The Effect of Honey on Nocturnal Cough and Sleep Quality for Children and Their Parents

Cough is a common symptom in pediatric practice and can be particularly troubling to children and their parents, resulting in discomfort, loss of sleep, and missed school days and workdays. Caregivers frequently administer over-the-counter (OTC) medications to their children in an attempt to treat cough. Apart from the costs associated with such medications, some OTC medications have unwelcome and potentially dangerous adverse effects. Dextromethorphan, an opiate-derived antitussive commonly found in OTC cough and cold preparations, is generally safe but on rare occasions can be associated with adverse effects such as dystonia, ataxia, lethargy, and even death. Furthermore, several studies have shown that dextromethorphan is not more effective than placebo at reducing cough symptoms. The American Academy of Pediatrics policy statement on the use of codeine- and dextromethorphan-containing cough remedies in children states that indications for the use of narcotics or dextromethorphan as antitussives in children have not been established given the lack of data for efficacy and the potential for adverse effects. The American Academy of Pediatrics recommends that physicians talk with parents about the risk associated with these drugs as well as the lack of data on the efficacy of codeine and dextromethorphan as antitussives.

See also page 1140

In addition to OTC preparations, a variety of home remedies and herbal medications, such as licorice, clove, lemon, and honey, are used by some caregivers to treat the symptoms associated with upper respiratory tract infections (URIs). The World Health Organization notes that many such preparations are inexpensive and encourages the use of safe antitussives such as lemon juice and honey for the treatment of cough if treatment is desired by the patient and family.

In the randomized, partially double-blinded study by Paul et al in this issue of the Archives, administration of honey is compared with administration of dextromethorphan and with no treatment for the reduction of nocturnal cough and sleep difficulty in children with URIs. This study enrolled 105 children aged 2 to 18 years from an acute care clinic in Pennsylvania. Children were randomized to receive honey, dextromethorphan, or no treatment at bedtime. Follow-up assessments were made by telephone the following day. Compared with children who received dextromethorphan or no treatment, children who received honey showed the greatest improvement in parent-reported cough frequency, cough severity, and quality of sleep for both the parent and the child. In pairwise comparisons between honey and no treatment, honey was better than no treatment for cough frequency and the combined symptom score. Paul and colleagues concluded that honey is an effective treatment for cough in children aged 2 to 18 years. We reviewed this study with regard to the validity of its results, size and precision of the treatment effect, and applicability to clinical practice using the framework recommended in the “User’s Guides to the Medical Literature.”

Are the Results in This Article Valid?

Was the Study Randomized?

Randomization helps to ensure that the baseline characteristics of the treatment groups are similar. Random assignment of participants to study groups controls for the influence of potential confounding factors on the study outcome. Ideally, the randomization technique will not allow for the prediction of group assignment by study personnel or participants. This can be accomplished through the generation of a randomization sequence by an independent party, which ensures that study personnel do not interject bias by assigning participants to one group over another. The study by Paul and colleagues used a randomization sequence generated by a statistician not affiliated with the study. The study coordinator assigned patients to their treatment groups according to the sequence generated by the statistician. Use of these randomization steps appears to be appropriate in this study.

Were the Groups Similar at the Start of the Trial?

The success of randomization can be assessed by comparing the characteristics of the treatment groups at baseline. Successful randomization makes it unlikely that known and unknown variables account for any differences seen in the final data analysis. In their Table 1, Paul and colleagues report that the 3 treatment groups in this study did not differ significantly in age, sex, ill-
ness duration, and symptom scores.\textsuperscript{8} It might have been helpful to include other baseline information that might affect study results, such as ethnicity. Other studies have shown differences in the use of complementary and alternative therapies or in modalities of therapy used among different ethnic groups.\textsuperscript{12,13} We recognize and support the position of the Archives that race and ethnicity should not be used “when there is no biological, scientific, or sociological reason for doing so.”\textsuperscript{14} However, if a preference for or against home remedies (such as honey) existed in a particular ethnic group, then group members might be less willing to participate in a study about honey. This would limit applicability of the results to only those ethnic groups included in the study. Information on other associated symptoms might also have been pertinent; it is feasible that parental perception of the quality of sleep or cough severity might be dramatically affected by URI symptoms other than cough, such as fever or chest pain.

Were Patients, Their Clinicians, and Study Personnel Blinded to Treatment?

Blinding reduces the potential for differential treatment or unintentional actions that might occur if the study personnel and/or study participants were aware of the patient’s group assignment, which could subsequently affect study outcome.\textsuperscript{9} Paul and colleagues were careful to keep study personnel blinded to treatment. Clinical personnel were given a sealed brown paper bag that contained a syringe with the study medication or an empty syringe; this was then provided to the study participant. Paul and colleagues even ensured that all of the bags were refrigerated so that no tactile or visual cues leading to knowledge of the treatment assignment would be evident. Unless there were perceivable differences in the weight of the filled and empty syringes, the clinicians involved in the study would be blinded to group assignment. Study personnel who conducted the follow-up surveys were also blinded to treatment group. However, the risk existed for unblinding of the interviewers during the follow-up telephone calls if the parents revealed that they had an empty syringe. Paul and colleagues did not report whether this occurred in any of the telephone surveys.

Figure 1. Flow of patients within the study. URI indicates upper respiratory tract infection.

Blinding of participants helps avoid a placebo effect, whereby participants might respond in a particular way because they know that they received a treatment. Paul and colleagues paid close attention to making the dextromethorphan and honey mixtures as similar as possible both in appearance and taste; therefore, participants assigned to the honey or dextromethoran groups were blinded to treatment. In contrast, participants assigned to the no-treatment group received an empty syringe and were not blinded to their treatment assignment. Participants in the no-treatment group showed the least improvement in all of the outcomes, and it is possible that awareness of not receiving any therapy may have biased their responses toward a lesser improvement in symptoms.

Aside From the Experimental Intervention, Were the Outcomes and Exposures Measured in the Same Way in the Groups Being Compared?

Differential treatment of experimental groups creates the possibility of alternative explanations for observed effects. Equal treatment of groups increases the likelihood that observed effects are attributable to the intervention. Paul and colleagues were meticulous in ensuring that all of the groups were treated equally. Figure 1 details the flow of participants in this study. After enrollment and randomization, all of the groups received opaque syringes in brown paper bags. Outcomes and exposures were measured in the same way in all of the groups. Blinded study personnel administered the second survey via telephone on the day following the treatment.

Were All Patients Who Entered the Trial Properly Accounted for and Attributed at Its Conclusion? Was Follow-up Complete?

Attrition occurs in nearly every study. It is important to know, however, how many patients do not complete the study. Differential loss of patients between groups could introduce bias if the lost patients are somehow different from those who completed the study or if they have different outcomes that are not considered in the final analysis.\textsuperscript{9} In this study, 130 children with URIs were enrolled. Study coordinators then administered the initial survey examining cough and sleep characteristics. For participation in the study, Paul and colleagues defined minimum symptom criteria (parents reporting severity of at least somewhat on at least 2 of the 3 cough frequency questions and on the parent and child sleep questions). Twenty-two children were excluded because they failed to meet these minimum symptom criteria; the remaining 108 children were then randomized to treatment groups. Follow-up was nearly complete in this study. Two participants were lost to follow-up and was excluded for discontinuing the intervention; 105 children were included in the final analysis (Figure 2). This attrition was minimal and is reasonable for this study size and design.
Were Patients Analyzed in the Groups to Which They Were Randomized?

When attrition does occur, it is helpful to perform an intention-to-treat analysis to maintain the integrity of the randomization. Differential loss between the groups limits the ability to assess study outcomes in a nonbiased fashion. Two participants were lost to follow-up in this study, and 1 participant was discontinued from the study. Otherwise, participants were analyzed in the groups to which they were randomized. If follow-up data were available from the 1 participant who was discontinued from the study, they should have been included in the final analysis. However, no follow-up scores were available. Loss of these 3 patients of 108 total patients would likely not have materially impacted the results of this study.

WHAT ARE THE RESULTS?

How Large Was the Treatment Effect?

Determination of the treatment effect allows readers to interpret the clinical significance of results. Depending on the design and size of the study, differences that are statistically significant may or may not be clinically significant. Paul and colleagues cite improvement among the statistically significant may or may not be clinically significant. Depending on the perspective of the observer, moving from a lot to a little may or may not represent a large treatment effect. However, if the perspective of parents is considered, this very well may be a large and important treatment effect, particularly in the case of sleep interruption. In this study, parents reported greater improvements in both the quality of their own sleep and that of their children's sleep after receiving honey. Although less than 1 point separated sleep quality scores between the 3 treatment groups, any improvement in sleep may be viewed as beneficial and significant by the parents.

How Precise Was the Estimate of the Treatment Effect?

In considering the precision of the treatment effect, it is important to understand the way in which the outcome is measured. Subjective measure of cough is, by nature, imprecise. Precision in cough measurement could be increased by using such techniques as ambulatory cough monitors or video recordings, but these methods are cumbersome and often impractical in the ambulatory setting.

The Pediatric Cough Questionnaire, the instrument used in this study, measures parental perception of their child's cough symptoms. Given the imprecision nature of subjective measures, the Pediatric Cough Questionnaire might be strengthened if scores on the instrument could be correlated with other variables related to cough in children, such as visits to physician offices or missed days of school or work. An abstract cited by Paul and colleagues reports acceptable reliability and validity for the Pediatric Cough Questionnaire, although it would be helpful to have more information on the test validation in a full publication.

It should be noted that there are few pediatric-specific measures of cough. A similar measure, the Canadian Acute Respiratory Illness and Flu Scale, assesses severity of cough and sleep disturbance in children with acute respiratory tract infections but also includes symptoms other than cough, such as sore throat, fever, and headache. The Canadian Acute Respiratory Illness and Flu Scale does not consider the effect of childhood illness on parental sleep.

A number of other questionnaires are used to assess cough-related quality of life but have not been studied in children. Measures such as the Leicester Cough Questionnaire and the Breathlessness, Cough, and Sputum Scale have been validated but only in adult populations with chronic cough. We recognize and appreciate the investigators’ use of a validated psychometric instrument, especially when considering the dearth of available scales in the pediatric population.

WILL THE RESULTS HELP ME IN CARING FOR MY PATIENTS?

Were All Clinically Important Outcomes Considered?

Paul and colleagues considered the outcomes of cough frequency, cough severity, bothersome nature of cough,
quality of the child’s sleep, and quality of the parent’s sleep. Taking into consideration the burden of respiratory illness in childhood, these are all clinically important outcomes to consider. In future studies, it might also be helpful to know the number of missed school days and workdays and the number of return visits to the physician for treatment of cough as well as whether these differ between the 3 treatment groups. Additionally, outcomes stratified by age might provide relevant information. Paul and colleagues stratified participants by age in the initial phase of the study, presumably for the purposes of different dosage sizes among the 3 age groups. The baseline data indicate that each group had a similar makeup with respect to age. However, it is feasible that the subjective experience of cough or interference of cough with sleep might be different in a 2-year-old when compared with that in an 18-year-old. Specific reporting of outcomes stratified by age would be helpful in determining whether such a difference exists.

Are the Likely Treatment Benefits Worth the Potential Harm and Costs?

Honey is generally affordable and often cheaper than OTC antitussives and has a low risk profile when used in patients older than 1 year. Processed honey is rarely associated with allergic reactions, although such reactions are more likely in persons with pollen allergy. The grayanotoxin-associated reaction cited by Paul and colleagues is rare and associated most commonly with unprocessed honey or honey from the Black Sea region.

One of the adverse effects that appeared more commonly in the group receiving honey was insomnia. However, this group also reported the greatest improvement in child and parent sleep. Larger studies could determine the extent to which improvement in sleep from cough suppression is offset by insomnia that may be associated with honey therapy.

Are the Results Applicable to My Practice?

Pediatric health care professionals see many children in the 2- to 18-year age group with URIs, of which cough is often a component. According to the 2005 National Ambulatory Medical Care Survey, URLs account for 11% of visits for children aged 1 to 12 years. The results of this study would be applicable to those patients. However, many parents bring their infants (aged < 1 year) to the pediatrician for evaluation of cough (10.7% of all ambulatory visits for infants are for URLs according to the survey), and in this age group, honey is not a viable therapeutic option given the rare but potential risk for infantile botulism.

When parents approach pediatricians asking for relief from their child’s cough symptoms, the pediatricians face a dilemma—balancing the desire to satisfy the parent’s request against the goals of protecting the child’s safety and recommending efficacious therapies. Many pediatricians are reluctant to prescribe dextromethorphan given the lack of evidence for its efficacy and the potential for adverse effects. Some may now view honey as a possible alternative for the treatment of cough. We recognize that other clinicians may not prescribe any therapy for the treatment of URI symptoms; for those clinicians, the results of this article may be less applicable.

It is unclear whether the observed improvements are related specifically to buckwheat honey or whether similar effects might be seen with other varieties of honey. Paul and colleagues note that darker honeys, such as the buckwheat variety, consist of more phenolic compounds than other varieties and that the associated antioxidant effect might have contributed to the improvement seen in those children treated with this kind of honey. Further research is needed to determine whether the observed improvement is specific to particular varieties of honey. If the effect is variety specific, then local availability of particular varieties of honey or cost to consumers may limit the applicability of the results. A nonscientific telephone survey of 15 national grocery chains and specialty food stores in Nashville, Tennessee, found that none of them stocked buckwheat honey. Buckwheat honey is readily available from Internet vendors at prices comparable to those of regular honey.

CONCLUSIONS

Findings by Paul and colleagues suggest that honey is better than no treatment for reducing cough frequency and improving combined symptom scores. The investigators were particularly thorough in their attempts to maintain blinding and were diligent in treating groups in a similar fashion aside from the interventions. The main limitation of the study is the lack of detailed psychometric data available for the questionnaire. Despite this, the study offers an interesting alternative to traditional OTC remedies for cough in children. Further randomized controlled trials could explore whether improvement is seen with varieties of honey other than buckwheat and whether consumption of other sweet liquids results in the same improvement as that seen after administration of honey. Additional trials could also be designed to address the potential bias associated with the lack of blinding between the groups who received honey and those who received no treatment.

For those pediatric health care professionals who choose not to treat cough symptoms associated with URIs, the potential benefits of any intervention may not be worth the risks associated with treatment. For those who do choose to offer therapy to children with cough, this study suggests that honey may be a reasonable option given its low cost, relatively low adverse effect profile, and potential benefit.
Correspondence: Dr Warren, Division of General Pediatrics, Department of Pediatrics, Vanderbilt University School of Medicine, AA-0216 MCN, 1161 21st Ave S, Nashville, TN 37232 (michael.warren@vanderbilt.edu).

Author Contributions: Study concept and design: Warren, Caples, and Cooper. Analysis and interpretation of data: Pont, Barkin, Callahan, Carroll, Plemmons, Swan, and Cooper. Drafting of the manuscript: Warren. Critical revision of the manuscript for important intellectual content: Warren, Pont, Barkin, Callahan, Caples, Carroll, Plemmons, Swan, and Cooper. Statistical analysis: Pont. Study supervision: Pont, Barkin, Plemmons, Swan, and Cooper.

Financial Disclosure: None reported.

REFERENCES

9. Guyatt GH, Sackett DL, Cook DJ. User’s guides to the medical literature, II: how to use an article about therapy or prevention, A: are the results of the study valid? JAMA. 1993;270(21):2598-2601.
10. Guyatt GH, Sackett DL, Cook DJ. User’s guides to the medical literature, II: how to use an article about therapy or prevention, B: what were the results and will they help me in caring for my patients? JAMA. 1994;271(1):59-63.