CLINICAL RESEARCH

A Prospective Multicentre Observational Study to Evolve the usefulness of Group of Homoeopathic Medicines in the Management of Acute Tracheobronchitis**

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Abstract : Sn open multicentre clinical trial was aimed to evolve the usefulness of a group of homoeopathic medicines in the management of acute tracheobronchitis with regard to improvement in its symptom complex. Patients presenting coryza with irritable dry or productive cough, oppression chest and neutrophillic leucocytosis were enrolled in the study from October 2005 to September 2008. Severity of patients' disease condition was evaluated as per tracheobronchitis symptom scale. Symptoms of disease as well as characteristic symptoms of individual patients were considered for selection of medicine from a group of 14 trial medicines. Selected medicine was prescribed in 6C potency (10-12 dilution) and was repeated from few minutes to few hours, as per the need of each case. There was significant reduction in the symptom score within 24 hours of starting the treatment ($p = 0.000 < .05$). At the end of study follow up, 91% of the patients reported either cured or markedly improved. Phosphorus (n = 58), Arsenicum album (n = 52), Bryonia alba (n = 21) and Pulsatilla nigricans (n = 16) were found most commonly indicated and useful medicines. It is inferred from this study that homoeopathy has a positive role in the management of acute tracheobronchitis but the trial may be repeated in better study design settings to make the study acceptable to the scientific community.

Keywords: Acute tracheobronchitis; Cough; Phosphorus; Arsenicum album; Pulsatilla nigricans

Introduction

The Acute respiratory infections (ARIs) are classified as upper respiratory tract infections (URIs) or lower respiratory tract infections (LRIs). The upper respiratory tract consists of the airways from the nostrils to the vocal cords in the larynx, including the paranasal sinuses and the middle ear. The lower respiratory tract covers the continuation of the airways from the trachea and bronchi to the bronchioles and the alveoli (Simoes et al., 2006). Except during the neonatal period, ARIs are the most common causes of both illness and mortality in children under five (Kamath et al., 1969). Estimates indicate that in 2000, 1.9 million of children died because of ARIs, 70 percent of them in Africa and Southeast Asia (Williams et al., 2002). The severity of LRIs in children under five is worse in developing countries (Black et al., 2003).

Acute tracheobronchitis accounts for 40% of all Lower Respiratory Infections (LRI) (Chapman et al., 1981). This condition consistently ranks as one of the top 10 diagnoses for which patients seek medical care, with cough being the most frequently mentioned symptom necessitating office evaluation (Slusarcick, 2000). Tracheobronchitis incidence is highest during the first two years of life, though the ratio of tracheobronchitis incidence to total LRI incidence increases with age. Over all age groups, peak incidence of tracheobronchitis, like that of pneumonia and bronchiolitis, occurs mainly during the winter months (Chapman et al., 1981).

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Patients with acute tracheobronchitis have no underlying lung disease, they present with the acute onset of cough associated

with sputum production, often in association with preceding coryza and fever. It is usually viral in origin and because there is no underlying lung disease, the illness is usually self limited and runs a benign course (Balter et al., 2003).

Studies demonstrate that viral pathogens such as parainfluenza virus, respiratory syncytial virus and influenza virus account for most of the agents identified among children with cough illness or bronchitis (Weissenbacher et al., 1990 & Suwanjutha et al., 1990). Taken together, the evidence is ample that cough illness or bronchitis in children is principally caused by viral pathogens. So, there is little or no benefit of using antimicrobial agents in children suffering from acute respiratory illnesses like cough and acute bronchitis. However, the magnitude of this benefit needs to be considered in a broader context of potential side effects, medicalization for a self-limiting condition, increased resistance to respiratory pathogens and cost of antibiotic treatment (Smith et al., 2004).

There are evidences in literature that homoeopathic medicines have better potential over conventional medicines in managing acute respiratory illnesses (Riley et al., 2001). Moreover, these studies also show that homoeopathic medicines are associated with less number of adverse events as compared to conventional therapies (Haidvogl et al., 2007). This study was designed with aim to evolve the usefulness of the group of homoeopathic medicines in the management of acute tracheobronchitis and also to deduce their characteristic and clinical symptoms. Attempt was also made to ascertain any specific relationship of these medicines with any particular seasonal or thermal changes.

MATERIALS AND METHODS

Setting and design

It was an open, multicentre, observational study, conducted by Central Council for Research in Homoeopathy (CCRH) at its six centres, viz. Regional Research Institutes at Shimla & Gudivada and Clinical Research Units at Ranchi, Siliguri, Shillong & Gangtok, from October 2005 to September 2008. In this study, a group of 14 trial medicines were pre-identified for the treatment of acute tracheobronchitis.

Pre-identification of 14 trial medicines

For identification of trial medicines, common disease symptoms of acute tracheobronchitis (Christopher et al., 2002) were converted into corresponding rubrics and were repertorized by CARA professional software using complete repertory (Witko, 1997). Repertorization was done by elimination method (Tiwari, 2003), using 'Coryza with cough' and 'Dry cough' as eliminating rubrics. Then, medicines appearing in first and second grade were sorted out and proposed as trial medicines.

Participants

264 patients (149 males, 115 females), attending the general Out Patient Department(OPD) of the Institutes/ Units enrolled in the study but 182 patients in the age group of 1-15 years with a history of coryza with irritating dry or productive cough, accompanied by oppression chest and neutrophillic leucocytosis, could complete the study. Patients suffering from any systemic disease(s), pneumonia, chronic pulmonary disease (CPD), acute exacerbation of chronic obstructive airways disease (COAD) and those having history of smoking, were excluded from the study. Written informed consent was obtained from the legal guardians of the patients. Protocol was approved by the Ethical Committee of the Council and study was conducted in accordance to the Declaration of Helsinki (2008) and Guidelines of Good Clinical Practice (1996).

Baseline evaluation

A tracheobronchitis symptom scale (TSS), was used to assess each patient's condition. This scale was developed by the CCRH. This scale consisted of 10 items with their corresponding sub-items viz. coryza with cough, irritable cough, dry cough (with subscale severity and duration), oppression chest, wheezing, respiration rate, cough painful (with subscale cough loose), expectoration (with subscale scanty, mucus, purulent, copious, blood streaked sputa), fever and neutrophillic leucocytosis. Total of score was done by adding score of above 10 items. Score was assigned between 0- 4 as per complaint of patient. Higher the score more the complaint. Maximum attainable score was 59. As per the baseline symptom score, patients were categorized into three groups - mild (d" 20), moderate (21 d" 35) and severe (e" 36).

Intervention

Repertorization chart, comprising of 15 common disease symptoms of acute tracheobronchitis (coryza with cough, irritable cough, dry cough, chest oppression, wheezing respiration, difficult respiration, painful cough, loose cough, scanty expectoration, mucous expectoration, purulent expectoration, profuse expectoration, blood stained spitting, heat sensation and pain in trachea) with the respective gradation of medicines as mentioned in the complete repertory

(Witco, 1997), was provided to the investigators. From this repertorization chart, symptoms present in the patient were highlighted, to sort out group of top ranking medicine. Final selection of medicine was done in consultation with materia medica. Cases which required medicines other than the trial group of medicines were treated in the general OPD and not included in the study. A record of such cases was also maintained. All medicines were prescribed in 6C potency (10-12 dilution) and were repeated every few minutes to hours depending on the frequency, duration and intensity (FDI) of the symptoms, till perceptible change appeared. All follow up actions were taken as per the guidelines of Hahnemann (Hahnemann, 1994) and Kent (Kent, 1997). All patients were called for daily follow-up till tenth day of infection. In the event of any adverse condition, patients were referred for appropriate medical care.

Outcome measures

Primary outcome measure was reduction in TSS score. Improvement was calculated using formula {[(baseline score – score at end) / baseline score] X 100}. Changes thereupon were graded as cured (100% improvement), marked improvement (75 to < 100 improvement), moderate improvement (50 to < 75% improvement), mild improvement (25 to < 50% improvement), not significant improvement (< 25% improvement), static (no change), worse (increase in symptom score).

Statistical analysis

Statistical analysis was carried out using SPSS 16.0 for windows (Statistical Package for Social Sciences, SPSS INC, CHICAGO). The data was examined for normality of distribution. For normally distributed data, comparisons of score at entry with score at end were done by using paired t test and one-way/single-factor ANOVA was used to analyze improvement between the groups. $P < 0.05$ was considered as significant.

RESULTS AND DISCUSSION

182 patients (104 males, 78 females) completed the follow-up. Out of 82 patients who could not complete the study followup, 37 patients lost to follow up where as 45 patients were dropped out due to protocol deviation. Mean age of patients was 7 ± 4 years. Besides presenting with coryza, irritable cough, oppression chest and neutrophillic leucocytosis, patients also presented other symptoms of acute tracheobronchitis like dry cough (73%), loose cough (27%), wheezing (60%), painful cough (36%), scanty expectoration (49%), mucus expectoration (46%), purulent expectoration (31%), copious expectoration (35%), bloody expectoration (28%) and fever (77%). At the baseline entry mean score of patients was 26.62 ± 6.152. Initially all patients were prescribed medicine in 6C (10 – 12 dilution) potency whereas in nine patients potency of the medicine had to be raised to 30C (10 – 60 dilution). On average patients required 6.96 ± 3.71 doses of indicated medicine. After prescription of homoeopathic medicine there was statistically significant reduction in symptom score within 24 hrs ($p = 0.000 < 0.05$). This reduction in score was consistent irrespective of the severity of disease (mild, moderate or severe) or lapse of days since onset of symptoms. After completing the study follow up 74% (n = 134) patients were completely cured, 17% (n = 31) were markedly improved, 6% (n = 10) moderately improved, 1% (n = 2) mildly improved, where as two patients did not improve significantly, one patient was static and two patients became worse after treatment and had to be referred for appropriate medical care. Out of Total 182 patients, 144 (79%) patients were enrolled within first 4 days of onset of their symptoms, out of which 94 (65%) patients were cured within 5 days of treatment from day of onset of symptoms. (Figure No. 1).

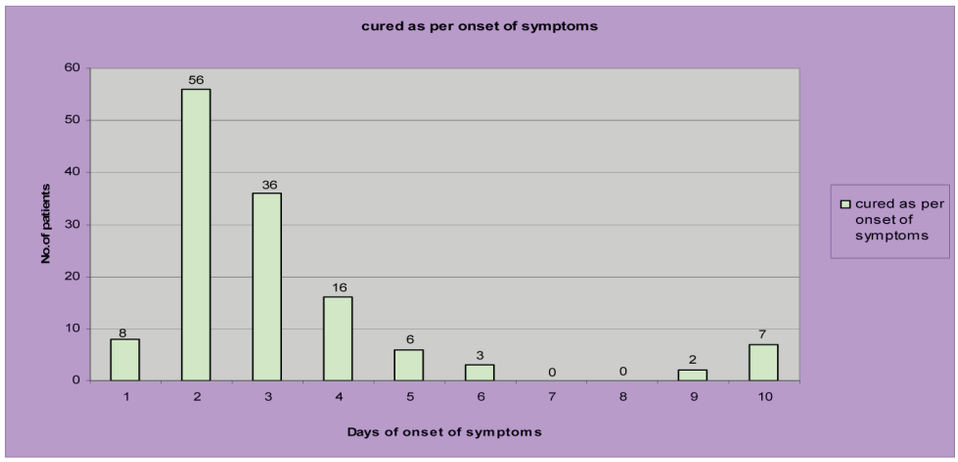

Fig 1: Cure rates in patients as per day of onset of symptom.

Patients cured after the treatment, in respect to days of treatment were shown in figure. No. 2.

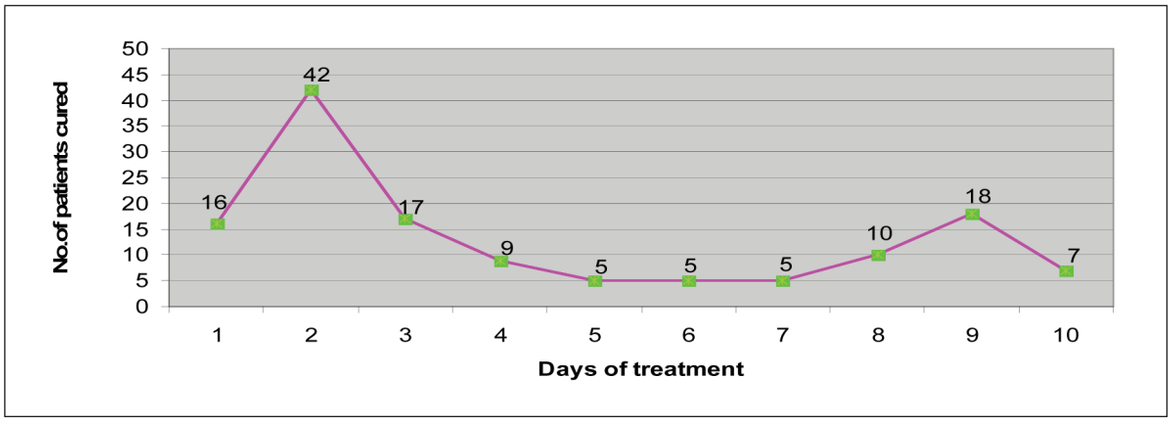

Fig. 2 Cure rate as per days of Treatment

Changes in symptom score at entry and at end were noted, they found statistically significant (p value < 0.000) in most of days except of 7th and 8th day. (Table No.1)

Table 1 : Symptom score at entry and at end of treatment

Days of enrollment of patient	No. of patients enrolled	Symptoms core (Mean ± SD)		P value	95% confidence
		At entry	At end		interval
1st day	9	28.11± 7.785	0.11 ± 0.333	0.000*	21.899 – 34.101
2nd day	61	28.48±5.378	0.46±2.953	0.000*	26.350 – 29.683
3rd day	46	23.98±6.648	0.72±2.167	0.000*	21.329-25.193
4th day	28	26.25±5.954	2.04±3.977	0.000*	21.957-26.471
5th day	14	24.46±6.630	6.07±6.662	0.000*	16.150-26.565
6th day	5	22.40±5.505	3.00±5.196	0.002*	12.398-26.402
7th day	3	31.67±4.619	11.67±20.206	0.156	-18.724-58.724
8th day	4	27.00±4.967	20.75±3.403	0.209	-6.237-18.737
9th day	3	30.00±2.646	0.33±0.577	0.002*	23.930-35.400
10th day	9	28.44±2.651	0.89±2.315	0.000*	26.112-28.909

*P value significant at < 0.05.

Patients were divided into mild (n=38), moderate (n=135) and severe (n=9) intensity subgroups as per their baseline score. When improvement rate was measured within these intensity subgroups, no significant difference was found, F (2, 181) = 0.207, p > 0.05. More than 83% of patients were covered by one of the four medicines namely, Phosphorus, Arsenicum album, Bryonia alba and Pulsatilla nigricans. Phosphorus (n = 58) was the most commonly indicated medicine, followed by Arsenicum album (n = 52), Bryonia alba (n=21) and Pulsatilla nigricans (n=16). (Table No.2)

Table 2: Medicine wise improvement status

Medicine	Cured	Improvement					
		Marked	Moderate	Mild	Not significant	Status quo	Worse
Phosphorus	44	10	4	-	1	1	-
Arsenic album	34	11	5	2	1	-	1
Bryonia alba	19	2	-	-	-	-	1
Pulsatilla nigricans	14	2	-	-	-	-	-
Lycopodium clavatum	4	-	1	-	-	-	-
Nux vomica	2	2	-	-	-	-	-
Kali carbonicum	7	-	-	-	-	-	-
Aconitum napellus	3	-	-	-	-	-	-
Spongia tosta	6	1	-	-	-	-	-
Ipecacuanha	1	-	-	-	-	-	-
Silicea	-	1	-	-	-	-	-
Natrum muriaticum	-	1	-	-	-	-	-
TOTAL	134	30	10	2	2	1	2

Indicated medicines showed some predilection to seasonal changes like Phosphorus patients showed a marked susceptibility to every change of weather, Arsenicum album patients to rainy season and Pulsatilla nigricans patients to hot weather. Bryonia alba acted more promptly in summer season. Future studies must explore the possibility of administering homoeopathic medicines in clinical conditions linked to particular season. Characteristic symptoms of these medicines which were repeatedly verified in the study are presented in Table 3.

Table 3 : Characteristic indications of leading medicines*

Phosphorus
Ailments from cold exposure (3)
Restless, irritable and sensitive (11)
Fear of being alone (10)
Mentally intelligent but physically weak (22)
Aggravation from change of weather (14)
Desire for cold food & drinks (39)
Aggravation from lying on left side, especially cough (13)
Profuse perspiration during fever (9)

Arsenicum album
Ailments from cold exposure (12)
Rainy season aggravation (4)
Ailments from eating ice-cream/ refrigerated food items (6)
Great anguish and restlessness (15)
Complaints < mid night, especially cough and fever ((21)
Thirst for small quantity of water at small intervals (21)
Wheezing and difficult respiration, < lying down, > by sitting and bending forward (7)
Violent dry cough with constant titillation in larynx, unable to lie down for fear of suffocation (5)

Bryonia alba
Wants to be quiet and undisturbed; every motion aggravates (12)
Profuse thirst for large quantity of cold water (6)
Dry cough with pain in chest; must hold the chest while coughing (4)
Pulsatilla nigricans
Fear of being alone (4)
Complaints < evening (9)
Amelioration in open air and from cold in general (9)
Aggravation from heat in general (3)

* First number in parenthesis denotes num

Few patients of acute tracheobronchitis could not be enrolled after screening because they were not covered by trial medicines. Some of the known seasonal symptoms of medicines are again verified during this study. Majority of these patients reporting in rainy season indicated to Natrum sulphuricum, Rhus toxicodendron or Dulcamara.

Acute tracheobronchitis is mainly a disease of childhood and early adolescence (Ayres et al., 1993), typically persisting for 10 to 20 days but occasionally may last for 4 or more weeks (Fleming, 2007), thus leading to increase in absenteeism in school. Findings of our study show that there was significant reduction in disease score within 24 hours and 41% of cases reported cure after three days of starting treatment. Similar to our results Riley et al also reported 67.3% improvement by homoeopathic medicines in 3 days, in patients suffering from acute respiratory infections. These facts suggest that by integrating homoeopathic treatment in primary health care service for management of acute tracheobronchitis, burden of disease can be minimized.

Antibiotic therapy is used in 65 to 80 percent of patients with acute bronchitis (Rossi et al., 2009; Gonzales, 1997), but a growing base of evidence puts this practice into question. Mainous AG III et al in their meta-analysis concluded that antibiotic therapy did not improve cough or clinical status, and patients had more side effects than those who did not take antibiotics. In our study, adverse events were reported in less than 1% of patients. The results are in consonance with Riley and Haidvogl.

Other studies have also been conducted which show that homoeopathic treatment can be used effectively in the management of acute illnesses, especially acute respiratory infections (Smith, 2004; Riley et al., 2001).

Phosphorus and Arsenicum album were found most frequently indicated and useful medicines in the treatment of acute tracheobronchitis. Similar to our results Srikanth (1997) also found that Arsenicum album is one of the most frequently prescribed medicines in acute respiratory allergies.

The present study had some limitations too. No provisions were made to evaluate any disease complication or treatment sequel, although other studies report that cases of acute bronchitis often show recurrences of complaint or receive new diagnosis of chronic bronchitis and asthma after 3 years (Spence et al., 2005; Jónsson et al., 1998).

Conflict of interest

Nil

Ethics

The study has been approved by the Ethical Committee of the CCRH.

Conclusion

It is inferred from this study that homoeopathy has a positive role in the management of acute tracheobronchitis but the trial may be repeated in better study design settings to make the study acceptable to the scientific community.

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