

Honey For Acute Cough in Children

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Introduction

Acute cough is one of the most common pediatric conditions and a major motive for outpatient visits.^{1,2} It is disruptive, can impact quality of life, causes anxiety and affects sleep in both parents and children.³⁻⁵ While parental expectations on cough management can vary from simple need for reassurance to preference for antibiotics, symptomatic relief is usually a common concern for most caregivers.⁶ Despite the frequent use of non-prescription / over-the-counter cough and cold medications such as decongestants and mucolytics, regulatory authorities have restricted their use in children due to unproven effectiveness and risk of serious harms.^{7,8} As an alternative, several recent studies have explored the use of honey as a treatment for acute cough.⁹⁻¹¹

Aim

In this Cochrane Corner we present and discuss the results of a systematic review from the Cochrane Database of Systematic Reviews which aimed to examine the comparative effectiveness and safety of honey to relieve acute cough in children in ambulatory settings. This was a 2018 update of reviews previously published between 2010 and 2014.¹²

Methods

The authors followed Cochrane review methodology. A systematic search of studies published up to February 2018 in CENTRAL (including the Cochrane Acute Respiratory Infections Group's Specialized Register), MEDLINE, EMBASE, CINAHL, EBSCO, Web of Science, LILACS and BIREME was conducted. World Health Organization International Clinical Trials Registry

Platform and ClinicalTrials.gov were also searched for ongoing and completed studies.

Randomized controlled trials including children aged 12 months to 18 years with cough lasting less than three weeks caused by acute viral or bacterial upper respiratory infections were considered eligible. The authors included two groups of comparisons:

- Honey alone was compared to cough syrups (with or without honey), placebo or no treatment;
- Honey plus antibiotics were compared with antibiotics (with or without non-honey cough syrups).

The primary outcomes were the duration of cough and its symptomatic relief (frequency, severity and bothersome cough). The secondary outcomes were quality of sleep in children and caregivers, quality of life, appetite, adverse effects and cost.

The risk of bias of included trials was assessed using Cochrane Risk of Bias Tool (2011 version) and the quality of evidence for the outcomes was assessed using the GRADE approach. Heterogeneity was quantified by the measurement of inconsistency through I^2 . Different effect measures were used depending on the outcome, including risk ratio (RR) for dichotomous variables and mean difference (MD) for continuous variables (including Likert scale items). The authors chose to analyze both within-group pre-post intervention changes (e.g. symptom scores measured before and after honey or one of the comparators were used), as well as the more relevant between-group pairwise interventions (e.g. honey *versus* placebo). The pairwise meta-analyses were based on a fixed-effects model, and a random-effects model was used when the I^2 statistic was $> 50\%$. The results were presented with 95% confidence intervals (95% CI). The authors performed subgroup analyses for different types of honey but did not conduct further subgroup or sensitivity analysis due to the reduced number of included studies.

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Results

The updated review included six studies conducted in Iran, Israel, United States of America, Brazil and Kenya, involving 899 children from 12 months to 16 years. No studies enrolled children with comorbidities.

Four studies included a placebo or no treatment arm, with or without an active comparator. Both the main interventions and active comparators were heterogeneous; different types of honey were compared to orally administered diphenhydramine, dextromethorphan and salbutamol, or to honey mixed with bromelain (pineapple-derived enzyme). Honey was given for one-night-only in four studies, three times on one day in one study and three times daily for five days in another study. No studies used honey plus antibiotics. The primary outcomes of the review were only partially reported across studies. Only one study assessed the duration of cough in days, while five studies evaluated one or more measures of symptomatic relief using 7-point Likert scales (lower scores indicating better symptom relief) with less than one week of follow-up.

The methodological aspects of randomization, allocation concealment, blinding and attrition bias were adequate in six, five, four and three studies, respectively. All six studies had low risk of bias for selective reporting. Two studies had a low risk for other potential sources of bias. The results of relevant pairwise comparisons in primary and secondary outcomes are summarized below in Table 1. Two studies were excluded from the

meta-analyses due to unclear reporting. The certainty of evidence ranged from low to moderate across comparisons and outcomes.

When given for a day, honey reduced the frequency of cough better than placebo (MD -1.62 points, 95% CI -3.02 to -0.22, two studies, n = 402, moderate-certainty evidence), with non-statistically significant improvements seen in cough severity, bothersome cough, and quality of reported child and parents sleep. Data from one study (n = 102) showed cough was relieved sooner in children who received honey for five days when compared to placebo (MD -0.72 days, 95% CI -1.31 to -0.13, moderate-certainty evidence). Cough frequency, severity, bothersome cough and impact on sleep were not significantly different by day five. All primary and secondary outcomes improved with significant differences when comparing honey to no treatment, except for bothersome cough. Data on duration of cough was not reported.

When considering active comparators, honey reduced cough frequency and severity by day one when compared to diphenhydramine (MD -0.57 points, 95% CI -0.90 to -0.24; and MD -0.60 points, 95% CI -0.94 to -0.26, respectively). Significant improvements were also noted for children and parents sleep (by days six and one, respectively). All results were based on one study (n = 80) with low-certainty evidence. Honey also significantly reduced cough duration (MD -0.54 days, 95% CI -0.98 to -0.10, one study, n = 100), as well as cough frequency, severity and bothersome cough

Table 1. Comparison between the effects on primary outcomes and adverse events of honey versus placebo

Outcomes and comparisons	Absolute effects (95% CI)	Relative effect (95% CI)	Participants (studies)	Certainty of evidence (GRADE)
Duration of cough	-0.72 days (-0.31 to -0.13)	-	102 (1)	Moderate
Frequency of cough				
Day 1	MD -1.62 (-3.02 to -0.22)		402 (2)	
Day 3	MD -1.13 (-1.71 to -0.55)		102 (1)	Moderate
Day 5	MD -0.48 (-2.95 to 1.99)		102 (1)	
Severity of cough				
Day 1	MD -1.07 (-2.43 to 0.30)		402 (2)	
Day 3	MD -0.85 (-1.41 to -0.29)		102(1)	Moderate
Day 5	MD -0.43 lower (-2,21 to 1,35)		102(1)	
Adverse events				
Stomachache, nausea, and vomiting		RR 1.91 (1.12 to 3.24)	402 (2)	Moderate

95% CI - 95% confidence interval; MD - mean difference; RR - risk ratio

more than oral salbutamol by day five, but salbutamol reduced cough impact on children and parents sleep. No differences were found between use of honey and dextromethorphan or bromelin mixed with honey across reported outcomes. Subgroup analysis by type of honey were only performed on pre-post intervention changes, and not between group differences.

No serious adverse events were reported in any of the treatment groups. Mild gastrointestinal symptoms (abdominal pain, nausea, and vomiting) were more common with honey than with placebo (RR 1.91, 95% CI 1.12 to 3.24) and with salbutamol.

Conclusion

The authors concluded that honey for up to three days is probably more effective in relieving cough symptoms and cough duration in children when compared to placebo. Honey is also likely more beneficial than diphenhydramine and comparable to dextromethorphan and bromelin mixed with honey, with no difference of non-severe adverse events. However, the authors state that these findings result from small studies with associated bias and highlight the need for larger randomized controlled trials.

Comments

Cough is a normal protective mechanism through which the respiratory system rids itself of excessive secretions and foreign inhaled material.⁹⁻¹³ Most cases of acute cough are due to transient, benign respiratory infections, without any serious underlying cause. However, only half of children recover from acute cough within 10 days, and 10% are still coughing by 25 days.^{9,14} The child and family impact of troublesome cough often leads families to use over-the-counter medications, despite their unproven effectiveness.

Honey is a mostly inexpensive sweet liquid with well-established antioxidant and antimicrobial biological effects. Importantly, it may reduce cough by its topical demulcent effect on the pharynx and larynx, which naturally induces reflex salivation and secretion of airway mucus.¹⁰ In 2001 the World Health Organization considered honey a cheap, popular and safe demulcent on the treatment of upper respiratory infections in young children.¹⁵ The results of this Cochrane review suggest that honey may be beneficial in improving cough symptoms and quality of sleep when compared to other management strategies, including first-generation

antihistamines, cough suppressants, or no treatment. However, it is important to point out that this evidence presents considerable limitations. All included studies were small, differences attributable to duration of administration and types of honey could not be adequately addressed, and there was short length of follow-up and scarce data for each comparison, leading to imprecise results with large confidence intervals. While the review suggests no significant harms were found, we should highlight the known risk of infantile botulism which restricts its use in infants aged under 12 months.¹⁶

In Portugal and elsewhere, the number and diversity of honey-containing products that may be used for pediatric cough has increased. These can range from pure foods to food supplements, or medical devices, often in a combination of honey with other substances. Different products imply heterogeneous regulatory requirements when it comes to submitting evidence for efficacy and safety, leaving considerable uncertainty for clinicians and families. Furthermore, a placebo effect related to glucose and sweet syrup formulations instead of a specific effect of honey cannot be ruled out.

The availability of any of these non-prescription products must not preclude addressing parents anxiety as a common driver for self-medication, with the option of no specific treatment based on the often-benign natural history of acute cough. Conversely, it is crucial to highlight that these easily accessible medicines can delay medical observation, and to keep in mind the differential diagnosis and red flags for more serious causes of acute cough, such as respiratory distress, wheezing and prolonged productive cough.

Keywords: Antitussive Agents/therapeutic use; Apitherapy; Child; Cough/therapy; Honey; Randomized Controlled Trials as Topic

Conflicts of Interest

The authors declare that there were no conflicts of interest in conducting this work.

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Protection of human and animal subjects

The authors declare that the procedures followed were in accordance with the regulations of the relevant clinical research ethics committee and with those of the Code of Ethics of the World Medical Association (Declaration of Helsinki).

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