A systematic review of nonpharmacological and nonsurgical therapies for gastroesophageal reflux in infants

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Authors' objectives
To conduct a systematic review of rigorously evaluated non-pharmacological and non-surgical therapies for gastroesophageal reflux disease (GERD) in infants.

Searching
MEDLINE (from 1966 to November 2000), EMBASE (as of November 2000), the Cochrane Controlled Trials Register (as of November 2000) and multiple alternative medicine databases (unspecified) were searched using the terms 'gastroesophageal reflux disease' and 'infants' as MeSH terms and keywords. The searches were restricted to papers in written in the English language. The references of any relevant review articles were also examined.

Study selection
Study designs of evaluations included in the review
Randomised controlled trials (RCTs) of a parallel or crossover design were included.

Specific interventions included in the review
Studies that examined any non-pharmacological or non-surgical intervention for GERD in infants were eligible for inclusion in the review. The specific interventions assessed were positioning (2 studies), thickened infant food (3 studies), formula changes (4 studies) and non-nutritive sucking (1 study).

Participants included in the review
The population of interest in the review were full-term infants with GERD who were otherwise healthy. GERD was defined as reflux into the oesophagus with a pH of less than 4.0 for at least 5% of the time, as diagnosed by means of pH probe study findings. Studies that included premature infants or infants with compound medical problems were, therefore, excluded. The included studies were of infants aged between 4 days and 28 months.

Outcomes assessed in the review
The authors did not state any inclusion criteria relating to the outcome measures. The outcomes assessed were reflux duration and frequency, emetic episodes and intra-oesophageal pH.

How were decisions on the relevance of primary studies made?
After the initial screening, three reviewers assessed the studies for inclusion. However, the authors do not state whether this was undertaken independently, or how any disagreements were resolved.

Assessment of study quality
The validity of the primary studies was assessed according to whether there was evidence of adequate inclusion criteria, randomisation and allocation concealment. Three reviewers assessed the validity of the included studies, and any disagreements were resolved by consensus. The authors do not state whether this was undertaken blind to the source.

Data extraction
The authors do not state how the data were extracted for the review, or how many of the reviewers performed the data extraction.

Data on the author, number of study participants, age range, intervention and the outcome measures (duration and frequency of reflux and emesis) were extracted and presented in tabular format.
Methods of synthesis
How were the studies combined?
The studies were combined narratively, grouped according to the type of intervention.

How were differences between studies investigated?
The studies were grouped by intervention type. However, due to the heterogeneous nature of the interventions examined, the authors do not report a formal statistical method for assessing differences between the studies.

Results of the review
Ten RCTs (n=323) were included. These were 2 parallel-group trials (n=44) and 8 crossover trials (n=279).

Positioning.
One RCT found that placement in an infant seat (inclined at 60 degrees) was detrimental with respect to GERD. Infants in the seat spent a greater proportion of time in a state of reflux (28.2%) than did those in the prone position (12.8%); they also had significantly more episodes of reflux (16.0 versus 10.1). Another RCT found no difference in any measure of reflux between infants in the prone position and those in the prone position with the head of the bed inclined at 30 degrees.

Nonnutritive sucking.
One study assessed infants randomised to a prone or seated position. In each position, the infants underwent the pH probe examination with and without pacifiers, in random order, for 3 hours. In the prone position, pacifier use increased the number of episodes of reflux in 2 hours from 7.2 to 12.8 (p=0.04). In the seated position, pacifier use decreased the number of reflux episodes in 2 hours from 21.1 to 14.8 (p=0.03), but this was insufficient to compensate for the negative effects of the seated position. The total reflux time and reflux clearance were not significantly affected by pacifier use in either position.

Thickened infant food.
Four RCTs assessed the effect of thickened food on GERD. Two studies compared formula thickened with rice flour to placebo, one compared carob bean gum-thickened formula with placebo, and one compared 2 different thickening agents. Thickening with rice flour.

The first RCT assessed infants given both thickened or non-thickened apple juice in the 4 positions of prone, prone and elevated 30 degrees, supine or unrestricted. There was no difference between the 2 types of juice in any position, except in the 30 degree elevated prone position, in which reflux time was increased with thickened juice. The second RCT compared thickened with normal infant formula. The type of formula had no statistically-significant impact on the amount of reflux. However, a significant decrease was found in the number of episodes of frank emesis (1.2 versus 3.9 per 90 postprandial minutes).

Thickening with carob bean gum.
There were improvements noted in both the group randomised to the control formula (80% casein and 20% whey) and the thickened formula. However, no significant differences were found between the two groups in terms of the pH monitoring results.

Carob bean gum versus rice flour thickening.
Parental diaries showed a reduction over time in the symptomatic scores for both formulas. However, the carob bean gum-thickened formula showed a significant reduction in both symptomatic score (70.4% versus 48.7%; p<0.01) and episodes of emesis (58.1% versus 34.1%; p<0.05).

Formula changes.
Two RCTs investigated the effect of the formula composition on GERD. The first study randomised the infants to receive casein predominant, soy-based, and whey-predominant formulas. No differences were noted on the outcome measures of spitting and vomiting and reflux between the formulas. The second small RCT examined casein versus whey-based formulas. All 3 infants showed improvement in emesis while receiving the whey-based formulas (1.3 versus 4.3; p<0.01), but the difference between the formulas was not significant when based on the results of the pH probe test.

Caloric density or osmolality changes.

One RCT assessed the effect of using dextrose 5% water (D5W), dextrose 10% water (D10W) and a glucose polymer solution when rehydrating children with carbohydrate solutions. The total minutes of oesophageal reflux were significantly lower while receiving the D5W and glucose polymer solutions than while receiving the D10W solution: the mean values were 12.0 (D5W) and 12.6 (glucose polymer) minutes, respectively, versus 28.6 minutes (D10W) (p<0.05). No significant difference was found in the results in the first postprandial hour, but the results became significant when observed for 2 hours postprandially.

Authors' conclusions
Many conservative measures commonly used to treat GERD in infants have no proven efficacy. While the thickened formulas do not appear to reduce measurable reflux, they may reduce vomiting.

CRD commentary
This was a reasonably well-conducted review. The authors addressed a clear review question in terms of the participants, interventions and study designs that were to be examined in the review. The literature search was adequate, although the studies were restricted to English language papers. This may mean that language bias was introduced into the review process and that other studies may have been missed. Likewise, there was no attempt to locate unpublished literature, which could have introduced publication bias.

The authors provided details of both how the studies were selected for inclusion in the review and how the validity of the studies was assessed. The methods used by the authors should have minimised selection bias, thus allowing the quality of the included studies to be judged. However, the authors did not state how the data were extracted; any errors in this process may, therefore, have been included in the results of the review. There was adequate information relating to the study characteristics in the paper; this allows the reader to judge whether the reviewers' results and conclusions are consistent with the evidence base reviewed. The use of a narrative synthesis was appropriate, as the studies were not sufficiently homogeneous to combine. However, differences between the studies could not be assessed due to the heterogeneous nature of the interventions examined.

Overall, the results of the review and the authors' conclusions appear to be consistent with the evidence base reviewed.

Implications of the review for practice and research
Practice: The authors state that there is no conclusive evidence that any non-pharmacological interventions for GERD are effective. However, many textbooks continue to recommend the use of conservative measures, including thickened juice and formula and the upright position, despite their lack of proven efficacy.

Research: The authors state that more larger scale studies are needed to answer the questions concerning efficacy definitively.

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Record Status
This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.