Early childhood: colic, child development, and poisoning prevention: a systematic review of treatments for infant colic

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Authors' objectives
To conduct a systematic review of rigorously evaluated treatments for infant colic.

Searching
MEDLINE, from January 1966 to May 1999, and the Cochrane Controlled Trials Register (May 1999) were searched using 'colic' as a MeSH term. The searches were restricted to RCTs conducted on human infants and published in the English language. The bibliographies of relevant review articles, meta-analyses, and all retrieved articles were also examined for additional studies. The Medical Editors Trial Amnesty was searched for unpublished trials.

Study selection
Study designs of evaluations included in the review
Randomised-controlled trials (RCTs) were included. Crossover trials were only included if all infants crossed over, and were therefore exposed to both treatment arms.

Specific interventions included in the review
The authors did not specify any intervention-related inclusion or exclusion criteria. The interventions evaluated in the included studies were: simethicone, dicyclomine, methylscopolamine, lactase enzymes, herbal teas, sucrose, low-allergen diet for breast-feeding mothers, hypoallergenic formulas for bottle-fed infants, soy-based formulas for bottle-fed infants, fibre-enriched formulas for bottle-fed infants, more frequent carrying of the infant, car ride simulators, intensive parent training and decreased infant stimulation. No details of dosage or study duration were reported.

Participants included in the review
The review included clinical trials of treatments for infant colic; no more specific inclusion criteria relating to trial participants were given. The participants were bottle- or breast-fed infants aged between 1 and 18 weeks. Studies of both hospital in-patients, and otherwise healthy infants with normal weight gain, were included. Some studies excluded premature infants and/or those with current medication use.

Outcomes assessed in the review
The authors did not specify any inclusion or exclusion criteria relating to outcomes. The outcome measures assessed were: parent diaries; observation by a health professional; parent interviews; frequency of crying; volume or intensity of crying; duration of crying; parent preference for placebo or active treatment in crossover trials; time spent sleeping; frequency of feeding; frequency of stools; clinical scores; frequency of night waking; transit times for total bowel and mouth to cecum; and hydrogen concentration from breath sample analysis.

How were decisions on the relevance of primary studies made?
The authors do not state how the papers were selected for the review, or how many of the authors performed the selection.

Assessment of study quality
The quality of the included trials was assessed by examining the adequacy of case definitions, randomisation, and double-blinding methods. A trial was considered to be adequately double-blinded if it was conducted in such a way, that there was no reason to assume that those responsible for outcome measurements would be able to distinguish between the active and placebo measurements. 'Adequate case definition' was defined as the use of Wessel criteria (see Other Publications of Related Interest no.1). The authors did not describe any method for assessing the adequacy of randomisation. The authors do not state how the papers were assessed for quality, or how many of the authors performed the quality assessment.
Data extraction
The authors do not state how the data were extracted for the review, or how many of the authors performed the data extraction.

Data were extracted from primary studies on the numbers of study participants, the participant characteristics, the interventions studied, the outcomes measured, adverse events (where reported) and the results.

Where sufficient data were available, the number-needed-to-treat was calculated from the absolute risk reduction associated with a given treatment (see Other Publications of Related Interest no.2) for each included study. Where results were reported in terms of resolution rates, these data were also extracted.

Methods of synthesis
How were the studies combined?
The authors presented a qualitative, narrative synthesis. Interventions were divided into pharmaceutical, dietary, behavioural, and naturopathic categories. Within each category the results were summarised by specific intervention and further subgrouped into studies presenting positive and negative results.

No formal attempt to assess publication bias was described.

How were differences between studies investigated?
No formal assessment of heterogeneity was described. The authors highlighted the wide variation in case definition and outcome measures used in the included trials, and the subsequent limitations imposed upon between-trial comparisons.

Results of the review
Twenty-two trials with a total of 1,217 participants were included in the review. Of these, 9 (n=593) used the Weasel case definition. The authors considered that all included trials had used adequate randomisation, and that 12 of the trials (n=638) had adequate double-blinding. Five trials (n=364) were considered adequate in all three categories.

Pharmaceutical interventions.

Of the 3 trials of simethicone, 1 reported significantly fewer episodes of crying, and the remaining 2 found no significant benefit.

All 3 trials of dicyclomine reported positive results. Two of the trials reported a higher (8%) incidence of adverse events in the treatment group than in the placebo group.

The single trial of methylscopolamine found that it had no significant impact on the symptoms of infant colic, but that adverse effects were more common in participants receiving the active treatment.

Dietary interventions.

A hypoallergenic diet was adopted by breast-feeding mothers in 2 studies. One found significantly positive results in terms of mean daily duration of symptoms, while the other found no statistically- significant effect on symptoms when eliminating cow’s milk from the maternal diet. Further analysis produced results in favour of a controlled diet.

There were 2 trials investigating the use of hypoallergenic formulas in bottle-fed infants. Both reported significantly positive results, although the data from one of these were not presented in a manner that allowed for comparable interpretation.

Of the 2 trials on the use of soy-based formulas in bottle-fed infants, one reported a significant reduction in mean weekly duration of symptoms, while the other did not report the data in a manner that allowed for analysis of the treatment effect.
Neither of the 2 trials of lactase found any significant differences between treatment and placebo groups.

One trial on the use of fibre-enriched formula in bottle-fed infants found no significant differences between the treatment and placebo groups.

Behavioural interventions.

Neither of the 2 trials of infant carrying showed any reduction of symptoms.

One trial investigating car ride simulators showed no significant differences between the treatment and control groups in either duration of crying or measures of maternal anxiety.

One trial found that parents who received intensive training in parent-infant communication skills and daily counselling reported a significant decrease in mean daily crying. However, this study had several major methodological flaws.

One trial showed a significant improvement in infants whose parents were advised to reduce stimulation, compared with the control group. However, this study also had methodological weaknesses.

Naturopathic interventions.

One trial of herbal tea found a significantly positive effect in the treatment group, in terms of reduced numbers of infants meeting the Weasel criteria for colic. No significant differences were seen in the average numbers of night awakenings, and no adverse events were reported in either the treatment or placebo groups.

One trial of sucrose found a significantly higher number of parent-reported responses in the treatment group than in the placebo group. However, it appeared that in the majority of cases the response lasted for less than 30 minutes. A second trial, which examined infants both with and without colic, found that whilst both groups responded to sucrose and not to placebo, the response in the colicky infants lasted, on average, for less than 3 minutes.

Authors' conclusions
There are some effective therapies for infant colic, but additional rigorous studies of existing and alternative therapies are needed.

CRD commentary
The review question was vague and treatments to be evaluated were unspecified. The title stated that the review was of ‘treatments for infant colic’, but the reviewers did not specify any inclusion or exclusion criteria relating to either participant age or definition of colic. No inclusion or exclusion criteria were specified with respect to interventions, participants or outcomes. This deficiency was compounded by the lack of any detailed description of the process used to select studies for inclusion in the review.

The search strategy described was crude, using only a single MeSH term and searching only one bibliographic database and the Cochrane Controlled Trials Register. In addition, the restriction of the search to English language publications may also lead to incomplete retrieval of the available literature. A limited attempt was made to locate unpublished trials, but there was no formal assessment of publication bias.

The quality assessment of included studies was restricted to assessments of adequacy of case definition, randomisation and blinding. 'Adequate case definition' was specified as the use of the Weasel definition. Whilst the authors state that all included studies had adequate randomisation, they neither defined this nor described the methods used to assess it. Similarly, their definition of adequate double-blinding was vague and there was no description of the methods used for assessment.

The participant characteristics of included trials were presented clearly and fully in tabular form, although the results of individual included trials were largely presented in a narrative summary. It is unclear what are primary data, and what has been calculated by the reviewers from data that are not presented.
The narrative summary was divided into broad categories based on treatment. In general, there was a reasonable
description of the findings of each included study, but a cohesive summary of the evidence was lacking for many of the
treatments evaluated.

The authors concluded that there were some effective therapies for infant colic, but the evidence presented was
generally very weak. The numbers of studies and participants was small and between-study heterogeneity was
potentially great for all treatments evaluated. The review did not appear to present sufficient evidence to support the use
of any of the interventions described.

**Implications of the review for practice and research**

**Practice:** The authors state that existing data do not demonstrate conclusive benefit of simethicone as a treatment for
infant colic.

The manufacturers of dicyclomine do not consider infant colic an indication for its use, and have contraindicated its use
in infants under 6 months old.

Methylscopolamine does not appear to be an either effective or safe treatment for infant colic.

Data regarding utilisation of hypoallergenic diets by breast-feeding mothers are inconclusive, but suggest that there may
be some therapeutic benefit. The use of hypoallergenic formulas in bottle-fed infants also appears to have a beneficial
effect.

Soy formula may be an effective treatment for infant colic.

There is some evidence for the effectiveness of herbal teas, and no adverse effects have been reported. However, there
are concerns about potential nutritional effects should prolonged intake lead to a decreased intake of milk.

There is no evidence that lactase is an effective therapy for infant colic.

Current data do not support supplemental carrying as an effective intervention for infant colic.

**Research:** The authors advocate further research in the areas of hypoallergenic diet and behavioural intervention. In
addition, they state 'Future randomised trials of treatments for infant colic should strive to avoid the methodological
flaws that have hampered the results of so many studies in this area. As double-blinding is not generally possible in
trials of behavioural interventions, it is especially important to use the most objective outcome measures possible in
these trials to reduce the potential for bias.'

The use of common case definitions (e.g. Weasel criteria), age ranges (2 to 8 weeks was the most common in the
studies reviewed), and outcome measures (e.g. mean daily duration of crying) would allow for a greater degree of
comparability between trials.

Future trials should subclassify infants with colic according to symptoms or suspected etiology. This might enable
researchers and clinicians to predict which interventions are most appropriate for a given infant.

**Bibliographic details**

Garrison MM, Christakis DA. Early childhood: colic, child development, and poisoning prevention: a systematic review
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**PubMedID**

10888690

**Original Paper URL**

http://pediatrics.aappublications.org/content/106/Supplement_1/184.abstract
Other publications of related interest

This additional published commentary may also be of interest. Treatments for infant colic. Bandolier 2000;79:4.

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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.