

# Cough Syrups – Do they Work in Acute Cough?

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**A**cute cough is perhaps the single most common presenting symptom in children wherein treatment is demanded and/or initiated. Often it is clinically trivial but very disturbing for the child and family; at other times it can appear harmless but reflect underlying disease. In addition, there is sometimes dichotomy between the physicians' and patients' perspectives; the former are concerned about cough representing respiratory disease requiring management, whereas the latter are anxious for immediate symptomatic relief. This dichotomy is the basis for a thriving pharmaceutical industry and the frequent (often injudicious) use of cough medications in our country and elsewhere.

## RELEVANCE

About 20% children suffer from cough at some stage(1) and nearly 5% of childhood visits to physicians are related to cough(2). The free availability of over-the-counter cough syrups, frequent self-medication, relatively lax regulation on the prescription and use of such medication, habit-forming potential with certain preparations and the massive industry drive promoting unrestricted usage, all contribute to making cough a relevant problem in our setting.

Thus the clinical question addressed in this systematic review of evidence is: "In children with acute cough (defined as less than 3-4 weeks duration)(3), (population), do cough syrups (*intervention*) alter the clinical outcome in terms of symptom relief, decreased frequency/severity, improved quality of life, adverse events etc (*outcome*) as compared to placebo or no treatment (*comparison*)?"

## CURRENT BEST EVIDENCE WITH CRITICAL APPRAISAL

A Cochrane Library search on 27 June 2009 with the term "cough" and filter "Record Title" identified 17 Cochrane reviews, 8 other systematic reviews, 625 methodologically-appraised clinical trials, and 3 health technology assessment (HTA) reports. Among these, two Cochrane reviews were relevant; one pertaining to over-the-counter medications in acute cough(4) and the other reporting the role of honey and lozenges in non-specific cough(5). The former included an updated literature search till January 2007, while the latter did not identify any eligible randomized trials. Therefore, an exhaustive literature search (restricted to RCTs) was undertaken in PubMed (Clinical queries). Five systematic reviews/meta-analyses were identified; four(6-9) did not yield additional data and one was in Norwegian(10) with an English summary only. TRIP database and BestBETS were also accessed on the same date. The search strategy and results are depicted in **Table I**.

The additional search revealed two trials evaluating a mixture of pharmacological agents(11, 12), and one assessing menthol(13). The small number of reports on herbal medicines and plant extracts had no data relevant to India. Thus the 2008 Cochrane review(4) and two additional trials(11,12) constitute current best evidence on the subject. A summary of the data from these RCTs is available from the author on request. Meta-analysis was not possible owing to a wide variety of dissimilar outcome measures used to assess efficacy. One of the additional trials(11) was an industry RCT evaluating a mixture of four pharmacologically active products

**TABLE 1** LITERATURE SEARCH STRATEGY FOR RANDOMIZED CONTROLLED TRIALS

Search terms	Filters	Output	Potentially relevant	Additional data
Central (2007-2009)				
Cough	Record title	56	4	1
Pubmed (Limits: All child, 01/01/2007 to 27/06/2009)				
cough	Systematic reviews	34	5	0
cough antiussive	AND	125	16	1
cough antihistamine	clinical[Title/Abstract]	33	4	0
cough decongestant	AND	22	8	0
cough expectorant	trial[Title/Abstract]OR	43	13	0
cough suppressant	clinical trials [MeSH	1028	103	0
cough mucolytic	Terms] OR clinical	6	1	0
cough syrup	trial[Publication Type]	13	3	1
cough over-the-counter	OR	55	6	0
cough dextromethorphan*	random*[Title/Abstract]	28	4	0
cough guaiphenesin/	OR random	7	2	0
guaifenesin	allocation[MeSH Terms]			
cough bromhexine	OR therapeutic	5	2	0
cough codeine	use[MeSH Subheading])	25	3	0
TRIP database ( <a href="http://www.tripdatabase.com">www.tripdatabase.com</a> )				
cough syrup	None	62	2	0
Best BETS ( <a href="http://www.bestbets.org/database/browse-bets.php">http://www.bestbets.org/database/browse-bets.php</a> )				
cough	None	5	1	0

Date of updated search: 27 June 2009

in children and assessing a composite score of symptom relief of runny nose, congestion, pain and cough. The mixture showed a significant benefit on the composite and individual symptom scores; this has been used by the authors to promote the combination. The other RCT(12) showed that dextromethorphan was no better than placebo for the treatment of cough.

The Cochrane review included eight RCTs with 616 participants having cough associated with upper respiratory infection (URI) and treated with various pharmacological agents singly or in combination. There was no difference between various pharmacological agents compared to placebo/no treatment. The reviewers reported the usual stringent methodological procedures that Cochrane Reviews are renowned for. They chose several relevant

outcome measures that quantified improvement in terms of change in severity or frequency of cough, comfort to the child in terms of impact on sleep, and parental assessment of improvement through scoring systems. They also introduced an additional refinement *viz* exclusion of parental or physician rating of ‘wellness’ that was not backed by objective measurements. This is methodologically appealing, but it could be argued that one of the roles of cough medication is to provide comfort to the patient and family, hence even subjective assessment of improvement may be a relevant outcome. In fact, this is a common argument used by many clinicians to prescribe cough syrups on the grounds that parents deserve fulfilment of their demands. However, two findings of this systematic review conclusively dispel such views. First, the trials showed that relief with cough syrups was not only comparable to

### EURECA CONCLUSION IN THE INDIAN CONTEXT

- Cough syrups are no better than placebo in children with acute cough, and have the risk of adverse effects. Therefore their use should be discouraged.

placebo, but both were of a fairly high magnitude, suggesting significant placebo effect. In other words, the symptomatic relief with cough syrups observed/reported in uncontrolled settings (loosely referred to as personal experience by physicians) is likely to be nothing more than placebo effect. In addition, sleep induced by cough syrups may be mistakenly attributed as a therapeutic rather than side effect, in some cases. The second observation that disallows exploiting even the ‘placebo effect’ of cough medications is the frequency and severity of adverse events reported with most pharmacological preparations. These range from insignificant and transient clinical events to serious adverse events and even death in rare instances. These observations argue strongly against using/prescribing/recommending cough syrups in children.

What then can be done for children with cough? The Cochrane review did not evaluate non-pharmacological preparations such as honey, *tulsi* leaves, and other herbal preparations and their role (if any) is still open to question. Literature search showed scanty data either in support or against such interventions and this area needs further research, particularly in the Indian context. There is limited data emerging to suggest that honey may have a better anti-tussive effect than the placebo-equivalent efficacy of cough syrups. This could become an interesting area of research provided methodologically well designed trials using population and age appropriate objective scoring systems are developed.

#### **EXTENDIBILITY**

None of the ten trials comprising current best evidence was conducted in India; and only one was performed in a developing country setting(13). However as mentioned previously, the clinical condition (acute cough), population (otherwise well children), intervention (nature and dosage of medication and metabolism thereof), and outcomes

of interest (clinical and social) are all extendible to our setting. Therefore the findings of this systematic review are applicable to our population.

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