Evidence Assessment: Summary of a Systematic Review

Who is this summary for?
For Doctors and Health Personal, Administrators and Managers of health facilities, Community Health Workers and the partners involved in child health.

Pain-relieving agents for infantile colic

Key findings

- No robust conclusions can be drawn on the effectiveness of pain-relieving agents for the treatment of infant colic because evidence is sparse and is prone to bias.
- Simethicone is not effective in reducing crying time or improving symptoms when compared with placebo.
- Compared with placebo, herbal agents, sugar, dicyclomine and cimetropium bromide may be beneficial in reducing crying time or relieving other symptoms of colic, but the quality of evidence is low or very low. Dicyclomine has been banned from the market due to side-effects.

Background

Infantile colic is a common disorder in the first months of life, affecting somewhere between 4% and 28% of infants worldwide, depending on geography and definitions used. Although it is self-limiting and resolves by four months of age, colic is perceived by parents as a problem that requires action. Pain-relieving agents, such as drugs, sugars and herbal remedies, have been suggested as interventions to reduce crying episodes and severity of symptoms.

Questions

What is the effectiveness and safety of pain-relieving agents for reducing colic in infants younger than four months of age?

Table 1: Summary of the systematic review		
	What the review authors searched for	**What the review authors found**
Studies	Randomised controlled trials (RCTs) and quasi-RCTs	All 18 studies were RCTs. Ten of 18 studies (56%) were cross-over trials
Participants	Infants younger than four months of age at enrolment who had infantile colic, as confirmed by a physician. Infantile colic is defined as a prolonged period of crying for no apparent reason in and otherwise healthy infant. For inclusion in this review, we accepted all definitions of excessive crying, and both breast fed and bottle fed infants were eligible.	The number of participants randomised to intervention and control groups ranged from 18 to 175. Participant age ranged from about one week to 16 weeks. Two studies did not provide the ages of enrolled infants.
Interventions	Any pain-relieving agent used for the treatment of infant colic, that is, pharmacological interventions (dicyclomine, cimetropium bromide, simethicone) and complementary interventions (herbal formulations, sucrose or glucose).	**Pain-relieving agents varied across studies.** • Simethicone was used in four studies. • Herbal formulations were used in four studies. • Sucrose or glucose was used in three studies. • Dicyclomine was used in five studies. • Cimetropium bromide (a drug that is distributed only in Italy and in Corea) was used in two studies. • Herbal tea was used in one study.
Controls	Placebo or with no treatment	In all but three studies, the control arm was given placebo. One study evaluated two different dosages of cimetropium bromide (1.2 mg/kg vs 2.0 mg/kg); One study compared sucrose or herbal tea versus no treatment; and one other compared simethicone medication against Mentha piperita.
Outcomes	**Primary outcomes** • Reduction in crying duration (post-treatment vs baseline) (available data may be continuous, for example, hours per day, or dichotomous, for example, reduction under a threshold defined by trialists) • Responders (dichotomous outcome), defined as proportions of participants who showed improvement by the end of treatment, according to the measures used by study authors **Secondary outcomes** • Reduction in frequency of crying episodes (post-treatment vs baseline) (available data may be continuous, for example, hours per day, or dichotomous, for example, reduction under a threshold defined by trialists) • Parental or family quality of life, including measures of parental stress, anxiety or depression (continuous outcome) • Sleeping time, that is, change in duration of peaceful sleeping (post-treatment vs baseline)* (continuous outcome) • Parental satisfaction, measured by Likert scales or on a numerical rating scale (NRS) (continuous outcome) • Adverse effects: constipation, vomiting, apnoea, apparent life-threatening events (ALTEs) and lethargy* (dichotomous outcome)	**Primary outcomes** All studies provided data on at least one primary outcome (e.g. reduction in crying duration, responders). Table 2 shows details on different definitions of responders as given by different study authors.
Date of the most recent search: May 2016		
Limitations: This is a moderate quality systematic review**, AMSTAR = 9/11**		
Citation: Biagioli E, Tarasco V, Lingua C, Moja L, Savino F. **Pain-relieving agents for infantile colic**. Cochrane Database of Systematic Reviews 2016, Issue 9. Art. No.: CD009999. DOI: 10.1002/14651858.CD009999.pub2.		

Table 2: Summary of findings

Simethicone versus placebo for infantile colic

Patient or population: infants with infantile colic
Settings: university primary care centre (Sweden) and general paediatric practices (USA)
Intervention: simethicone versus placebo

Outcomes	Illustrative comparative risks*(95%CI)		Relative effect (95%CI)	No. of participants (studies)	Quality of the evidence (GRADE)
	Assumed risk	Corresponding risk			
	Control	Simethicone vs placebo			
Reduction in crying duration Difference between final values (hours per day of crying) Follow-up:mean7days	Mean crying duration in control groups was 4. 37hours/d	Mean crying duration in intervention groups was 0.13 lower (1.4 lower to1.14 higher)	MD-0.13 (1.40to1. 14)	27 (1study)	Very low
Responders Number of infants who improved after treatment Follow-up:mean7days	**Study population**		RR0.95 (0.73to1.23)	110 (2 studies)	Low
	591 per 1000	561 per 1000 (431 to 727)			
	Moderate				
	604 per 1000	574 per 1000 (441 to 743)			

Additional summary of findings

Herbal agents versus placebo for infantile colic

Patient or population: patients with infantile colic
Settings: multi - speciality clinics (Russia); university hospitals (Turkey, Italy); primary community-based clinics (Israel)
Intervention: herbal agents versus placebo

Outcomes	Illustrative comparative risks*(95%CI)		Relative effect (95%CI)	No. of participants (studies)	Quality of the evidence (GRADE)
	Assumed risk	Corresponding risk			
	Control	Herbal agents vs placebo			
Reduction in crying duration Difference before and after treatment (hours per day of crying) Follow-up:mean7days	Mean reduction in crying duration in control groups was 0.22 hours/ d.	Mean reduction in crying duration in intervention groups was1. 33 higher (0.71to1.96 higher).	MD1.33(0.71to1.96)	279 (3 studies)	Low
Responders Number of infants who improved after treatment Follow-up:mean7days	**Study population**				Moderate
	326 per 1000	669 per 1000 (509 to 881)	RR2.05 (1.56 to 2.7)	277 (3 studies)	
	Moderate				
	257 per 1000	527 per 1000 (401 to 694)			

Sugar versus placebo for infantile colic

Patient or population: infants with infantile colic
Settings: university hospital (Turkey)
Intervention: sugar versus placebo

Outcomes	Illustrative comparative risks*(95%CI)		Relative effect (95%CI)	No. of participants (studies)	Quality of the evidence (GRADE)
	Assumed risk	Corresponding risk			
	Control	Sugar vs placebo			
Reduction in crying duration Difference before and after treatment (hours per day of crying) Follow-up: mean7days	Mean reduction in crying duration in control groups was 0.09 hours/d of crying.	Mean reduction in crying duration in intervention groups was1. 72 higher (1.38to2.06 higher).	MD1.72 (1.38to2.06)	70 (1study)	Very low

Cimetropium bromide versus placebo for infantile colic

Patient or population: infants with infantile colic
Settings: university hospital (Italy)
Intervention: cimetropium bromide versus placebo

Outcomes	Illustrative comparative risks*(95%CI)		Relative effect (95%CI)	No. of participants (studies)	Quality of the evidence (GRADE)
	Assumed risk	Corresponding risk			
	Control	Cimetropium bromide vs placebo			
Reduction in crying duration Difference between final values(minutes per crisis of crying) Follow-up: mean 3 days	Mean reduction in crying duration in control groups was 47.5minutes per crisis of crying	Mean reduction in crying duration in intervention groups was 30.2 lower (39.51to20.89 lower)	MD-30.20 (-39.51to- 20.89	86 (1study)	Very low
Responders Number of infants who improved after treatment Follow-up: mean 3 days	**Study population**				
	326 per 1000	746 per 1000 (469 to 1000)	RR2.29 (1.44 to 3.64)	86 (1 study)	Very low
	Moderate				
	326 per 1000	747 per 1000 (469 to 1000)			

Applicability

This review included 18 studies enrolling a total of more than one thousand infants, and evaluated the effects of several pain- relieving agents (i.e. simethicone, herbal remedy, sugar, dicyclomine, cimetropium bromide) in the treatment of infant colic. Eleven studies were conducted in Europe, three in America, two in Asia, one in Russia and one in Australia.

Conclusions

Pain-relieving agents may not reduce crying time or pain symptoms in children aged less than 4 months with infantile colics.

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