

The therapeutic role of honey for treating acute cough in the pediatric population. A systematic review

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Abstract

An acute cough is a common reason for medical consultation in the pediatric age group, particularly in the setting of an upper respiratory tract infection (URTI). Traditionally, honey is used as a home remedy for treating an URTI in many parts of the world. Its use is supported by the fact that honey has both antimicrobial and wound-healing properties. Due to its inexpensiveness, easy availability and safety (in children above the age of 12 months), the World Health Organization endorsed the use of honey as a demulcent in the symptomatic relief of a cough and sore throat. A literature review of PubMed identified 6 randomized controlled trials that compared honey against over-the-counter (OTC) cough medications, and no treatment, in the pediatric population. It was shown that honey was more efficacious than no treatment and at least as efficacious as OTC cough medications. As OTC cough medications are associated with morbidity and mortality in pediatrics, the potential utilization of honey as an alternative therapeutic option in pediatrics warrants further objective research in the context of clinical practice.

Keywords

Honey, cough, treatment, pediatrics, upper respiratory tract infection.

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Introduction

An acute cough is one of the most frequent reasons for medical consultation in the pediatric age group, particularly in the setting of an upper respiratory tract infection (URTI). In the United States, it is estimated that 3% of all outpatient consultations are related to cough [1]. Although commonly viral in origin and typically self-resolving [2], coughs can be distressing to both children and parents, leading to poor sleep and potentially interfering with school or work. As a result, parents commonly turn to over-the-counter (OTC) medications to treat their child's cough, such as levodropropizine or dextromethorphan. However, the utilization of such medications in pediatrics is subject to controversy due to their safety profile [3], their unproven efficacy and disapproval by professional organizations such as the American Academy of Paediatrics [4-5]. Despite this, consumers regularly spend several billions of dollars on OTC cough medications [2].

Traditionally, honey is used as a home remedy for an URTI in many parts of the world. Its use is supported by the fact that honey has both antimicrobial and wound-healing properties [6]. Due to its inexpensiveness, easy availability and safety (in children above the age of 12 months), the World Health Organisation endorsed the use of honey as a demulcent in the symptomatic relief of a cough and sore throat [7, 8].

The focus of this systematic review is to assess the potential therapeutic use of honey as a remedy for cough in the pediatric age group.

Methods

The PubMed database was used and the keywords "honey AND cough AND pediatric" yielded 16 results. The inclusion criteria included studies in English, conducted in the last 12 years (since 2007), and the presence of a control group. Cohort studies, randomized controlled trials (RCTs) and systematic reviews were also included.

6 articles were identified from PubMed after fulfilling the inclusion criteria and were analyzed for this review (Fig. 1).

Results

In Miceli Sopo et al.'s open randomized study, 134 children with non-specific cough were randomized into 2 groups; both groups had participants who were given 90 ml of cow milk mixed with 10 ml of

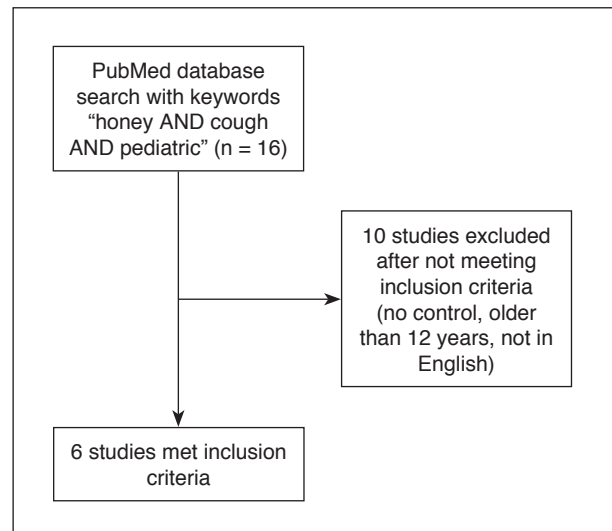


Figure 1. Flowchart of study inclusion.

wildflower honey and the controls for each group were dextromethorphan and levodropropizine respectively, both common OTC antitussive agents. These were administered over 3 days before bedtime, after which the parents completed a 5-item subjective questionnaire about the cough. The study showed an 84% therapeutic success rate amongst all groups, indicating that honey is at least as efficacious as dextromethorphan and levodropropizine. However, this study had no placebo control group and was not blinded for both participants and physicians thus raising concerns about potential bias. Blinding may have been difficult due to the recognizable consistency and taste of honey compared to the other medications [9].

Regarding Cohen et al., 300 children with URTIs and cough were randomized in a double-blinded study in 2012. The randomized study participants into 4 groups; each group was given a specific type of honey (eucalyptus, citrus, and labiatae honey), with 1 group being given silan date extract (date syrup) instead as a placebo due to its similar taste and consistency to honey. In contrast to Miceli Sopo et al., a single dose (10 g) was given before bedtime. Subjective questionnaires were administered to the parents before and 2 days after treatment, with cough frequency being the primary measured outcome. The study found that all groups with honey consistently reported greater symptomatic relief of coughing compared to the placebo. There were no significant differences between the types of honey. However, this study did not exclude participants who used other OTC medications like paracetamol and ibuprofen, thus compounding the study. Furthermore, there are observable differences

in the physical features and aroma of the different types of honey thus raising the possibility of bias in the results and skepticism about the nature of the study's blindness [10].

In Paul et al. study, 103 children with URTI-associated cough were enrolled in a double-blinded RCT comparing the effects of a nocturnal dose of buckwheat honey, honey-flavored dextromethorphan, and no treatment, on cough and sleep quality. A 7-point Likert scale questionnaire was administered to parents before, 1 day, and 2 days after the intervention. The study found that all groups improved, with the most significant decrease in cough severity and frequency seen in the honey group, followed by dextromethorphan, and no treatment. Both children and parental sleep improved the greatest in the honey group. However, no significant difference was found between the efficacy of honey and dextromethorphan. Blindness was not applicable for the no-treatment group as no placebo was provided. Furthermore, it should be noted that the National Honey Board funded this study and therefore it may represent a potential conflict of interest [11].

Shadkam et al. conducted a RCT that divided 160 children aged below 5 years, with an URTI and cough, into 4 groups. One group was given a single dose of 2.5 ml of Kafi-Abad honey before sleep, the second group was given single dose dextromethorphan, the third group received a single dose of diphenhydramine, and the fourth group received supportive therapy such as saline nose drops and nebulizers. The fourth group was not adequately blinded as a result. A subjective questionnaire was administered to the parents in the presence of a pediatrician before and after 1 day of intervention to assess the outcome on the cough. The study found that the honey group had the most considerable reduction in cough severity, frequency, and improved sleep in both children and parents. Dextromethorphan and diphenhydramine were also identified as relieving agents but not as efficacious as honey. Limitations identified by the authors include limited intervention; only 1 dose was given in each group. Furthermore, this study was not blinded, and as such, the results are very likely affected by this [12].

Ayazi et al. conducted a randomized clinical trial that divided 87 children into 3 groups that compared 2 variants of Iranian honey (*Kimia* and *Shahde-Golhe*, respectively) with a control group that was administered diphenhydramine. Parents were administered a 7-point Likert scale

questionnaire (similar to Paul et al.) on cough severity and sleeping difficulties. All groups were given 1 dose of their allocated treatment before bedtime for 2 days, after which the questionnaire was administered again to the same parent over a telephone interview. The study reported symptomatic improvement in all 3 groups; however, both honey groups were shown to be significantly more effective than diphenhydramine, echoing the results of Shadkam et al. Potential limitations to the study include the allocation method which was not completely randomized, and the fact that patients who were administered analgesics such as paracetamol were not excluded: that could have influenced the outcome of the study. The study could not be blinded due to the different physical appearance and taste of the treatment types [13].

In 2017, Cohen et al. organized a single-blinded multicentre RCT that recruited 150 children with acute uncomplicated URTIs into 2 groups and compared the efficacy of a polysaccharide-resin-honey (PRH) cough syrup with that of carbocysteine mucolytic cough syrup. Both groups were given 1 dose on the night of enrollment and after that received 3 daily doses for 3 days afterward. The study administered a subjective cough severity questionnaire (Likert scale) to parents on the day of enrollment and each treatment day afterward, with the study's primary outcome focusing on night cough score changes in the first 2 nights. The study showed improvement in cough severity in both groups, with the most significant reduction observed in the PRH group showing a reduction in combined cough severity score by 5.16 ± 0.85 (compared to 1.77 ± 0.67 in the carbocysteine group, p -value = 0.005). Limitations of the study included the lack of double-blinded protocol, and the inability to assess adherence to the treatment regimen. Furthermore, this study does not exclusively study honey as a solitary therapeutic agent and therefore confounding effects of the polysaccharide resin cannot be ruled out [14].

Discussion

The above studies consistently showed that, in a total of 934 patients, honey was more efficacious than no treatment and at least as effective as conventional OTC cough suppressants, if not better (**Tab. 1**). Due to the ease of availability of honey and its inexpensiveness, this is significant for families of poor socioeconomic status.

Table 1. Summary of the studies included.

Authors	Sample size	Design	Intervention	Primary outcome	Conclusion
Paul et al., 2007 [11]	103 children	Double-blinded RCT	A nocturnal dose of buckwheat honey, honey-flavored dextromethorphan, and no treatment groups	7-point Likert questionnaire administered to parents before, 1 day, and 2 days after the intervention, focusing on cough symptoms	Honey saw the most significant decrease in cough severity, frequency and sleep problems, followed by dextromethorphan, and no treatment. No significant difference reported between the efficacy of honey and dextromethorphan
Shadkam et al., 2010 [12]	160 children	Unblinded RCT	A single dose of Kafi-Abad honey, diphenhydramine, dextromethorphan, and supportive therapy groups	A subjective questionnaire administered to parents before and 1 day after treatment	Honey had the most significant reduction in cough severity, frequency, and improved sleep in both children and parents. Dextromethorphan and diphenhydramine were not as efficacious as honey
Cohen et al., 2012 [10]	300 children	Double-blinded RCT	3 variants of honey (eucalyptus, citrus, and labiatae) controlled with silan date syrup, 10g dose at bedtime	A subjective questionnaire administered to parents before and 2 days after treatment, focusing on cough frequency	Honey saw the most significant decrease in cough severity, frequency and sleep quality
Miceli Sopo et al., 2015 [9]	134 children	Unblinded open RCT	A 3-day course of honey (10 ml in 90 ml cow milk) compared to either dextromethorphan or levodropropizine at bedtime	A subjective questionnaire filled by parents on the improvement of cough before and 3 days after treatment	Honey was as efficacious as dextromethorphan and levodropropizine in symptomatic relief of cough
Ayazi et al., 2017 [13]	87 children	Unblinded RCT	2 variants of honey (<i>Kimia</i> and <i>Shahde-Golhe</i>) controlled with diphenhydramine, 1 dose at bedtime for 2 days	7-point Likert questionnaire administered to parents before and 2 days after treatment, focusing on cough and sleep symptoms	Both variants of honey were significantly more effective than diphenhydramine in the symptomatic improvement of cough
Cohen et al., 2017 [14]	150 children	Single-blinded RCT	PRH cough syrup compared to carbocysteine syrup, 1 dose on enrollment night and 3 doses a day for 3 days after	Subjective Likert questionnaire filled by parents to assess night cough score changes in the first 2 nights	Both groups resulted in symptomatic improvement of cough, with the PRH group being more effective than the carbocysteine group in reducing overnight cough scores

RCT: randomized controlled trial; PRH: polysaccharide-resin-honey.

The potential benefit of utilizing honey over common OTC medications is the excellent safety profile of honey. In the studies mentioned, only Paul et al. reported mild adverse events from treatment with honey, and that was limited to only 5 children reporting hyperactivity, insomnia, and nervousness [11]. Honey was long known to have antimicrobial and antioxidant properties. These activities are predominately due to the presence of inhibines such as hydrogen peroxide, flavonoids and phenolic acids in honey [15]. The combination of both properties is believed to be the reason for improved wound healing and protection against

oxidative stress [16]. However, honey should not be used in children below the age of 12 months due to the risk of infantile botulism [7]. Due to the risk of dental caries in the pediatric age group, it is advised to utilize a short course [17].

According to the literature, OTC cold and cough medicines are sources of morbidity and mortality in children due to medication errors resulting in accidental overdoses, and adverse drug events [18]. Dextromethorphan has been associated with (but not limited to) dependence particularly amongst adults, psychosis, hallucinations, mania, dystonia, anaphylaxis, peripheral neuropathy,

megaloblastic anemia, and death [12]. Health Canada, the Canadian department of public health, recommended against the use of OTC cough suppressants in children less than 6 years of age [19]. Surprisingly, Paul et al. stated there was no statistically significant difference between treatment with dextromethorphan and no treatment being given. It had been hypothesized that the sweet taste of cough syrup and its subsequent stimulation of taste receptors influences the cough reflex via inhibition of the solitary nucleus, the component of the brainstem that mediates the cough reflex as well as taste [20].

Both Cohen et al. and Miceli Sopo et al. relied on the administration of a subjective questionnaire to parents on perceived symptomatic relief of nocturnal cough; Paul et al. first used that. The possibility that honey is merely a consistent placebo cannot be ruled out. As such, further objective RCTs are needed and must be conducted with a different but more objective assessment of the primary outcome, such as daily assessment by pediatricians although, in reality, this would be unfeasible. In the studies above, no physical examination by pediatricians was conducted unless warranted by the patients' clinical condition.

Furthermore, the issue of appropriately blinding participants remains. Blindness was inapplicable in the no-treatment groups of Paul et al. and Shadkam et al. studies due to the nature of the intervention. This deprived the groups of any placebo and raised the likelihood of bias compounding the results of the studies. As previously stated for Cohen et al., blindness cannot be fully guaranteed as the different varieties of honey and silan date extract could still be differentiated from each other based on appearances, consistency, and taste. Furthermore, both Cohen et al. and Paul et al. studies were funded by separate honey boards respectively, raising questions over a potential conflict of interests.

It should be noted that all the studies above focused primarily on acute uncomplicated cough in the pediatric population and had excluded patients with significant co-morbidities or symptoms suggestive of other pathologies such as asthma, laryngotracheobronchitis, pneumonia, and sinusitis. As such, limited data if any exists on the usage of honey in these population groups. Therefore, an accurate diagnosis by qualified medical professionals is needed so as not to delay treatment of the underlying condition.

Conclusion

In conclusion, multiple randomized controlled studies confirm that honey has some therapeutic properties in the treatment of cough. It can be reasonably stated that honey is at least as efficacious as OTC cough suppressants such as dextromethorphan and other OTCs, if not better. However, more objective means of measuring outcomes must be established in future randomized controlled studies as all the studies mentioned above relied on subjective questionnaires wherein the possibility of a placebo effect cannot be ruled out.

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Declaration of interest

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