

A spoonful of honey helps a coughing child sleep. *J Fam Pract.* 2012;61:145-147.

Potential PURL Review Form: Randomized controlled trials

SECTION 1: IDENTIFYING INFORMATION

1. Citation Cohen HA, Rozen J, Kristal H, et al. Effect of honey on nocturnal cough and sleep quality: a double-blind, randomized, placebo-controlled study. *Pediatrics.* 2012;130:465-471.
2. Hypertext link to PDF of full article <http://pediatrics.aappublications.org/content/130/3/465.long>
3. First date published study available to readers August 6, 2012
4. PubMed ID 22869830
5. Nominated By Umang Sharma
6. Institutional Affiliation of Nominator University of Chicago
7. Date Nominated August 8, 2012
8. Identified Through *Pediatrics*
9. PURLS Editor Reviewing Nominated Potential PURL Kate Rowland
10. Nomination Decision Date
11. Potential PURL Review Form (PPRF) Type Randomized controlled trial
12. Other comments, materials or discussion
13. Assigned Potential PURL Reviewer Anne Mounsey
14. Reviewer Affiliation University of North Carolina
15. Date Review Due August 24, 2012

16. Abstract

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.

SECTION 2: CRITICAL APPRAISAL OF VALIDITY

- | | |
|--|--|
| 1. Number of patients | 75 patients in each of 3 treatment arms and one placebo arm; total N=300 |
| 2. Main characteristics of study patients (inclusions, exclusions, demographics, settings, etc.)? | Aged 1-5 years with a nocturnal cough due to a URI defined as cough and rhinorrhea of <7 days. Pts excluded if asthma, pneumonia, croup sinusitis or allergic rhinitis, or had used cough/cold meds the night before the study. Had to score at least 3/7 for a minimum of 2 of the 3 questions related to nocturnal cough frequency, effect on child's, and parental sleep on the previous night. |
| 3. Intervention(s) being investigated? | Eucalyptus, labiatae, or citrus honey |
| 4. Comparison treatment(s), placebo, or nothing? | Silan date extract similar in color and taste to honey. |
| 5. Length of follow up? Note specified end points, eg, death, cure, etc. | One night |
| 6. What outcome measures are used? List all that assess effectiveness. | Validated 5-item questionnaire, each item graded on 7-point Likert scale. Primary outcome was the change in the cough frequency between the 2 nights. Secondary outcome was the change in cough severity, bothersomeness of cough to child, effect of cough on the child's and parents' sleep, and a combined score of these 5 measures. |
| 7. What is the effect of the intervention(s)? Include absolute risk, relative risk, NNT, CI, p- | Improvement in cough frequency (total score possible=6): Eucalyptus honey=1.77 improvement Citrus honey=1.95 Labiatae honey=1.82 |

values, etc.

Placebo=1.0 ($P<.001$). No significant differences according to type of honey.

There were significant improvements in cough severity with honey (1.77-1.94) vs placebo (0.99; $P<.001$) and in cough bothersomeness (honey 2.0-2.16 vs placebo 1.25; $P<.04$). Both children's and parents' sleep improved more with honey (1.70-2.16) than placebo (1.21-1.28; $P<.018$).

When the results for these outcomes were combined into total scores by adding the scores from the individual categories, honey again proved to be the most effective treatment. Total scores improved by:

E honey= 9.88

L honey= 9.51

C honey= 10.10

Placebo=5.82 ($P<.001$).

8. What are the adverse effects of intervention compared with no intervention?

Four children in the honey groups and one in the placebo group had stomach pain, nausea, or vomiting. No statistically significant difference among the groups.

9. Study addresses an appropriate and clearly focused question - **select one**

Well covered

10. Random allocation to comparison groups

Poorly addressed

11. Concealed allocation to comparison groups

Poorly addressed

12. Subjects and investigators kept "blind" to comparison group allocation

Well covered

13. Comparison groups are similar at the start of the trial

Adequately addressed

Comments: There were fewer boys in the placebo group.

14. Were there any differences between the groups/arms of the study other than the intervention under investigation? If yes, please indicate whether the differences are a potential source of bias.

Well covered

15. Were all relevant outcomes measured in a standardized, valid, and reliable way?

Adequately addressed

16. Are patient-oriented outcomes included? If yes, what are they?

Cough severity and frequency and child and parental sleep disturbance.

- 17.** What percent dropped out, and were lost to follow up? Could this bias the results? How?
The honey groups had a total of 26 lost to follow-up compared with 4 in the placebo group. It was not clear why the dropout rate differed, but this difference was unlikely to bias the results.
- 18.** Was there an intention-to-treat analysis? If not, could this bias the results? How?
Yes
- 19.** If a multi-site study, are results comparable for all sites?
Pediatric community clinics in Israel
- 20.** Is the funding for the trial a potential source of bias? If yes, what measures were taken to insure scientific integrity?
No
- 21.** To which patients might the findings apply? Include patients in the study and other patients to whom the findings may be generalized.
Children aged 1-5 years
- 22.** In what care settings might the findings apply, or not apply?
Pediatrics and primary care
- 23.** To which clinicians or policy makers might the findings be relevant?
Pediatricians and primary care physicians

SECTION 3: REVIEW OF SECONDARY LITERATURE

1. DynaMed excerpts

2. DynaMed citation/access date

3. Bottom line recommendation or summary of evidence from DynaMed (1-2 sentences)

4. UpToDate excerpts

5. UpToDate citation/access date

Pappas DE, Hendley JO. The common cold in children: treatment and prevention. In: Basow DS, ed. UpToDate [database online]. Waltham, Mass: UpToDate; 2012. Available at: <http://www.uptodate.com>. Last updated June

2012. Accessed August 2012.

6. Bottom line recommendation or summary of evidence from UpToDate
(1-2 sentences)

UpToDate recommends avoiding the use of over-the-counter (OTC) common cold medications in children up to the age of 12 years. Such medications have no proven efficacy and their use has been associated with serious side effects, including death.

The US Food and Drug Administration recommend against the use of OTC cough medications in children younger than 2 years, and the American Academy of Pediatrics have issued strict warnings over the use of OTC cough and cold preparations in children younger than 6 years.

7. PEPID PCP excerpts
www.pepidonline.com
username: fpinauthor
pw: pepidpcp

8. PEPID citation/access data

9. PEPID content updating

1. Do you recommend that PEPID get updated on this topic?

Yes, there is important evidence or recommendations that are missing

2. Is there an EBM Inquiry (HelpDesk Answers and Clinical Inquiries) as indicated by the EB icon (EB) that should be updated on the basis of the review?

No, this topic is current, accurate and up to date.

10. Other excerpts (USPSTF; other guidelines; etc.)

The FDA recommends against cough and cold medications in children younger than 6 years.

11. Citations for other excerpts

12. Bottom line recommendation or summary of evidence from other sources (1-2 sentences)

SECTION 4: CONCLUSIONS

1. Validity: How well does the study minimize sources of internal bias and maximize internal validity? Give one number on a scale of 1 to 7 (1=extremely well; 4=neutral; 7=extremely poorly) 2

2. If 4.1 was coded as 4, 5, 6, or 7, please describe the potential bias and how it could affect the study results.

Specifically, what is the likely direction in which potential sources of internal bias might affect the results?

3. Relevance: Are the results of this study generalizable to and relevant to the health care needs of patients cared for by “full scope” family physicians? Give one number on a scale of 1 to 7 (1=extremely well; 4=neutral; 7=extremely poorly)

1

4. If 4.3 was coded as 4, 5, 6, or 7, please provide an explanation.

5. Practice-changing potential: If the findings of the study are both valid and relevant, does the practice that would be based on these findings represent a change from current practice? Give one number on a scale of 1 to 7 (1=definitely a change from current practice; 4=uncertain; 7=definitely not a change from current practice)

2

6. If 4.5 was coded as 1, 2, 3, or 4, please describe the potential new practice recommendation. Please be specific about what should be done, the target patient population and the expected benefit.

Consider recommending one and a half teaspoons of honey to parents of children over the age of one year with a cough to decrease the frequency and severity of the cough.

7. Applicability to a Family Medical Care Setting:

1

Is the change in practice recommendation something that could be done in a medical care setting by a family physician (office, hospital, nursing home, etc), such as a prescribing a medication, vitamin or herbal remedy; performing or ordering a diagnostic test; performing or referring for a procedure; advising, educating or counseling a

patient; or creating a system for implementing an intervention? Give one number on a scale of 1 to 7 (1=definitely could be done in a medical care setting; 4=uncertain; 7=definitely could not be done in a medical care setting)

8. If you coded 4.7 as a 4, 5, 6 or 7, please explain.

9. Immediacy of Implementation: Are there major barriers to immediate implementation? Would the cost or the potential for reimbursement prohibit implementation in most family medicine practices? Are there regulatory issues that prohibit implementation? Is the service, device, drug or other essentials available on the market? Give one number on a scale of 1 to 7 (1=definitely could be immediately applied; 4=uncertain; 7=definitely could not be immediately applied)

10. If you coded 4.9 as 4, 5, 6, or 7, please explain why.

11. Clinical meaningful outcomes or patient-oriented outcomes: Are the outcomes measured in the study clinically meaningful or patient oriented? Give one number on a scale of 1 to 7 (1=definitely clinically meaningful or patient oriented; 4=uncertain; 7=definitely not clinically meaningful or patient oriented)

12. If you coded 4.11 as a 4, 5, 6, or 7 please explain why.

Most scores improved by 2 (one more than placebo). We thought this could be a clinically meaningful increase in scores for exhausted parents with a coughing toddler. Moreover, it's a safe intervention.

13. In your opinion, is this a Pending PURL? Give one number on a scale of 1 to 7 (1=definitely a Pending

PURL; 4=uncertain;
7=definitely not a Pending
PURL)

Criteria for a Pending PURL:

- Valid: Strong internal scientific validity; the findings appears to be true.
- Relevant: Relevant to the practice of family medicine
- Practice changing: There is a specific identifiable new practice recommendation that is applicable to what family physicians do in medical care settings and seems different than current practice.
- Applicability in medical setting:
- Immediacy of implementation

14. Comments on your response in 4.13

They used 3 types of honey that were all effective thus it is likely that any honey would help.