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Role of honey in children with acute cough in upper respiratory tract infection: randomized, placebo-controlled study

Abstract

Introduction: Cough is one of the common complaints for which parents seek medical attention. There is no accepted therapy for this annoying symptom. World Health Organization has recognized honey as a potential treatment for acute cough

Objective: To evaluate the role of single nocturnal dose of honey to placebo in symptomatic treatment of nocturnal cough and sleep difficulties in children with acute cough due to Upper Respiratory Tract Infection (URTI).

Methods: Randomized placebo controlled double blinded trial was done in children aged 1-5 years with diagnosis of URTI<14 days. Ninety participating parents were asked a five-item questionnaire regarding subjective assessment of child's cough and sleeping difficulty on two consecutive days, first on day of presentation when no medication was given and second on the day after 10ml of honey or placebo was given at bedtime. Main outcome measures included the cough frequency; cough severity, bothersome nature of cough, and child and parent sleep quality. Each of the five items was scored on a 7-point Likert scale.

Results: Baseline characteristics were comparable in both the groups. After intervention, statistically significant improvement was noted in all the study outcome variables except in bothersome nature of cough in honey group compared to the placebo group. Greatest improvement was seen in cough severity and effect on parent's and child's sleep.

Conclusion: Honey is effective in symptomatic relief of child's nocturnal cough and sleep difficulties related to URTI. Honey can be used as an alternative therapy to cough medications.

Keywords: children, cough, honey, sleep

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Abbreviations: AAP, american academy of pediatrics; IOM, Institute of Medicine; OTC, over-the-counter; URTI, upper respiratory tract infection; WHO, world health organization

Introduction

Cough is an important defensive reflex that enhances the clearance of secretions and particles from the airways and helps to protect the lower airways from the aspiration of foreign material.[1] It can be of infectious origin i.e. bacterial or viral and/or due to irritant or allergen in the respiratory tract.[2] Acute cough in majority of children is from Upper Respiratory Tract Infection (URTI) i.e. common cold. Hallmarks of the common cold include runny nose, cough, and congestion. Mostly cough from acute URTIs are due to viral infections.[3] Cough can be distressing for parents especially when it interferes with child's daily activities and disturb parents and child's sleep. It also results in absenteeism from school. As it is a major concern for parents, it is the most common presenting symptom to the general practitioners.[4] Though an immediate remedy is usually sought by the caregiver, there is no effective treatment beyond ordinary supportive care. *American Academy of Pediatrics (AAP)* strongly recommends against the use of over-the-counter cough and cold medications in infants and children below two years of age. It also highlights that cold and cough products do not work in children younger than 6 years and can have potentially serious side effects.[5] The *World Health Organization (WHO)* has noted honey as a potential treatment of cough and cold symptoms, and it is considered as a demulcent that is inexpensive, popular, and safe(outside of the infant population).[6] The objective of this trial was to compare the effects of a single nocturnal dose of honey to placebo on nocturnal cough and the sleep difficulty associated with URTI.

Methods

Children between one to five years of age with nocturnal cough attributed to URTI were included in the study between November 2014 to August 2015. URTI was defined by the presence of cough and rhinorrhea of ≤14days duration. Children with signs or symptoms of asthma, pneumonia, laryngotracheobronchitis, sinusitis, and/or allergic rhinitis were excluded. Children with history of reactive airways disease, asthma, or chronic lung disease were considered ineligible. Intake of Over the Counter (OTC) Cough Cold medication on prior evening was not included in the study. Double-blinded randomized design was used to conduct this study in Pediatric Out-patient Department of Tribhuvan University Teaching Hospital, Nepal. On the basis of previously published study[7] we calculated that the sample size necessary to detect a 0.75-point difference between any 2 treatment groups (using analysis of variance) with 80% power and an alpha of 0.05 was 40 subjects per treatment group. Considering 10% drop out rate, the sample size chosen for this study was 90.

All participating parents were asked to complete a 5-item pre-intervention questionnaire regarding their subjective assessments of the child's cough and sleep difficulty on the previous night. The questionnaire used was previously validated pediatric cough questionnaire[8] (Table 1). Survey responses were graded on a 7-point Likert scale. Each child was randomly assigned in a double-blinded fashion to receive either buckwheat honey or placebo and was sent home with a bottle of suspension. Parents were instructed to administer 10ml solution at bedtime. Drugs and placebo for the study were provided by a *WHO* registered pharmaceutical company of Nepal, National Pharmaceutical. Each placebo had Golden syrup (sucrose) solution of same color, viscosity and flavor and taste. Both honey and placebo were packed in small bottle of 20ml each and marked with the letters A,B. Sample size and randomization sequence was constructed by a statistician not affiliated with the study and was then used by the study coordinators to assign treatment groups. A second survey was done via telephone interview the following day to the same parent. Post-intervention same questions as those answered at enrollment were read to them and scores were graded accordingly. Parents were asked about their child's compliance with solution and if they have came across any adverse events. Reasons for not giving solution to child were noted if any. Those who could not be contacted were labelled as lost to follow-up. Outcome measure was the change in the frequency of cough, cough severity, the bothersome nature of the cough, the effect of the cough on sleep for both the child and the parent, and the combined score of these five measures between the 2 nights. Permission was taken *from Institutional review board (IRB*) IOM and an informed consent with assent was obtained before enrolling the subjects in the study.

Table 1 Pediatric cough questionnaire (PCQ) Scoring

Sl. No	Cought question	Pre-intervention	Post-intervention
1	How frequent was your child's coughing last night?		
2	How severe was your child's cough last night?		
3	How bothersome was last night's cough to your child?		
4	How much did last nighte's cough affect your child's ability to sleep?		
5	How much did last night's cough affect your (parent's) ability to sleep?		

0 = not at all 1 = not much, 2 = a little, 3 = somewhat, 4 = a lot, 5 = very much, 6 = extremely

Results

Total of 177 patients between 12 months to 60 months presenting with acute cough were screened. Ninety eligible patients were enrolled in the study. Figure 1 summarizes the enrollment of children. The mean age of the children in drug and placebo groups was 28.95+13.27 months and 30.79+13.9 months respectively. Table 2 shows baseline characteristic of the study population. Most children in both groups presented with cough of less than 7 days duration. In addition (Table 3), there were no significant differences between measures of symptom severity at baseline. As shown in Figure 2, when symptom scores were compared between treatment group and placebo group after intervention, significant differences were detected in the amount of improvement reported for all study outcome variables except in bothersome nature of cough. For cough frequency, those who received honey had a mean 1.32- point improvement compared with a 0.70-point change for those received placebo and it was statistically significant (p=0.003).

Table 2 Baseline characteristic of the study population

	Treatment group		Placebo group		
Characteristics	**Mean**	**Standard deviation**	**Mean**	**Standard deviation**	**P-Value**
Age (Months)	29.04	12.74	30.4	13.83	0.63
Sex Male	46.88%		52.11%		1
Female	53.12%		47.89%		1
Duration of cough (days)	5.09	2.68	5.53	3.11	0.47
Temp (°F)	98.77	0.72	98.58	0.62	0.9

Table 3 Baseline pre- intervention coughs score

	Treatment group		Placebo group		
Categories	**Mean**	**Standard deviation**	**Mean**	**Standard deviation**	**P-Value**
Cough frequency score	4.41	0.77	4.44	0.76	0.87
Cough severity score	4.24	1.13	4.02	0.8	0.3
Cough bothersome score	3.93	0.98	3.93	0.96	0.96
Cough child sleep	4.12	1.05	3.77	0.92	0.1
Cough parents sleep	4.07	1.03	3.74	1.09	0.16
Combined total score	20.78	4.02	19.91	3.25	0.27

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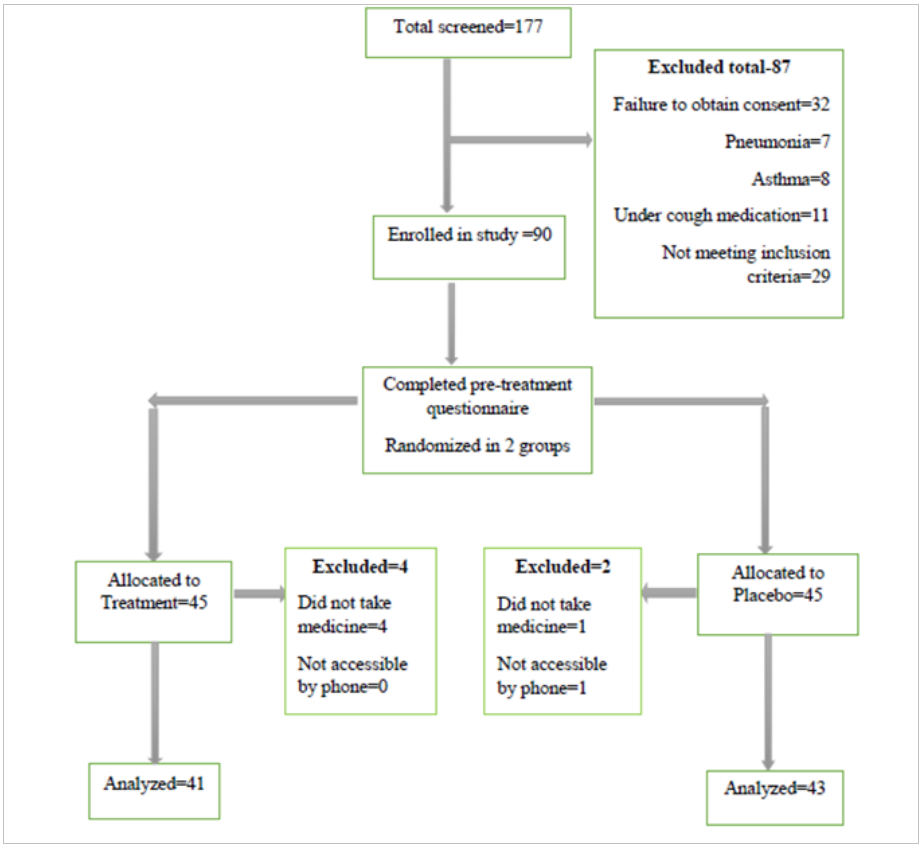

Figure 1 Flow diagram of the study population.

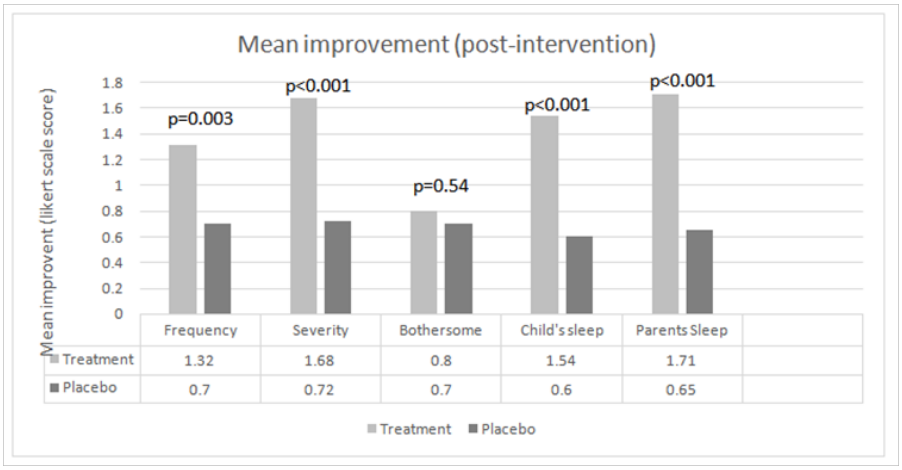

Figure 2 Mean improvement in Likert scale score after intervention between 2 groups.

Parents also noted similar improvements in the severity of their children's cough; 1.68 point with honey group, 0.72 point with placebo group (p=<0.001). There was a mean 0.80point improvement in bothersome nature of cough in honey group compared to 0.70-point improvement in placebo group which was insignificant (p=0.54). Parents felt their children slept better after receiving honey, with improvement by 1.54 point compared to 0.60-point improvement in placebo group (p=<0.001). Parental sleep also improved in the similar way to that of their children, with the honey treatment arms having mean improvement of 1.71 compared to only 0.65 improvement in placebo arms (p=< 0.001). When the results for these individual categories outcomes were combined by adding scores - honey treated group again proved to be the effective treatment. The children improved by an average of 7.05 point with honey and 3.37 point in placebo groups which was statistically significant (p=<0.001). Few adverse events occurred in this investigation. Vomiting and diarrhea was noted in five children in honey group compared to seven children in placebo group. The adverse events were not significantly different between two groups (Table 4).

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Table 4 Adverse effects noted between 2 groups

Side effects		Treatment n (%)	Placebo (%)	p value
Vomiting	Present	3(7.3%)	4(9.30)%	1
	Absent	38(92.6%)	39(90.69%)	
Diarrhea	Present	2(4.87%)	3(6.97%)	1.07
	Absent	39(95.12%)	40(93.02%)	1
Rash	Present	0(0%)	1(2.32%)	1
	Absent	41(100%)	42(97.67%)	

Discussion

Acute cough due to viral URTI is one of the common complaints for which patients and parents seek medical attention. People often use OTC cough and cold medication which are easily available. The results of our study showed honey was more effective than placebo for the treatment of outcomes related to nocturnal cough frequency, severity and effect on child and parental sleep. Paul et al. were the first to study about the effects of honey on acute cough in children. His study showed Buckwheat honey was more effective compared to no treatment, especially on cough frequency and total cough score (calculated by adding the scores from the five individual categories). On the other hand, it had the same effectiveness of dextromethorphan. [9] Cohen et al study showed that, all three types of honey (eucalyptus honey, citrus honey, or labiatae honey) were effective without any significant difference between each other and they were all superior comparing to date syrup (placebo). The Cohen et al. study proved that several honey products can beef fective[7] S. Miceli Sopo et al. evaluated the effect of wildflower honey, given for three subsequent evenings, on non-specific acute pediatric cough, compared to dextromethorphan (DM), and therapeutic success was achieved by 80% in the honey and milk group and 87% in OTC medication group ($p = 0.25$).[10]

The results of our study strengthen the observation made by Cohen et al and Paul et al that honey products may have a beneficial effect for symptomatic relief of no cturnal cough. Paul et al compared the effect of one type of honey (buckwheat) to dextromethorphan and a no-treatment but they included children of wide range of age group (2 to 17 years). Similarly, Shadkam et al. also reported that honey hada more alleviating effect on URI-induced cough compared with dextromethorphan and diphenhydramine, however their study was not blinded.[11] Thus, our study further supports the recommendations of the World Health Organizatio*n* to use honey as a potential treatment of cough. In current study, vomiting and diarrhea were noted in five children in honey group compared to seven children in placebo group. In contrast with observation made by Paul et al, which was telephone-based survey on second day, symptoms of hyperactivity, nervousness, and insomnia was not noted both group as these are minor symptoms parents may not recognize or given importance to these symptoms.[9]

The World Health Organization has noted honey as a potential treatment of cough and cold symptoms.[6] Honey is a natural sweetener available all over the world. Honey has well-established antioxidant and antimicrobial effects,[12,13] which helps to explain its superiority in this study, the antimicrobial potential of this natural product was first described a century ago. It is a sweet, viscous liquid with acomplex chemical composition. It is made up of a mixture of approximately 25carbohydrate, free amino acids, vitamins, trace elements and flavonoids.[14] Honey has broad-spectrum antimicrobial actions, against various gram-negative and gram-positive bacteria, and is active against common bacteria found in the upper respiratory tract such as *Staphylococcus aureus, Streptococcus faecalis, Candidaalbicans, Klebsiella pneumonia, Pseudomonas aeruginosa, Escherichia coli, Salmonellaspp* and *Shigelladysenteriae.*[15,16] It is seen that honey also has antiviral properties. Due to these properties, honey has been used in traditional medicine for the treatment of cough. It is also used in modern medicines to treat infected wounds.[17,18] Buckwheat honey which was used in this study is a dark variety of honey, and darker honeys tend to have a higher content of phenolic compounds. These compounds have been associated with the antioxidant properties of honey that may have contributed to its effect in this study.[19,20] In general, honey is inexpensive and has an excellent safety profile. However, honey might contain dormant endo spores of *Clostridium botulinum*. These can transform in to toxin-producing bacteria in infant younger than one year of age, leading to infantile botulism. Hence, pasteurized honey can safely be used in children older than one year of age. [21]

Another theory for explaining some of the beneficial effects of honey was described in a review by Eccles.[22] He hypothesized that sweet substances naturally cause reflex salivation and may also cause the secretion of airway mucus that leads to a demulcent effect on the pharynx and larynx, thereby reducing cough. He suggested that an interaction between closely related sensory nerve fibers that initiate cough and the gustatory nerves fibers that taste sweetness may help to produce the antitussive effects of sweet substances via a central nervous system mechanism. But in our study significant difference noted between the honey and the placebo group suggests that other factors in addition to the sweet taste of honey contribute to its beneficial effect on children with cough. Study in our part of world showed that 75% of the mothers of children less than 5 years of age gave their children OTC cough medicines as access to these medicines is very easy.[23] However, these medications are potentially dangerous. Many of the adverse events reported were caused by inadvertent overdoses when parents gave the drug to a child too often or at a higher than recommended doses. OTC availability in especially concerning as a result of numerous serious adverse events described in medical literature such as dystonia, anaphylaxis, psychosis, mania, hallucination, ataxia, somnolence and death with higher doses.[24–26] Rimsza et al., reported 10 unexpected deaths associated with the use of OTC cough and cold medications in a 1-year period. [27] Subsequently, because of concern about its safety profile American Academy of Pediatrics has issued warnings against the use of OTC cough and cold preparations in children younger than 6 years.[5] Cochrane review suggests that honey may be better than "no treatment" for reducing cough frequency, cough severity, resolving bothersome cough and improving sleep quality for both children and parents. Its effect on cough frequency, cough severity and quality of sleep for children and parents is also likely to be better than diphenhydramine which is an over-the counter (OTC) cough remedy.[28] This study is somewhat limited by the fact that subjective survey was used for this study but clinicians and parents often make decisions based on subjective assessment of symptom severity as discussed earlier. Though most of the parents did report that the treatment was given to their child without difficulty compliance with medication administration could not be guaranteed. We could not determine the effect of honey on duration of cough associated with URTI. Another limitation is the fact that the effect of only a single dose was evaluated. Outcomes could

have been different if treatment and follow-up were longer than one night.[29]

Conclusion

This study showed honey to be effective in symptomatic relief of child nocturnal cough and sleep difficulties related to URTI which further confirms findings of previous studies.[7,9] In the absence of safe and effective anti-tussive drugs, honey should be considered as an effective and safe treatment of cough in children above one years of age group. Future studies are recommended to confirm our findings and should include longer treatment and follow-up periods, and measure other out-comes such as improvement in appetite, level of physical activity, school attendance and cost, all of which are relevant to caregivers.

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Conflicts of interest

None.

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