A Comparison of the Effect of Honey, Dextromethorphan, and Diphenhydramine on Nightly Cough and Sleep Quality in Children and Their Parents

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Abstract

Objectives: Coughing is a prevalent symptom of upper respiratory infections (URIs) that cause disturbance in the sleep of children and their parents. There is as yet no reliable treatment to control URIs and their related cough; however, drugs such as dextromethorphan (DM) and diphenhydramine (DPH) are now mainly used in the world. The aim of this study is to compare the effect of honey, DM, and DPH on the nightly cough and sleep quality of children and their parents.

Design: This was a clinical trial study in which 139 children aged 24–60 months suffering from coughing due to URIs were selected and assigned randomly to 4 groups. The first group received honey (HG), the second one DM (DMG), the third DPH (DPHG), but the fourth group or control group (CG) was assigned to a supportive treatment.

Outcome measures: After approximately a 24-hour intervention, the 4 groups were reexamined and their cough frequency, cough severity, and sleep quality in children and their parents were recorded by using the questionnaire with Likert-type questions.

Results: The mean of cough frequency score HG is 4.09 ± 0.72 and 1.93 ± 0.65 before and after the intervention, respectively, while these figures for the CG are 4.11 ± 0.78 and 3.11 ± 0.57, respectively. After the intervention, the difference of the mean score of the variables in all groups became statistically significant. The mean score of all variables in HG has stood significantly higher than those in other groups. There is also a significant relationship between the DMG and CG groups, even though there is no statistically difference between DMG and DPHG groups.

Conclusions: The result of the study demonstrated that receiving a 2.5-mL dose of honey before sleep has a more alleviating effect on URIs-induced cough compared with DM and DPH doses.

Introduction

Upper respiratory tract infections (URIs) are the prevalent diseases among children, sending many of these patients to physicians every year.1,2 Each year, children are usually affected 6–8 times by the disease; however, its prevalence among adults is 2–3 times.2 Normally, viruses, and in less than 10% of the cases, bacteria, are the producers of these infections.1 The URIs are usually ameliorated spontaneously. Even though they are not associated with disability and mortality, they can cause morbidity and medical costs. The typical signs and symptoms of the disease are the following: rhinorrhea, sneeze, malaise, a slight fever, and cough.2 These, in around 50% of people, are in the form of dry and sore throat, while in 40% others they appear in the form of cough. Most of the symptoms emerge during the first 3 days but are fortunately relieved in a week; the cough, however, may remain for a longer time.3 Coughing, especially during the night, can cause trouble and disturbance for the children’s and parents’ sleep.4 Each year, billions of dollars are spent to control and cure cough while the cough medicines’ real effect is not clear.5

There is as yet no appropriate and acceptable treatment for URIs and the resultant cough. The antitussive drug that is frequently utilized for children is dextromethorphan (DM); however, this drug has not yet been confirmed by the Pediatrics Academy of America.6,7 Diphenhydramine (DPH) is also another drug that is used in relation to coughs, but its relieving effect is controversial.1 In the present study, the effect of both DM and DPH has been compared with honey.
especially in a larger population, whereas in Paul’s study there is no such comparison.

In traditional medicine, honey is used to treat the signs and symptoms of URIs, especially coughing. Honey has also been used to repair sores and injuries in children. Also, the World Health Organization recently recommended honey for controlling cough and other URI symptoms. Compared with the drugs, honey is less expensive, more available, and especially safer to be used for children. The relieving effect of honey has been known to be from its antioxidant and cytokine-releasing features, thus justifying its antimicrobial effect. Regardless of these, honey is also considered a food substance consisting of various nutrients, energy, and different phytochemicals, which have both curative and nutritive effects.

In view of the prevalent problems of coughing due to URIs in children and the fact that a reliable treatment for this has not yet been found, the aim of this study was to compare the effects of DM, DPH, and honey on the nightly cough and sleep quality of children and their parents.

Materials and Methods

Design and subjects

This is a clinical trial study that began in December 2008 and ended in May 2009. The subjects were 160 children aged 24–60 months suffering from URI-induced cough. On the basis of the previous studies (i.e., power = 80% and α = 0.05), a total of 140 children were randomly assigned to 4 groups (35 in each group). To be on the safe side (i.e., if a subject would not come back or would not perform the medical orders appropriately), 5 others were added to each group, thus totaling 160 children (40 in each group) who participated in the study. All or some of these children were suffering from symptoms such as rhinorrhea, sneeze, sore throat, and stuffed nose. Their coughing had lasted 5 days. Those with the diseases such as asthma, pneumonia, laryngotracheobronchitis, sinusitis, allergic rhinitis, chronic lung disease, congenital heart disease, malignancy, and diabetes were not included in the study. Those who had consumed antihistamine, DPH, or DM 4 hours before sleep or had consumed cytochrome P450 inhibitors simultaneously (i.e., serotonin-reabsorption selective inhibitors) were also excluded from the study. Parents were also excluded if they were using a drug and herbal that had an effect on sleeping, such as sedatives.

Measurements

A standard researcher-made questionnaire previously designed for the purpose and formerly used in other studies was filled in by asking questions of the children’s mothers. The questionnaire in the first part included demographic variables such as age and gender. In the second part (i.e., the main part), it included four key questions related to cough, severity of cough, sleep quality of the child as well as those of parent, respectively (Fig. 1). The answers to the questions were categorized on the basis of a Likert-type scale graded from 0 (= not at all) to 6 (= extremely). The questionnaire was completed by each mother in the presence of a pediatrician before and after a 1-night intervention. (Note that in Iran, children are referred to physicians mostly through their mothers; mothers also take care of children at home.) Any ambiguous question for the mother, if any, was answered by a pediatrician. Thus, after a physician visited the patient, the questionnaire was completed and on the following day each mother and child revisited the doctor and the relevant questionnaire was completed once more but after the intervention.

Dosage and prescriptions

Using Table of Random Numbers, the subjects were placed in 1 of the 4 groups. The first group (HG) received 2.5 mL of natural honey from Kafi-Abad (a village in Yazd) before sleep. The second (DMG) and third (DPHG) groups received 2.5 mL of DM syrup (7.5 mg, Pour-Sina drug manufacturing company in Tehran, registered No. 1228051241), and 2.5 mL of DPH syrup (6.25 mg, Ramoofarmon drug manufacturing company, Registered No. 1228056772), respectively, before sleep. The honey and other

![FIG. 1. Survey questions about nightly cough and sleep difficulty. Adapted with permission from the study by Paul et al., Arch Pediatr Adolesc Med 2007;16(12):1140–1146. ©2007 American Medical Association. All rights reserved.](image-url)
drugs are usually used at room temperature of about 22–26°C. The fourth group (CG), however, was given only supportive treatment recommended for other groups as well. The supportive treatments included saline nose drops, water vapor, cleaning a blocked nose, and using acetaminophen if fever existed. All mothers were offered the same standard on how to use liquids, nose drops, and humidifier by a pediatrician. All 4 groups were examined the following day and the same questionnaire was completed for them once more. The subjects who for any reason had consumed an inappropriate dose of the drugs were excluded from the survey.

Data analysis

Data were analyzed by SPSS software version 11 (SPSS Inc., Chicago, IL). For comparing the average mean of each of the quantifiable variables for pre- and postintervention, a paired *t*-test was used; one-way analysis of variance and multiple comparison tests were used for comparing the average mean of quantifiable variables for pre- and postintervention, a paired *t*-test was used to compare the frequency distribution between groups. The *p*-values were considered significant at *p* < 0.05.

Ethical considerations

A consent form was obtained from each child’s mother. They could quit the study freely whenever they liked. The Research Ethics Committee of the Shahid Sadoughi University of Medical Sciences approved the relevant research proposal.

Results

Of 160 participants, 21 were excluded from the study for not visiting the physician as scheduled or inappropriately using the drugs (7, 4, 6, and 4 patients from HG, DMG, DPHG, and CG groups, respectively), so 139 patients’ data were finally analyzed. In general, the average mean age of the children was 37.75 ± 11.12 months. Of the patients, 71 (51.1%) were girls and 68 (48.9%) were boys.

### Table 1. Mean and Frequency of Variables of the 4 Groups at the Beginning of the Study

<table>
<thead>
<tr>
<th>Variables</th>
<th>HG (N = 33)</th>
<th>DMG (N = 36)</th>
<th>DPHG (N = 34)</th>
<th>CG (N = 36)</th>
<th>p-valuea</th>
</tr>
</thead>
<tbody>
<tr>
<td>Duration of illness (day)</td>
<td>3.03 ± 1.16b</td>
<td>3.14 ± 1.12</td>
<td>3.09 ± 1.16</td>
<td>3.0 ± 1.26</td>
<td>0.98</td>
</tr>
<tr>
<td>Cough frequency score</td>
<td>4.09 ± 0.76</td>
<td>4.08 ± 0.91</td>
<td>4.23 ± 0.70</td>
<td>4.20 ± 0.79</td>
<td>0.81</td>
</tr>
<tr>
<td>Cough severity score</td>
<td>3.85 ± 0.83</td>
<td>3.86 ± 0.93</td>
<td>3.94 ± 0.74</td>
<td>3.90 ± 0.80</td>
<td>0.96</td>
</tr>
<tr>
<td>Cough impact on child sleep score</td>
<td>3.67 ± 0.69</td>
<td>3.64 ± 0.68</td>
<td>3.62 ± 0.70</td>
<td>3.64 ± 0.72</td>
<td>0.99</td>
</tr>
<tr>
<td>Cough impact on parent sleep score</td>
<td>3.94 ± 0.70</td>
<td>3.92 ± 0.70</td>
<td>3.91 ± 0.71</td>
<td>3.86 ± 0.64</td>
<td>0.97</td>
</tr>
<tr>
<td>Age (month)</td>
<td>37.7 ± 11.4</td>
<td>37.4 ± 11.1</td>
<td>38.0 ± 11.4</td>
<td>37.8 ± 10.9</td>
<td>0.99</td>
</tr>
<tr>
<td>Gender</td>
<td>17 (51.5)c</td>
<td>17 (47.2)</td>
<td>17 (50.0)</td>
<td>17 (47.2)</td>
<td>0.98d</td>
</tr>
<tr>
<td>Male</td>
<td>16 (49)</td>
<td>19 (53)</td>
<td>17 (50)</td>
<td>19 (53)</td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*a*One-way analysis of variance.

*b*Mean ± standard deviation.

*N* (%).

*c*χ².

HG, honey group; DMG, dextromethorphan group; DPHG, diphenhydramine group; CG, control group.

### Table 2. Mean of Variables of the Four Groups Before and After the Study

<table>
<thead>
<tr>
<th>Variables</th>
<th>HG</th>
<th>DMG</th>
<th>DPHG</th>
<th>CG</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cough frequency score</td>
<td>Before 4.09 ± 0.76</td>
<td>After 1.93 ± 0.65</td>
<td>0.001</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cough severity score</td>
<td>Before 3.84 ± 0.83</td>
<td>After 1.51 ± 0.61</td>
<td>0.001</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cough impact on child sleep score</td>
<td>Before 3.66 ± 0.66</td>
<td>After 1.42 ± 0.56</td>
<td>0.001</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cough impact on parent sleep score</td>
<td>Before 3.93 ± 0.70</td>
<td>After 1.54 ± 0.56</td>
<td>0.001</td>
<td></td>
</tr>
</tbody>
</table>

*a*Paired *t*-test.

HG, honey group; DMG, dextromethorphan group; DPHG, diphenhydramine group; CG, control group.
The mean and frequency of variables of the 4 groups at the beginning of the study are shown in Table 1. As is indicated, none of the variables were statistically significant between the 4 groups.

In Table 2 the mean scores of cough frequency, cough severity, and sleep quality in children and their parents in all groups have been compared and as demonstrated the difference in each group before and after the intervention is statistically significant. This difference is not, however, the same in all groups. As an example, the mean of cough frequency for HG is 4.09 ± 0.76 and 1.93 ± 0.65 before and after the intervention, respectively, while these figures for the CG are 4.19 ± 0.78 and 3.11 ± 0.57, respectively.

A comparison of the average mean score of the dependent variables in all groups after the intervention is also shown in Tables 3 and 4. As is evident from Table 3, after approximately a 24-hour intervention the difference of the mean score of the variables in all groups has become statistically different. However, in order to check the difference among the groups, the multiple comparison test was used, the result of which is summarized in Table 4. According to the results, the mean score of all variables in the HG has stood significantly higher than those in other groups. On the other hand, there is also a significant relationship between DMG and CG group even though there is no statistically significant difference between the DMG and DPHG groups.

**Discussion**

The results of this study demonstrated that honey compared with other groups had a significantly more effective curing impact on cough frequency, cough severity, and sleep quality of children and their parents. DM and DPH had also a relieving effect on the factors mentioned compared with CG. However, no difference was found between the two groups statistically. Also, in a study by Paul et al., it was demonstrated that honey could have a curing effect on cough and sleep pattern of children and their parents; however, the study

### Table 3. Mean of Variables of the 4 Groups at the End of the Study

| Variables                        | HG     | DMG   | DPHG  | CG     | p-value <
|----------------------------------|--------|-------|-------|--------|-----------
| Cough frequency score            | 1.93 ± 0.65 | 2.47 ± 0.72 | 2.50 ± 0.70 | 3.11 ± 0.57 | <0.001    
| Cough severity score             | 1.51 ± 0.61 | 2.16 ± 0.69 | 2.11 ± 0.68 | 2.69 ± 0.66 | <0.001    
| Cough impact on child sleep score| 1.42 ± 0.56 | 1.91 ± 0.69 | 1.97 ± 0.62 | 2.50 ± 0.65 | <0.001    
| Cough impact on parent sleep score| 1.54 ± 0.56 | 1.94 ± 0.53 | 2.02 ± 0.52 | 2.44 ± 0.69 | <0.001    

*One-way analysis of variance.
HG, honey group; DMG, dextromethorphan group; DPHG, diphenhydramine group; CG, control group.

### Table 4. Multiple Comparisons Between Groups at the End of the Study

| Dependent variables               | Group vs | Groups | Mean difference | p-value <
|-----------------------------------|----------|--------|----------------|-----------
| Cough frequency score             | HG       | DMG    | -0.53          | 0.001     
|                                   |          | DPHG   | -0.56          | 0.001     
|                                   |          | CG     | -1.17          | <0.001    
|                                   | DMG      | DPHG   | -0.02          | 0.86      
|                                   |          | CG     | -0.63          | <0.001    
|                                   | DPHG     | CG     | -0.61          | <0.001    
| Cough severity score             | HG       | DMG    | -0.65          | <0.001    
|                                   |          | DPHG   | -0.60          | <0.001    
|                                   |          | CG     | -1.17          | <0.001    
|                                   | DMG      | DPHG   | 0.04           | 0.36      
|                                   |          | CG     | -0.52          | 0.001     
|                                   | DPHG     | CG     | -0.57          | <0.001    
| Cough impact on child sleep score| HG       | DMG    | -0.49          | 0.002     
|                                   |          | DPHG   | -0.54          | 0.001     
|                                   |          | CG     | -1.07          | <0.001    
|                                   | DMG      | DPHG   | -0.05          | 0.72      
|                                   |          | CG     | -0.58          | 0.001     
|                                   | DPHG     | CG     | -0.52          | 0.001     
| Cough impact on parent sleep score| HG      | DMG    | -0.39          | 0.005     
|                                   |          | DPHG   | -0.48          | 0.001     
|                                   |          | CG     | -0.89          | <0.001    
|                                   | DMG      | DPHG   | -0.08          | 0.50      
|                                   |          | CG     | -0.50          | <0.001    
|                                   | DPHG     | CG     | -0.41          | 0.003     

*Post hoc multiple comparisons.
HG, honey group; DMG, dextromethorphan group; DPHG, diphenhydramine group; CG, control group.
found that DM compared with the no-treatment group did not have a better effect on URI-induced cough. In another study carried out by Yoder et al. on 37 children aged 6–18 years old, no significant relationship was found for the relieving effect of DM and DPH and placebo on the cough produced by URI-induced cough. Also, the results of the study by Bjornsdottir et al. indicated that DM and DPH would have no relieving effect on the nightly symptoms of URI.

Our study confirmed the results of the previous studies regarding the curing effect of honey on children’s nightly cough induced by URIs. This study, however, indicated that DM and DPH also have a relieving effect on this cough but compared with honey, their effect is less, which is statistically significant.

Several studies have also reported the antimicrobial and antioxidant effect of honey. It has been suggested that these effects can lead to healing of wound, thus justifying our results. Honey possesses various phenolic compounds as well, which are related to its antioxidant feature. Eccles has recently demonstrated some useful effects of honey. He has suggested that the sweet substances of honey normally reflexively secrete saliva, which might cause secretion of mucus in the airways. The secretion of mucus can have a relieving effect on the larynx and pharynx, thus alleviating cough, especially the dry cough. He also adds that consuming sweet substances causes the production of internal opioids as well. The interaction effect between the sensory fibers responding to opioids and gustatory sensory fibers may help in producing the antitussive effect of the sweet substances associated with a central nervous system mechanism.

DM is currently used to cough in the United States. Although in a cohort study it was found that this is well tolerated, over-the-counter studies reveal that this drug can produce side-effects such as dystonia, anaphylaxis, mastocytosis, dependence, psychosis, mania, hallucination, ataxia, somnolence, insulin-dependent diabetes, peripheral neuropathy, cerebral degeneration, megaloblastic anemia, and death if used at a high dose. There are reports that DPH is increasingly misused by adults. DPH, as the first-generation antihistamine, also has its own side-effects. This type of antihistamine has been known to cause somnolence but occasionally it may also cause restlessness, nervousness, and sleeplessness. standard doses of DPH have some relation with acute dystonia and impaired driving ability. Long-term use and high dose of this drug can cause habit formation, psychosis, cardiac dysrhythmia and long QT, rhabdomyolysis, epilepsy, and death.

In this study, 2 children, who had been affected by otitis media on their following visit, were then treated by antibiotics. Otitis is seemingly a side-effect of URIs and has nothing to do with DPH. Although our study demonstrated that DM and DPH have a relieving effect on children’s cough, honey is apparently more effective. However, in children younger than a year old, honey may cause botulism. The parents of 2 children in the honey group complained of their children’s nervousness. Paul et al. also indicated that hyperactivity, nervousness, and loss of sense of smell were more prevalent in those treated with honey.

The parents of 3 children in the DPH group also complained of their children’s somnolence. In addition, in a study by Yoder et al., it was indicated that somnolence can be taken as one of the complications of DPH. No complication was found for the DM group in our study.

A limitation of this study has been its intervention period. As was explained, each patient received just one dose of honey or drugs, and it is clear that if the intervention period had been longer (i.e., each patient had used more than one dose of drugs), the results would be more reliable and of more value. On the other hand, there would be more opportunity for the demonstration of complications, if any. Therefore, for further studies this limitation has to be taken into consideration. The fact that this study was not blinded can be regarded as another limitation for this study, thus affecting the results.

In conclusion, the finding of the study suggests that receiving a 2.5-mL dose of honey before sleep has a more relieving effect on the nightly cough of children and others compared with DM or DPH. Thus, in these conditions it is recommended to be used.

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Disclosure Statement

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