor gastrostomy explode all trees
#2 gastrostom* in All Text
#3 (#1 or #2)
#4 MeSH descriptor fundoplication explode all trees
#5 fundoplicat* in All Text
#6 (nissen in All Text and operation* in All Text)
#7 thal in All Text
#8 toupet in All Text
#9 belsey in All Text
#10 anti-reflux in All Text
#11 (anti in All Text and reflux in All Text)
#12 antireflux in All Text
#13 (#4 or #5 or #6 or #7 or #8 or #9 or #10 or #11 or #12)
#14 MeSH descriptor child explode all trees
#15 MeSH descriptor infant explode all trees
#16 MeSH descriptor adolescent explode all trees
#17 (baby in All Text or babies in All Text)
#18 infant* in All Text
#19 toddler* in All Text
#20 child* in All Text
#21 girl* in All Text
#22 boy* in All Text
#23 pre-school* in All Text
#24 preschool* in All Text
#25 teen* in All Text
#26 adolescen* in All Text
#27 (#14 or #15 or #16 or #17 or #18 or #19 or #20 or #21 or #22 or #23 or #24 or #25 or #26)
#28 MeSH descriptor cerebral palsy explode all trees
#29 (cerebral in All Text and palsy in All Text)
#30 (little* in All Text and disease in All Text)
#31 (spastic in All Text near/6 diplegia in All Text)
#32 (spastic in All Text near/6 quadriplegia in All Text)
#33 (neuro* in All Text near/6 disab* in All Text)
#34 (neuro* in All Text near/6 impair* in All Text)
#35 (#28 or #29 or #30 or #31 or #32 or #33 or #34)
#36 (#3 and #13 and #27 and #35)

Appendix 2. MEDLINE search strategy

MEDLINE searched through OVID, (1966 to June 2006)
1 Gastrostomy/
2 gastrostom$.tw.
3 or/1-2
4 Fundoplication/
5 fundoplicat$.tw.
6 nissen operation$.tw.
7 thal.tw.
8 toupet.tw.
9 belsey.tw.
10 anti-reflux.tw.
11 anti reflux.tw.
12 antireflux.tw.
13 or/4-12
14 exp Child/
15 Infant/
16 Adolescent/
17 (baby or babies).tw.
18 infant$.tw.
19 toddler$.tw.
20 child$.tw.
21 girl$.tw.
22 boy$.tw.
23 pre-school$.tw.
24 preschool$.tw.
25 teen$.tw.
26 adolescen$.tw.
27 or/14-26
28 Cerebral Palsy/
29 cerebral palsy.tw.
30 little$ disease.tw.
31 (spastic adj3 diplegia).tw.
32 (spastic adj3 quadriplegia).tw.
33 (neuro$ adj3 disab$).tw.
34 (neuro$ adj3 impair$).tw.
35 or/28-34
36 3 and 13 and 27 and 35
37 randomized controlled trial.pt.
38 controlled clinical trial.pt.
39 randomized controlled trials.sh.
40 random allocation.sh.
41 double blind method.sh.
42 single-blind method.sh.
43 or/37-42
44 (animals not human).sh.
45 43 not 44
46 clinical trial.pt.
47 exp Clinical Trials/
48 (clin$ adj25 trial$).ti,ab.
49 ((singl$ or doubl$ or trebl$ or tripl$) adj25 (blind$ or mask$)).ti,ab.
50 placebos.sh.

51 placebo$.ti,ab.
52 random$.ti,ab.
53 research design.sh.
54 or/46-53
55 54 not 44
56 55 not 45
57 comparative study.sh.
58 exp Evaluation Studies/
59 follow up studies.sh.
60 prospective studies.sh.
61 (control$ or prospectiv$ or volunteer$).ti,ab.
62 or/57-61
63 62 not 44
64 63 not (45 or 56)
65 45 or 56 or 64
66 36 and 65

Appendix 3. EMBASE search strategy

EMBASE, searched via OVID, (1980 to Week 33 2006)
1 Gastrostomy/
2 gastrostom$.tw.
3 or/1-2
4 Fundoplication/
5 fundoplicat$.tw.
6 nissen operation$.tw.
7 thal.tw.
8 toupet.tw.
9 belsey.tw.
10 anti-reflux.tw.
11 anti reflux.tw.
12 antireflux.tw.
13 or/4-12
14 exp Child/
15 Infant/
16 Adolescent/
17 (baby or babies).tw.
18 infant$.tw.
19 toddler$.tw.
20 child$.tw.
21 girl$.tw.
22 boy$.tw.
23 pre-school$.tw.
24 preschool$.tw.
25 teen$.tw.
26 adolescen$.tw.
27 or/14-26
28 Cerebral Palsy/
29 cerebral palsy.tw.
30 little$ disease.tw.
31 (spastic adj3 diplegia).tw.
32 (spastic adj3 quadriplegia).tw.

33 (neuro$ adj3 disab$).tw.
34 (neuro$ adj3 impair$).tw.
35 or/28-34
36 3 and 13 and 27 and 35
37 clin$.tw
38 trial$.tw.
39 (clin$ adj3 trial$).tw.
40 singl$.tw.
41 doubl$.tw.
42 trebl$.tw.
43 tripl$.tw.
44 blind$.tw.
45 mask$.tw.
46 ((singl$ or doubl$ or trebl$ or tripl$) adj3 (blind$ or mask$)).tw.
47 randomi$.tw.
48 random$.tw.
49 allocat$.tw.
50 assign$.tw.
51 (random$ adj3 (allocat$ or assign$)).tw.
52 crossover.tw.
53 52 or 51 or 47 or 46 or 39
54 exp Randomized Controlled Trial/
55 exp Double Blind Procedure/
56 exp Crossover Procedure/
57 exp Single Blind Procedure/
58 exp RANDOMIZATION/
59 54 or 55 or 56 or 57 or 58 or 53
60 36 and 59

Appendix 4. CINAHL search strategy

CINAHL, searched via OVID, (1982 to May, week 4 2006)
1 Gastrostomy/
2 gastrostom$.tw.
3 or/1-2
4 fundoplicat$.tw.
5 nissen operation$.tw.
6 thal.tw.
7 toupet.tw.
8 belsey.tw.
9 anti-reflux.tw.
10 anti reflux.tw.
11 antireflux.tw.
12 exp Child/
13 Infant/
14 Adolescent/
15 (baby or babies).tw.
16 infant$.tw.
17 toddler$.tw.
18 child$.tw.
19 girl$.tw.
20 boy$.tw.

21 pre-school$.tw.
22 preschool$.tw.
23 teen$.tw.
24 adolescen$.tw.
25 or/12-24
26 Cerebral Palsy/
27 cerebral palsy.tw.
28 little$ disease.tw.
29 (spastic adj3 diplegia).tw.
30 (spastic adj3 quadriplegia).tw.
31 (neuro$ adj3 disab$).tw.
32 (neuro$ adj3 impair$).tw.
33 or/26-32
34 or/4-11
35 3 and 25 and 33 and 34
36 randomi$.mp. [mp=title, subject heading word, abstract, instrumentation]
37 clin$.mp. [mp=title, subject heading word, abstract, instrumentation]
38 trial$.mp. [mp=title, subject heading word, abstract, instrumentation]
39 (clin$ adj3 trial$).mp. [mp=title, subject heading word, abstract, instrumentation]
40 singl$.mp. [mp=title, subject heading word, abstract, instrumentation]
41 doubl$.mp. [mp=title, subject heading word, abstract, instrumentation]
42 tripl$.mp. [mp=title, subject heading word, abstract, instrumentation]
43 trebl$.mp. [mp=title, subject heading word, abstract, instrumentation]
44 mask$.mp. [mp=title, subject heading word, abstract, instrumentation]
45 blind$.mp. [mp=title, subject heading word, abstract, instrumentation]
46 (40 or 41 or 42 or 43) and (44 or 45)
47 crossover.mp. [mp=title, subject heading word, abstract, instrumentation]
48 random$.mp. [mp=title, subject heading word, abstract, instrumentation]
49 allocate$.mp. [mp=title, subject heading word, abstract, instrumentation]
50 assign$.mp. [mp=title, subject heading word, abstract, instrumentation]
51 (random$ adj3 (allocate$ or assign$)).mp.
52 Random Assignment/
53 exp Clinical Trials/
54 exp Meta Analysis/
55 51 or 47 or 46 or 39 or 36 or 52 or 53 or 54
56 55 and 35

Appendix 5. ISI Web of Science search strategy

ISI Web of Science, searched via Web of Knowledge, (1970 to June2006)
reflux
reflux AND child*
reflux AND child* AND gastrostom*
reflux AND child* AND gastrostom* AND fundoplicat*
reflux AND child* AND gastrostom* AND fundoplicat* AND neuro*

Appendix 6. The Child Health Library search strategy

The Child Health Library search June 2006
reflux
gastrostomy* AND reflux

Appendix 7. National Research Register search strategy

National Research Register searched 2006 (Issue 2)
#1 GASTROSTOMY single term (MeSH)
#2 gastrostom*
#3 (#1 or #2)
#4 FUNDOPLICATION single term (MeSH)
#5 fundoplicat*
#6 (nissen next operation*)
#7 thal
#8 toupet
#9 belsey
#10 anti-reflux
#11 (anti next reflux)
#12 antireflux
#13 (#4 or #5 or #6 or #7 or #8 or #9 or #10 or #11 or #12)
(#3 and #13) (1)

Appendix 8. LILACS search strategy

LILACS searched 1982 to June 2006
Tw gastrostomy and (Tw fundoplicat$ or Tw nissen operation$ or Tw thal or Tw toupet or Tw belsey or Tw anti-reflux or Tw anti reflux or Tw antireflux)

WHAT'S NEW

Last assessed as up-to-date: 31 May 2006.

15 September 2008	Amended	Converted to new review format.

HISTORY

Protocol first published: Issue 3, 2006

Review first published: Issue 1, 2007

14 November 2006	New citation required and conclusions have changed	Substantive amendment

CONTRIBUTIONS OF AUTHORS

Both authors (AVR and PB) contributed to writing the text of this review. The search strategy was developed by Joanne Abbott (TSC of the Cochrane Developmental, Psychosocial and Learning Problems Group).

Selection of abstracts, review of potential trials, assessment of methodological quality, data extraction and data entry was independently done by both authors (AVR and PB).

DECLARATIONS OF INTEREST

None known.

SOURCES OF SUPPORT

Internal sources

- No sources of support supplied

External sources

- Cerebra (Charity for Brain Injured Children and Young People), UK.

INDEX TERMS

Medical Subject Headings (MeSH)

Cerebral Palsy [*complications]; *Fundoplication; Gastroesophageal Reflux [*therapy]; Gastrointestinal Agents [*therapeutic use]; *Gastrostomy; Proton Pumps [*therapeutic use]

MeSH check words

Child; Humans