CRO for Natural Healthcare Products

Special Reprint 2012

AN OPEN LABEL, PHASE II, CLINICAL TRIAL OF ENCOF LOZENGES IN THE TREATMENT OF PATIENTS WITH COUGH.

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ABSTRACT

BACKGROUND
Encof Lozenges, a polyherbal formulation was tested for its efficacy in patients with cough.

Methods: A total of 35 male or female adult patients who were diagnosed clinically were recruited in the study. Encof Lozenges was given 1 Lozenge, four times a day for 1 week and the patients were assessed on day 4 and day 7 for its efficacy. After 7 Days treatment the signs & symptoms of cough were noted and compared with baseline. Physician's Global Assessment, Patient's Global Assessment and Adverse events were noted.

Results: The cough signs & symptoms were significantly reduced in after treatment as compared to baseline ($p < 0.05$). In patient's global assessment, patients treated with Encof were more satisfied than patients treated with placebo. Physicians' global assessment showed significant reduction in the severity of illness and better tolerability. There were no adverse events noted in study population.

Conclusions: This clinical trial demonstrates that the Encof Lozenges reduces the signs & symptoms of cough within 7 days.

Key words: Cough, Cough signs & symptoms, Global Assessment

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INTRODUCTION

Cough is the most common symptom presented to general practitioners (Britt 2002; Cherry 2003). Cough impairs quality of life (French 2002) and results in various other complications. Cough is usually divided into acute or chronic according to its duration and age group. It is defined as chronic if over eight weeks duration in adults; and over three to four weeks in children (Chang 2005).This reflects the different conditions causing chronic cough in different age groups.

Acute cough is a common presentation of upper respiratory tract infections (URTI) encountered in general practice [1]. In Australia in 1999, cough was treated in 7.5% of general consultation [2]. Cough can lead to high morbidity and cause debilitating symptoms such as exhaustion, insomnia, hoarseness, musculoskeletal pain, sweating and even urinary incontinence [3, 4]. The pressure produced during coughing could also potentially cause some kind of complication in nearly all organ systems [3]. More importantly, cough can be so profound that it may have an adverse effect on the patient's quality of life [4].

In the management of acute cough, in the ambulatory setting, combination rather than single drugs showed a benefit (Schroeder 2004). However, antihistamines, neither singly nor in combination, were effective for relieving acute cough (De Sutter 2003; Schroeder 2004). Moreover they are associated with potentially significant adverse events including altered consciousness, arrhythmia and death (Gunn 2001; Kelly 2004). Neither of these reviews included patients with pneumonia (De Sutter 2003; Schroeder 2004).

It is well known that not every ill person consults a health care professional. [5] Social and cultural factors may influence the pattern of symptomatology and phenomenology [6]. Patients disappointed with ineffective conventional treatments and naturally look for alternatives. Ayurved has been practiced in India for over 5000 years: Ayurved is considered to be a very acceptable alternative in South Asia and a sizable segment of the population consults Ayurved practitioners for their health problems.

This study was designed to evaluate the effectiveness of Encof, a polyherbal lozenges in treating acute and chronic cough of uncomplicated URTIs in adults. Encof is made from commonly used herbs in treating cough and, their functions and side effects are well documented. Encof Lozenges consists of Yashtimadhu (Glycyrrhiza glabra), Vasaka (Adhatoda vasica), Haridra (Curcuma longa), Talispatra (Flacourtia catapracta), Clove oil (Eugenia caryophyllus), Khadir (Acacia catechu), Cinnamon oil (Cinnaamomum zeylanicum), Elaichi powder (Elettaria cardamomum), Saffron (Crocus sativus). Ingredients like Yashtimadhu (Glycyrrhiza glabra), Cinnamon oil (Cinnaamomum zeylanicum), Khadir (Acacia catechu) and Talispatra (Flacourtia catapracta) have both anti-tussive and expectorant activities including the promotion of salivary and bronchial secretions. Vasaka (Adhatoda vasica) has expectorant activities and broncho-dilatative effect. Haridra (Curcuma longa) and Clove oil (Eugenia caryophyllus) have antimicrobial activity.

It contains standardised extracts of the following herbs equivalent to:

Yastimadhu	(Giycyrrhiza glabra)	200mg
Vasaka	(Adhatoda vasica)	25mg
Haridra	(Curcuma longa)	10mg
Talisptra	(Flacourtia cataphracta)	3mg
Clove oil	(Eugenia caryophyllus)	7mg
Khadir	(Acacia catechu)	5mg
Cinnamon oil	(Cinnaommum zeylanicum)	3mg
Elaichi powder	(Elettaria cardamomum)	3mg
Saffron	(Crocus sativus)	0.25mg
Sugarbase		q.s

METHODS

Study design

This was an open label, outpatient-based, single-center drug - trial study with cough resulting from uncomplicated upper respiratory tract infections.. The trial was conducted at Life Veda Treatment and Research Center, Mumbai, India. Detailed medical history, general physical examination, and respiratory evaluation were recorded at the screen by the designated Principal Investigator (PI) of the trial. Laboratory tests were carried out as per protocol. Subsequently, all patients were examined by PI at every visit during the trial.

Male or female patients above the age of 18 diagnosed clinically having acute or chronic cough. Patients suffering with other pulmonary disease such as TB, Sarcoidosis, Pneumonia etc were excluded from the study. Patients incapable of giving informed consent and those unlikely to follow the treatment schedule and patients who continue to smoke tobacco in any form were excluded. Those dependent on legal/illegal drugs, steroids and patients with significantly reduced hepatic renal clearance to affect drug metabolism were excluded from the study.

STUDY MEDICATION AND DOSAGE

Polyherbal cough Lozenges consists of Yashtimadhu (Glycyrrhiza glabra), Vasaka (Adhatoda vasica). Haridra (Curcuma longa), Talispatra (Flacourtia catapracta), Clove oil (Eugenia caryophyllus), Khadir (Acacia catechu), Cinnamon oil (Cinnaamomum zeylanicum), Elaichi powder (Elettaria cardamomum), Saffron (Crocus sativus).

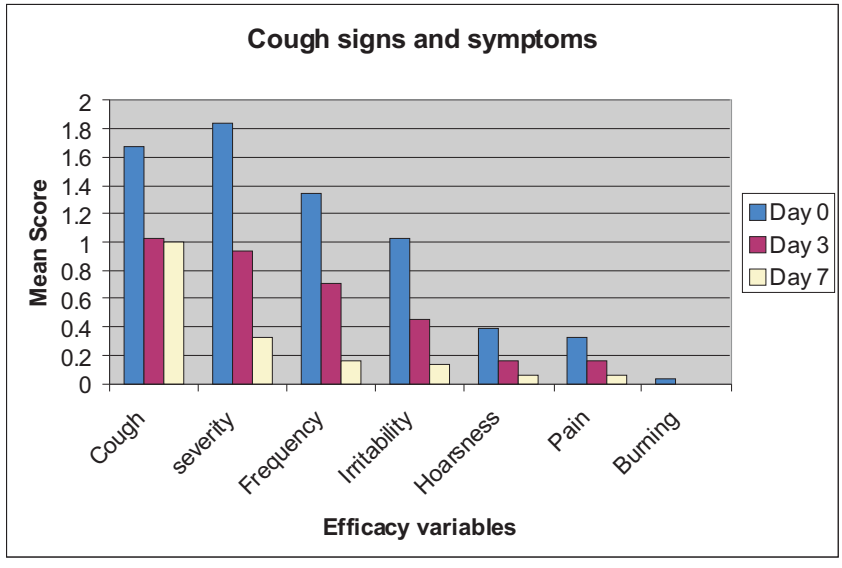
Dosage: 1 Lozenge four times a day for 7 days.

Efficacy parameters assessed were i) severity of pain measured on Visual Analog Scale (VAS) of 0-10, ii) Functional Disability of joint was assessed by measuring pain while a) walking distance b) squatting c) crossing legs & d) climbing steps and scored as 0- no pain, 1-mild pain, 2-moderate pain, 3-severe pain and 4-acute pain. After 3 months of treatment again the blood investigations were carried out and patients' and physicians' global assessment was made. The variation in VAS and functional disability of joint was assessed by paired t-test and ANNOVA respectively.

RESULTS: Outcome measures and data analysis

Treatment period lasted for 7 days. During which, clinical assessments including history, examination and tests were performed at day 4 and day 7. The participants were asked to fill a questionnaire to grade the severity of a range of symptoms related to cough and the functional disturbance of cough. The first primary safety outcome is Severity of Cough (Intensity, Frequency etc.), The second efficacy outcomes was tolerability which was defined as a permanent discontinuation of the study drug Encof lozenges as the result of an adverse event, Patient's and physician's global assessment. Subjects were encouraged to withdraw from the trial and to be treated accordingly if there were any signs of deterioration in clinical presentation. This study was done on intention-to-treat basis that patients initially treated but subsequently dropouts were included in the final analysis.

Group data was expressed as the frequency unless otherwise specified. To analyse differences in the baseline parameters, student t-test was performed. The statistical significance of change differences within groups was tested by the Student's t-test.



The result indicates encouraging outcome in clinical signs and symptoms of cough. There was However there was significant reduction in Cough during Day 0 to Day 7(t=6.3, S, P<0.001). 1. In case of Severity, frequency, irritability and hoarseness during Day 0 to Day 3 and Day 0 to Day 7 there was significant change noted (P < 0.001). There was no significant reduction in Pain noted during Day 0 to Day 3, however, significant reduction in Pain during Day 0 to Day 7. (t=2.4, S, P=0.03). Only one case was found with burning symptoms and there was no change seen for the same. (Appendix: Table-III). The laboratory investigations were insignificant. (Table II) During the study no adverse events were noted. According to 74.19 % patients the recovery with Encof lozenges is accepted as good to excellent whereas, according to physician 77.42 % patients showed recovery as good to excellent. (Appendix: Table - IV)

Table I: Demographic Data

Demographic and Vitals:

Data: Mean ± SD

1. Age (yrs): 37.06 ± 10.82 (Minimum=19, Maximum=59), n=31.
2. Sex: Male = 25(80.6 %), Female = 6 (19.4 %).
3. Systolic Blood Pressure (mmHg): 125.55 ± 7.44 (Minimum=110, Maximum=140), n=31.
4. Diastolic Blood Pressure (mmHg): 82.35 ± 5.40 (Minimum=70, Maximum=92), n=31.
5. Pulse/Min: 70.94 ± 4.22 (Minimum=62.0, Maximum=78.0), n=31.
6. Temperature (F): 36.70 ± 0.05 (Minimum=36.7, Maximum=37.0), n=31.
7. Respiration/Min: 22.61 ± 0.80 (Minimum=22, Maximum=24), n=31.

Table II: Laboratory Investigations:

Data: Mean ± SD

Statistical test: Student's paired t test, Level of Significance P=0.05, S= Significant, NS=Not Significant, N=Number of observations

SR	Parameter	N	Before	After	t value, Significance, P value
1	RBC (/cmm)	31	5.41± 0.67	5.42 ± 0.66	0.17, NS, P = 0.87
2	WBC Total	31	6841.94 ± 1677.85	6677.42 ± 1473.71	1.1, NS, P = 0.29
3	Nutrophils	31	62.00 ± 14.45	14.37 ± 10.00	1.92, NS, P = 0.06
4	Lymphocytes (%)	31	31.06 ± 8.38	30.82 ± 8.09	0.18, NS, P = 0.86
5	Eosinophils (%)	31	3.08 ± 3.34	2.44 ± 4.21	0.92, NS, P = 0.36
6	Monocytes (%)	31	0.00 ± 0.00	0.00 ± 0.00	0,NS P = 1
7	Basophills	31	0.00 ± 0.00	0.00 ± 0.00	0, NS, P = 1
8	ESR	31	17.84 ± 5.65	16.68 ± 4.58	1.8, NS, P = 0.09

Table III: Cough signs and symptoms

Symptoms	Day 0	Day 3	Day 7	Comparison bet. Day 0 - Day 3	Comparison bet. Day 0 - Day 7
Cough	1.68 ± 0.60	1.03 ± 0.18	1.00 ± 0.00	t=1.0, NS, P=0.33	t=6.3, S, P<0.001
Severity	1.84 ± 0.64	0.94 ± 0.57	0.32 ± 0.48	t=12.6, S, P<0.001	t=12.5, S, P<0.001
Frequency	1.35 ± 0.80	0.71 ± 0.59	0.16 ± 0.37	t=7.4, S, P<0.001	t=8.9, S, P<0.001
Irritability	1.03 ± 1.11	0.45 ± 0.62	0.13 ± 0.43	t=4.8, S, P<0.001	t=4.3, S, P<0.001
Hoarseness	0.39 ± 0.72	0.16 ± 0.37	0.06 ± 0.25	t=3.0, S, P<0.001	t=2.8, S, P=0.01
Pain	0.32 ± 0.75	0.16 ± 0.45	0.06 ± 0.25	t=1.98, NS, P=0.06	t=2.4, S, P=0.03
Burning	0.03 ± 0.18	0.00 ± 0.00	0.00 ± 0.00	t=1.0, NS, P=0.33	t=1.0, NS, P=0.33

Table IV: Recovery:

1 By Patient 2. By Physician
Scale: 1= Excellent, 2= Good, 3 = Fair, 4 = Poor, 5 = Very Poor

Data: Frequency (Percentage %)

	Patient	Physician
Excellent (1)	8 (25.8 %)	5 (16.1 %)
Good (2)	15 (48.4%)	19 (61.3 %)
Average (3)	5 (16.1 %)	3 (9.7 %)
Poor (4)	3 (9.7 %)	4 (12.9 %)
Total	31 (100 %)	31 (100 %)

Table V: Tolerability

	Patient
Excellent (1)	27 (87.1 %)
Good (2)	4 (12.9 %)
Average (3)	0 (0.0 %)
Poor (4)	0 (0.0 %)
Total	31 (100 %)

DISCUSSION

About 80% of all antimicrobials are prescribed in primary care, and up to 80% of these are for respiratory tract indications, including acute cough. Respiratory tract infections are by far the most common cause of cough in primary care. Broad spectrum antibiotics are often prescribed for cough, including acute bronchitis and many of these prescriptions will benefit patients only marginally if at all, and may cause side effects. Unnecessary prescribing, especially of broad spectrum antibiotics, drives antimicrobial resistance, wastes money and raises wrong expectations for patients. Microbial resistance topped the list of priority intervention needs in the World Health Organization report on Priority Medicines.

The results from the present study to analyze the efficacy if Encof lozenges in treatment of cough resulted from uncomplicated URTI,confirmed that URTI was a usually self-limiting disease with its symptoms improved in the first week of presentation. This formulation was well tolerated with no adverse effects reported. Encof lozenge contains ingredients including Yashtimadhu (Glycyrrhiza glabra), Cinnamon oil (Cinnaamomum zeylanicum), Khadir (Acacia catechu) and Talispatra (Flacourtia catapracta) has both anti-tussive and expectorant activities including the promotion of salivary and bronchial secretions. Vasaka (Adhatoda vasica) has expectorant activities and broncho-dilatative effect. Haridra (Curcuma longa) and Clove oil (Eugenia caryophyllus) antimicrobial activity. The formulation shows comprehensive property for treating cough of uncomplicated URTI and its associated symptoms.

CONCLUSION

An Encof lozenge is very effective in treating cough and associated symptoms of uncomplicated URTI. It showed good tolerability and significant recovery from the associated symptoms of cough. No adverse event is noted through out the study indicates that Encof lozenge is safe for treatment of cough.

ACKNOWLEDGEMENT

Authors are thankful to M/s. Millennium Herbal Care Limited, Mumbai for providing medicines and financial support and experts from fields including plant chemistry, clinical pharmacology and Ayurveda who have significantly provided their expertise to this study.

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