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Pediatrics 2012;130;465; originally published online August 6, 2012;
DOI: 10.1542/peds.2011-3075

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http://pediatrics.aappublications.org/content/130/3/465.full.html

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Effect of Honey on Nocturnal Cough and Sleep Quality: A Double-blind, Randomized, Placebo-Controlled Study

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KEY WORDS
cough, children, honey

ABBREVIATIONS
FDA—Food and Drug Administration
OTC—over-the-counter
URI—upper respiratory tract infection

[†]Deceased.

Dr Cohen was responsible for conception and design of study, data acquisition, analysis and interpretation of data, and he drafted and revised the article and approved the final version; Dr Rozen was responsible for data acquisition, data analysis and interpretation, and critical revision of the article; Drs Kristal, Laks, Berkovitch, Uziel, Kozer, and Pomeranz were responsible for data acquisition, data analysis and interpretation, revising the article, and approving the final version; and Mr Haim was responsible for preparing blinded specimens.

This trial has been registered at www.clinicaltrials.gov (identifier NCT01575821).

www.pediatrics.org/cgi/doi/10.1542/peds.2011-3075

doi:10.1542/peds.2011-3075

Accepted for publication Apr 23, 2012

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PEDIATRICS (ISSN Numbers: Print, 0031-4005; Online, 1098-4275).

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FINANCIAL DISCLOSURE: *The authors have indicated they have no financial relationships relevant to this article to disclose.*

FUNDING: This study was supported in part by a research grant from the Israel Ambulatory Pediatric Association, Materna Infant Nutrition Research Institute, and the Honey Board of Israel. The funders had no role in the study design, data collection or analysis, decision to publish, or preparation of the manuscript.

WHAT'S KNOWN ON THIS SUBJECT: Honey is recommended as a cough medication by the World Health Organization. To date, the efficacy of this treatment has been shown in 2 studies: one tested only buckwheat honey and the other study was not blinded.

WHAT THIS STUDY ADDS: In a randomized controlled trial, we compared 3 types of honey versus placebo as a treatment of upper respiratory tract infection–associated cough. These types of honey were superior to placebo in alleviating cough.

abstract

FREE

OBJECTIVES: To compare the effects of a single nocturnal dose of 3 honey products (eucalyptus honey, citrus honey, or labiatae honey) to placebo (silan date extract) on nocturnal cough and difficulty sleeping associated with childhood upper respiratory tract infections (URIs).

METHODS: A survey was administered to parents on 2 consecutive days, first on the day of presentation, when no medication had been given the previous evening, and the following day, when the study preparation was given before bedtime, based on a double-blind randomization plan. Participants included 300 children aged 1 to 5 years with URIs, nocturnal cough, and illness duration of ≤7 days from 6 general pediatric community clinics. Eligible children received a single dose of 10 g of eucalyptus honey, citrus honey, labiatae honey, or placebo administered 30 minutes before bedtime. Main outcome measures were cough frequency, cough severity, bothersome nature of cough, and child and parent sleep quality.

RESULTS: In all 3 honey products and the placebo group, there was a significant improvement from the night before treatment to the night of treatment. However, the improvement was greater in the honey groups for all the main outcome measures.

CONCLUSIONS: Parents rated the honey products higher than the silan date extract for symptomatic relief of their children's nocturnal cough and sleep difficulty due to URI. Honey may be a preferable treatment for cough and sleep difficulty associated with childhood URI. *Pediatrics* 2012;130:465–471

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Cough is a common symptom in pediatric practice. It can be particularly troubling to children and their parents. It often results in discomfort to the child and loss of sleep for both the child and parents. As a result, children miss day care or school and parents miss a day of work. In an attempt to treat cough, caregivers frequently administer over-the-counter (OTC) medications to their children, with their attendant risks,[1–7] lack of proven efficacy,[8–11] and the disapproval of professional organizations such as the American Academy of Pediatrics,[12] and the Food and Drug Administration (FDA).[13]

A variety of home remedies and herbal medications, such as licorice, cloves, lemon, and honey, are used by some caregivers to treat the symptoms associated with upper respiratory tract infections (URIs).[14,15] The World Health Organization 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).[14] Honey has antioxidant properties and increases cytokine release, which may explain its antimicrobial effects.[16–21]

The objective of this trial was to compare the effects on nocturnal cough and the sleep difficulty associated with URIs of a single nocturnal dose of 3 honey products compared with placebo.

METHODS

Patients

Subjects were recruited from patients who presented to 1 of 6 general pediatric community clinics for an acute care visit between January 2009 and December 2009. Eligible patients were those between the ages of 1 and 5 years complaining of nocturnal cough that was attributed to a URI. A URI was defined by the presence of cough and rhinorrhea of ≤7 days' duration. Other symptoms might have included but were not limited to nasal congestion, fever, sore throat, myalgia, and headache. Patients were excluded if they had signs or symptoms of asthma, pneumonia, laryngotracheobronchitis, sinusitis, and/or allergic rhinitis. Patients were also excluded if they had used any cough or cold medication or honey on the night before entering the study. Patients were not excluded when analgesic medications such as acetaminophen or ibuprofen were administered on either night of the study.

Preintervention Study Questionnaire

After attaining informed consent, all participating parents were asked to complete a 5-item questionnaire regarding their subjective assessments of the child's cough and sleep difficulty on the previous night. The questionnaire used was a Hebrew version of a previously validated questionnaire[22] (Fig 1). Survey responses were graded on a 7-point Likert scale. Minimum symptom severity score criteria were established to determine which children should enter the randomized trial. Only children whose parents rated a severity of at least 3 for a minimum of 2 of the 3 questions related to nocturnal cough frequency, effect on the child's sleep, and effect on parental sleep on the previous night were included.

Study Design

A double-blind randomized design was used to conduct this study. Eligible children were randomized to 4 treatment groups: 3 groups were given 1 of 3 types of honey (eucalyptus honey (family Myrtaceae), labiatae honey (family Labiatae), or citrus honey (family Rutaceae), or a placebo. Silan date extract was selected as the placebo because its structure, brown color, and taste are similar to that of honey.

Intervention

The 3 honeys and the silan date extract were prepared by the staff of the Zerifin Breeding Apiary of the Volcani Agricultural Research Center in Rechovot, Israel. All 3 types of honey and the silan date extract were packed in small plastic containers of 10 g each and marked with the letters A, B, C, or D. The study preparations were distributed to the pediatric community clinics in blocks of 4. Parents were instructed to administer 10 g of their child's treatment product within 30 minutes of the child going to sleep. The parents were instructed that the preparation could be given undiluted or together with a noncaffeinated beverage.

The parents, the physicians, and the study coordinator did not know the content of the preparation that was dispensed. The envelopes containing the codes of the study preparations were stored at the office of the Ministry of Agriculture, Extension Service, Beekeeping Department, and were not opened until after the statistical analysis was completed.

Postintervention Study Questionnaire

The day after the treatment, the parent who completed the preintervention questionnaire was contacted by telephone. Trained research assistants who were blinded to the treatment group

How frequent was your child's coughing last night?
How severe was your child's cough last night?
How bothersome was last night's cough to your child?
How much did last night's cough affect your child's ability to sleep?
How much did last night's cough affect your (parent's) ability to sleep?

FIGURE 1
Cough Severity Assessment Questionnaire. Scoring: 0 = not at all, 1 = not much, 2 = a little, 3 = somewhat, 4 = a lot, 5 = very much, 6 = extremely.

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asked the parent the same 5 questions that had been answered in writing before the intervention, this time regarding the previous evening when the child had received the treatment. No physician examination was performed on the second study day unless dictated by illness progression.

Outcome Measures

The primary outcome was the cough frequency. The primary outcome measure was the change in the frequency of cough between the 2 nights. Secondary outcome measures of importance were changes in the 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.

Sample Size Analysis

On the basis of previously published data,[8] we estimated that the sample size necessary to detect a 0.75-point difference between any 2 treatment groups (using analysis of variance) with 90% power and an α of .05 was 60 subjects per treatment group.

To compensate for possible dropouts and abnormal data distribution, we attempted to recruit 75 patients per group.

Statistical Analysis

Statistical comparisons of variables between treatment groups were performed by using the χ^2 test for nominal variables and analysis of variance for continuous variables. For comparisons of cough evaluation before and after treatment, a paired Student *t* test was used. A *P* value $<$.05 was considered statistically significant. All statistical analyses were done by using the SPSS package for Windows (version 15.0.1, SPSS, Chicago, IL).

Ethics

The study was approved by the Committee for Ethics in Human Subjects Research, Meir Medical Center, Kfar Saba, Israel.

RESULTS

Three hundred children with URIs were enrolled and 270 (89.7%) completed the single-night study (Fig 2). Sixty-four children received eucalyptus honey, 62 received citrus honey, 73 received labiatae honey, and 71 received placebo (silan date extract). The dropout rate was higher in the citrus and eucalyptus groups (P = .006).

The median age of the patients completing the study was 29 months (range 12–71 months), with no significant difference in age among the treatment groups (Table 1). One hundred forty-six of the children (54%) were boys. The participants were ill a mean $\pm$ SD of 2.8 $\pm$ 2.0 days before enrollment, with no significant differences among treatment groups (P = .161). Almost half (47%) of the children had $>$3 days of coughing, with no difference among groups (P = .9). In addition, there were no significant differences between measures of symptom severity at baseline.

When symptom scores were compared for each treatment group from the night before treatment to the night of treatment, significant differences were detected in the amount of improvement reported for all study outcome variables (Fig 3). No significant differences were found among the different types of honey; however, each of the honey groups had a better response compared with the silan date extract. For cough frequency, those who received eucalyptus honey had a mean 1.77-point improvement compared with a 1.95-point change for those receiving citrus honey, 1.82 change for those receiving labiatae honey, and a 1.00 point change for those who were treated with silan date extract (placebo group) on the second night (F = 5.708, $P <$ .001). Parents also noted similar improvements in the severity of their child's cough: 1.78 points with eucalyptus honey, 1.77 points with citrus honey, 1.94 points with labiatae honey and 0.99 points with silan date extract (F = 5.78, $P <$ .001). Parents felt the cough also was less bothersome on the second night, with honey providing the greatest relief with a 2.0-point change with eucalyptus honey, a 2.16-point change with citrus honey, and a 2.07-point change with labiatae honey, compared with a 1.25-point change with silan date extract group (F = 4.63, $P <$ .04). Parents rated their children's sleep better after receiving honey, with improvement by 2.13 points with eucalyptus honey, 1.98 points improvement with citrus honey, and 1.70 points with labiatae honey, compared with a 1.21-point change with silan date extract (F = 3.61, $P <$ .014). As might be expected, parental sleep improved in a fashion similar to that of their children, with the honey-treatment arms improving the most, a mean of 2.16 points with eucalyptus honey, 2.10 points with citrus honey, 1.90 points with labiatae honey, and 1.28 points with silan date extract (F = 3.40, $P <$ .018). When the results for these outcomes were combined by adding the scores from the individual categories, honey again proved to be the most effective treatment. The children improved by an average of 9.88 points with eucalyptus honey, 10.10 points with citrus honey, 9.51 points with labiatae honey, compared with 5.82 points for those treated with silan date extract (F = 5.33, $P <$ .001).

Stomachache, nausea, or vomiting were reported by the parents of 4 patients in the honey treatment group (2 in the citrus, 1 in the eucalyptus, and 1 in the labiatae honey group) and 1 in the placebo group. The adverse events were not significantly different between the groups.

DISCUSSION

The results of this study (Fig 3) demonstrate that each of the 3 types of

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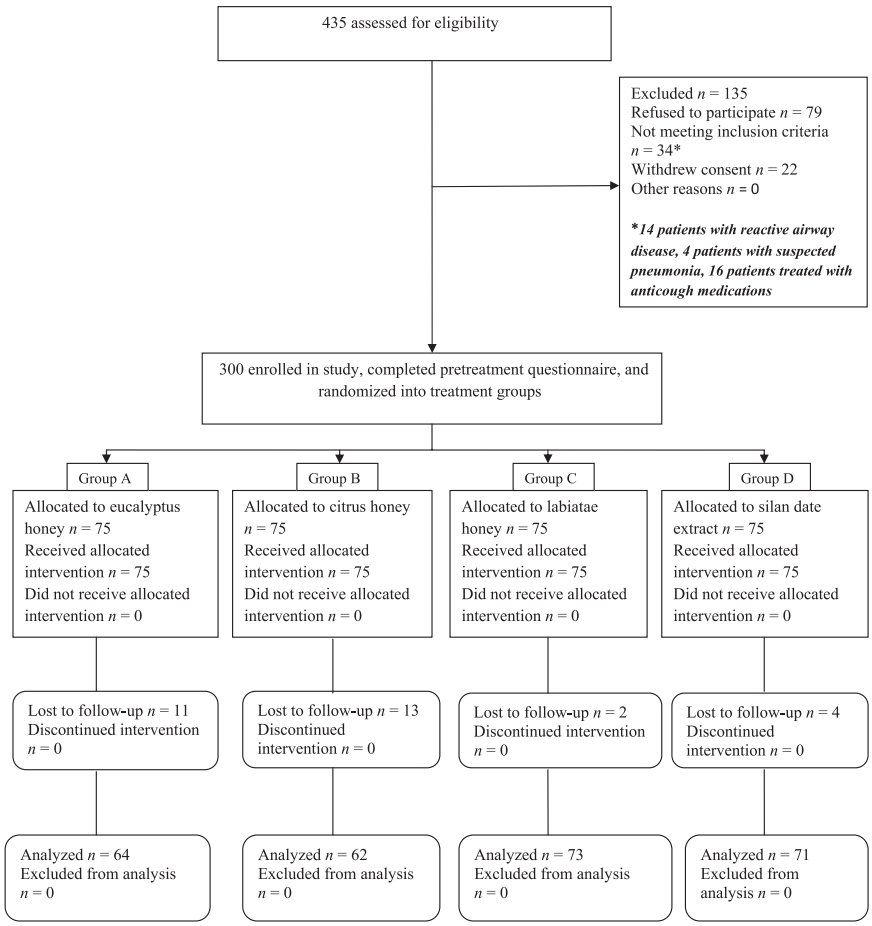

FIGURE 2
Patient flow diagram.

TABLE 1 Baseline Patient Characteristics by Group

Characteristic	A (n = 64)	B (n = 62)	C (n = 73)	D (n = 71)	P Value
Age in months (mean ± SD)	27.5 ± 13.9	29 ± 13.5	30 ± 16.6	29 ± 14.9	.235
Male gender					
Number (%)	36 (56)	26 (36)	39 (53)	23 (32)	.018
Days of illness (mean ± SD)	2.4 ± 1.4	3.5 ± 3.1	2.7 ± 1.6	2.7 ± 1.8	.16
Cough frequency score (mean ± SD)	3.72 ± 1.02	3.76 ± 1.14	3.68 ± 0.9	3.58 ± 0.82	.73
Cough severity score (mean ± SD)	3.66 ± 0.96	3.71 ± 1.08	3.75 ± 0.91	3.55 ± 0.77	.59
Cough bother score (mean ± SD)	3.78 ± 1.15	3.85 ± 1.13	3.85 ± 1.05	3.70 ± 1.07	.84
Child sleep score (mean ± SD)	3.72 ± 1.40	3.61 ± 1.31	3.49 ± 1.32	3.69 ± 1.19	.74
Parental sleep score (mean ± SD)	3.75 ± 1.60	3.66 ± 1.38	3.75 ± 1.26	3.70 ± 1.35	.98
Combined symptom score (mean ± SD)	18.63 ± 5.62	18.60 ± 5.00	18.48 ± 4.59	18.23 ± 4.55	.96

A, eucalyptus honey; B, citrus honey; C, labiatae honey; D, silan date extract.

honey (eucalyptus, citrus, and labiatae) was more effective than the placebo for the treatment of all of the outcomes related to nocturnal cough, child sleep, and parental sleep.

The results of our study strengthen the observation made by Paul et al[8] that honey products may have a beneficial effect for symptomatic relief of nocturnal cough associated with URIs. Our study differs, however, from the study of Paul et al because they compared the effect of 1 type of honey (buckwheat) to dextromethorphan and a no-treatment group, whereas our study compared the effectiveness of 3 types honey to placebo.

In contrast with Paul et al, we did not document symptoms of hyperactivity, nervousness, and insomnia in the honey treatment groups versus the placebo group. Shadkam et al[23] also reported that honey had a more alleviating effect on URI-induced cough compared with dextromethorphan and diphenhydramine. That study was not blinded, however. Thus, our study further supports the recommendations of the World Health Organization to use honey as a potential treatment of cough.[14]

Honey is a remarkably complex natural liquid that is reported to contain at least 181 substances.[24] It has well-established antioxidant and antimicrobial effects

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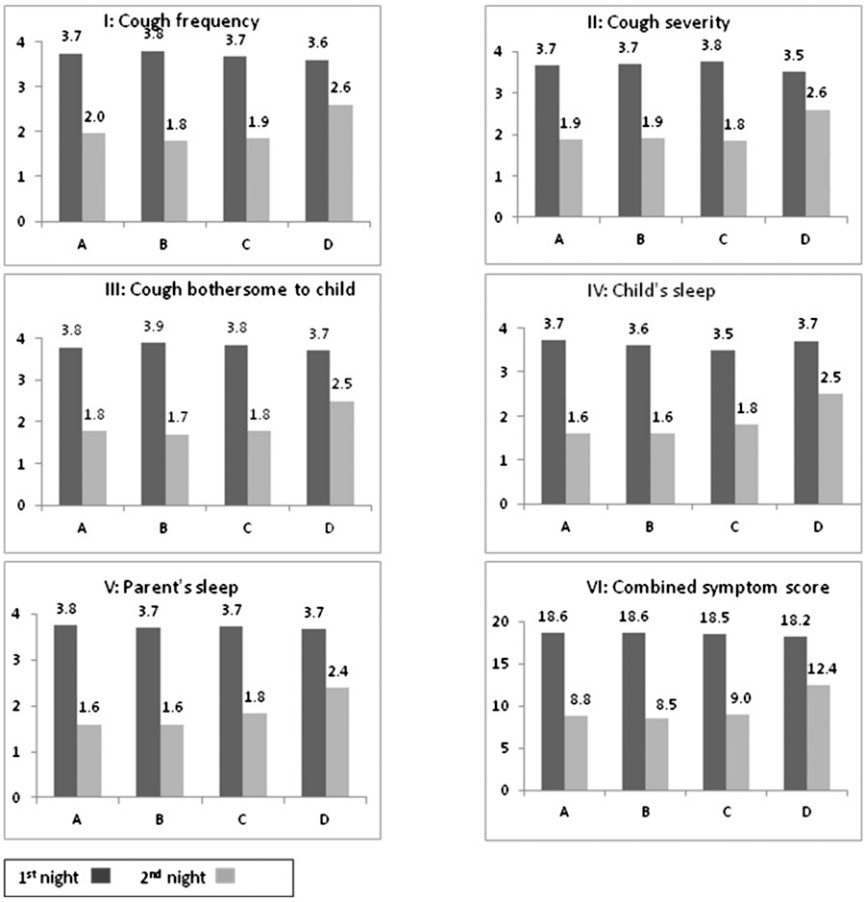

FIGURE 3

The effect of different types of honey and silan date extract on cough frequency (I), cough severity (II), cough bothersome to child (III), the child's sleep (IV), parent's sleep (V), and combined symptoms score (VI). $P < .05$ for the comparisons between group D and the other groups. A, eucalyptus honey; B, citrus honey; C, labiatae honey; D, silan date extract.

that have been suggested as the mechanism for honey's efficacy in wound healing and may help to explain its superior results in this study.[16–21]

The antioxidants present in honey come from a variety of sources, such as vitamin C, monophenolics, flavonoids, and polyphenolics. Although there is a wide spectrum of antioxidant types, monophenolics such as 4-hydroxybenzoic and 4-hydroxycinnamic acids predominate in many honeys.[21,25] Most of the antioxidant components in processed honey are water, not lipid, soluble.[21]

Different types of honey vary widely in the quantity of water-soluble antioxidants they contain.[26,27] This variability is dependent on the honey's floral source, as well as seasonal, environmental, and other external factors. It was observed that the darker a honey's color, the higher its antioxidant capacity. The levels of certain antioxidant components decrease with processing and storage of honey.[21] However, available data show that phenolic antioxidants from processed honey are bioavailable and increase the antioxidant activity of plasma.[19]

Eccles[26] provided another possible explanation for some of the beneficial effects of honey. Because of the close anatomic relationship between the sensory nerve fibers that initiate cough and the gustatory nerve fibers that taste sweetness, an interaction between these fibers may produce an antitussive effect of sweet substances via a central nervous system mechanism. This theory may explain some of the observed effect in patients treated with silan date extract because this is also a sweet substance. However, the significant difference between the honey products and the silan date extract suggests that other factors in addition to the sweet taste of honey contribute to its beneficial effect on children with cough.

Silan was used as placebo in this study. An alternative hypothesis is that silan date extract could worsen cough and cold symptoms. However, our data clearly show that patients treated with silan date extract actually improved. There is also no reason to believe silan caused allergic symptoms or bronchospasm because dates are not a common food allergen in the Israeli population.[27]

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Cough due to a viral URI is generally self-limited. However, parents often wish some active intervention. This tends to lead to the use of OTC cough medications. 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 dose. Some overdoses were caused when the parents gave a child a combination of cold and cough medicines, not realizing the product containing the same ingredient.

Dart et al[28] reported 118 cases of fatalities in children younger than 12 years of age that were judged as possibly, likely, or definitely related to a cough and cold ingredient. Of these 118 cases, 103 involved a nonprescription medication, and the ingredients most often mentioned were pseudoephedrine (n = 45), diphenhydramine (n = 38), and dextromethorphan (n = 36). Of these cases, the evidence indicated that 88 involved an overdose. Several contributing factors were identified, age <2 years, use of medication for sedation, use in day-care settings, use of 2 medicines with the same ingredient, failure to use a measuring device, product misidentification, and use of a nonprescription product intended for adult use.

Rimsza et al reported 10 unexpected deaths that were associated with the use of OTC cough and cold medications in a 1-year period.[29] The authors recommended that such medications should not be given to infants because they may present a serious health hazard, and there is no evidence to support the efficacy and safe dosage of these medications in infants. Rimsza et al also suggest that educational campaigns to decrease the use of OTC cough and cold medications in infants need to be increased.[29]

Lokker et al reported that unintentional misuse of OTC cold products is common and could result in harm if medications are given inappropriately. Label language and graphics seem to influence inappropriate interpretation of OTC product age indications.[30] As a result of these studies, an FDA advisory committee recommended against the use of OTC cough and cold medications in children aged <6 years, and a subsequent FDA public health advisory was issued recommending against the use of these medications in children <2 years of age.[13]

Honey is an alternative that is generally regarded as safe for children older than 1 year. Allan et al[31] stated that evidence for honey in acute pediatric cough supports a small effect, but clinical significance is uncertain. Our randomized, placebo-controlled study seems to indicate that treatment with honey can be clinically effective.

We suggest, in concordance with the FDA[13] and the Israeli Ministry of Health Pharmaceutical Administration, that caregivers and clinicians should be aware of the risk of serious adverse events from administering cough and cold medications to children <2 years of age and use several precautions when using them in older children (2–11 years). We believe that educational campaigns to decrease the use of OTC cough and cold medications in children need to be increased. On the basis of our findings, honey can be offered as an alternate treatment to children >1 year of age. Honey should not be given to children <1 year of age because of the risk of infantile botulism.[32] Because frequent use of honey can cause dental caries, the recommendation should be for a short course of honey.

The study is limited by the subjective nature of the survey used. However, clinicians and parents often make decisions based on subjective assessments of symptom severity. It should also be noted that it is possible that some of the improvement measured could also be attributed to the natural history of URIs, which generally improve with time and supportive care. Furthermore, compliance with honey and placebo administration could not be guaranteed. However, every parent reported that their child took the treatment as recommended. Another limitation is the fact that the effect of only a single dose was evaluated. If the intervention period would have been longer and more than 1 dose given, the results would have been more reliable and more valuable.

The dropout rate was higher for children receiving citrus and eucalyptus honey. The exact reason for the higher dropout rate in these groups is not known. Because these types of honey are more aromatic, it is possible that some children disliked the honey taste.

CONCLUSIONS

Parents rated each of the honey products more favorably than the silan date extract for symptomatic relief of their children's nocturnal cough and sleep difficulty due to URI. Honey may be a preferable treatment of cough and sleep difficulties associated with childhood URI. In light of this study, honey can be considered an effective and safe treatment of children >1 year of age.

ACKNOWLEDGMENT

We thank Dorit Krash of Clalit Health Services for statistical analysis.

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Effect of Honey on Nocturnal Cough and Sleep Quality: A Double-blind, Randomized, Placebo-Controlled Study

Herman Avner Cohen, Josef Rozen, Haim Kristal, Yoseph Laks, Mati Berkovitch, Yosef Uziel, Eran Kozer, Avishalom Pomeranz and Haim Efrat

Pediatrics 2012;130;465; originally published online August 6, 2012;
DOI: 10.1542/peds.2011-3075

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