Original Article

Management of early years of simple and mucopurulent chronic bronchitis with pre-defined homeopathic medicines – a Prospective Observational Study with 2-Years Follow-Up

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Abstract

Background Simple and mucopurulent chronic bronchitis (SMCB) is characterized by recurrent mucoid or mucopurulent expectoration in absence of localized suppurative disease. This observational open label study was undertaken to evaluate the effects of homeopathic medicine in SMCB. **Methods** 1902 patients were screened from 07 centres out of which 1305 were excluded. 597 patients were enrolled as per the inclusion and exclusion criteria. A total of 14 pre-defined homeopathic medicines were shortlisted for prescription after repertorizing the pathological symptoms of SMCB. Outcomes were assessed through chronic bronchitis symptom scale (CBSS) and FEV1/ FVC ratio with spirometry for over a period of two years. Appearance of any change (relief/ worse)/ status quo was immediately followed by placebo/ change in dilution/ change in remedy. Statistical analysis was done using SPSS version 20. **Results:** 532 patients were analyzed based on the intention to treat principle using last observation carry forward method. Mean CBS score reduced from 29.86±4.5 at baseline to 12.33±7.6 at completion of 2 years. Repeated measures ANOVA, at time points 0 (baseline), 3, 6, 9, 12, 15, 18, 21 and 24 months, showed significant reduction in CBS scores [Wilk's Lambda 0.104, F=564, df 524; p=00001]. The FEV1 and FEV1/FVC was maintained within normal limits. 86% prescriptions included *Lycopodium*, *Arsenicum album*, *Pulsatilla*, *Phosphorus*, *Stannum metallicum*, *Calcarea carbonica*, *Silicea*, *Bryonia alba*. **Conclusion:** The result suggests effectiveness of homeopathic treatment in early years of SCMB patients. Controlled trials are warranted.

Keywords: chronic bronchitis, homeopathy, pre-defined medicines, early years

Introduction

Chronic obstructive pulmonary bronchitis (COPD) is a common, preventable and treatable disease characterized by persistent respiratory symptoms and airflow limitation due to airway and/or alveolar abnormalities, usually caused by significant exposure to noxious particles or gases [1]. It is a broad spectrum disease with chronic bronchitis (CB) at one end and emphysema at the other. Chronic bronchitis (CB) is a common but variable phenomenon defined as chronic productive cough for more than 3 months in each of 2 consecutive years [2,3]. It is a chronic progressive disease associated with exacerbations and remissions and often goes through three stages: simple chronic bronchitis, in which there is a recurrent increase in the volume of mucoid bronchial secretion sufficient to cause expectoration; chronic or recurrent muco-purulent bronchitis, when the sputum is persistent or intermittently purulent owing to secondary bacterial infection in the lung and chronic obstructive bronchitis, in which there is persistent, widespread narrowing of the intrapulmonary airways, at least on expiration, causing increased resistance to airflow [4].

The occurrence of CB in the general population has been documented to vary between 3% to 7% of healthy adults. However, it is estimated to be as high as 74% among those diagnosed to have COPD. Many among those in the general population experiencing symptoms of chronic bronchitis may not have a definitive respiratory diagnosis [3]. Patients under the age of 50 years who are otherwise healthy and have CB are at a higher risk of morbidity and mortality when compared to healthy subjects [4]. The 'Indian Study of Asthma, Respiratory Symptoms and Chronic Bronchitis' (INSEARCH) on 85,105 men and 84,470 women from 12 urban and 11 rural sites reported the prevalence of CB to be 3.49% in adults > 35 years [5]. According to DALYs 2016, India, COPD, is leading cause of death next to ischemic heart disease [6].

If not treated, patients with chronic bronchitis symptoms had a threefold increased risk of developing new COPD compared to the asymptomatic population [3]. Each pharmacologic treatment regimen should be individualized and guided by the severity of symptoms, risk of exacerbations, side effects, co-morbidities, drug availability and costs, and the patient's response, preference, and ability to use various drug deliveries [1]. The primary aim of treatment for chronic bronchitis is to relieve symptoms, prevent complication and slow the progression of the disease. The classes of medications used are bronchodilators, antimuscarinic drugs, glucocorticoids, antibiotic therapy, and Phosphodiesterase-4 inhibitors. However, long term users will land into several complications/adverse effects [1].

In clinical practice, spirometry helps in the management of CB by documenting the extent of reversibility of airflow obstruction and provides valuable therapeutic information about the patient's responsiveness to inhaled bronchodilator therapy. A measured forced expiratory volume in one second (FEV₁) /forced vital capacity (FVC) i.e. FEV₁/FVC ratio of less than 70 defines obstructive airways [1]. The airflow limitation measured though provides important information to the physician to enable optimization of management [7] but these pulmonary functions gradually deteriorate even when treated with bronchodilators, antibiotics and inhaled steroids.

A less expensive method as compared to modern medicine, is to treat the episodes as soon as they begin and to control the causative factors which exacerbate the condition [3]. Large cohort studies have shown that patients who chose to consult GPs certified in homeopathy used less antibiotics and antipyretic/anti-inflammatory drugs for URTI than those seen by GPs prescribing conventional medications [8].

WHO has acknowledged Homeopathy as second mainly applied and used system of medicine internationally [9]. Homeopathic treatment is associated with improvement of symptoms in a range of chronic and recurring pathologies [10,11,12,13] and respiratory disorder [8,14]. A study on critically ill patients by Frass. et al [15] suggested that potentized potassium dichromate may help to decrease the amount of stringy tracheal secretions in COPD patients. Homeopathic treatment for respiratory diseases was associated with a significant reduction in the use and costs of conventional drugs [16]. Most real-world outcome studies in adults and children have shown benefits of homeopathy in respiratory disorders [17]. However, no studies have been carried out on the patients in early years of simple and mucopurulent chronic bronchitis. Peters et al [18] suggested certain homeopathic medicines after repertorizing the disease symptoms of sinusitis but to be prescribed after individualization according to homeopathic principles. Similar pattern was adopted in this study too for arriving at 14 pre-defined medicines for SMCB. The present study was undertaken to evaluate the role of a group of 14 pre-defined homeopathic medicines in management of simple and mucopurulent chronic bronchitis.

Objectives

Primary objective was to evaluate the usefulness of homeopathic medicine(s) in the management of simple and mucopurulent chronic bronchitis (SMCB). Secondary objective was to evaluate the effect of homeopathic medicines in the spirometry (FEV₁ and FEV₁/ FVC) findings.

Material and methods

Study design and Setting

This was a prospective observational study carried out during Oct. 2005 to Sept. 2010 at seven research centres under Central Council for Research in Homoeopathy namely: *Dr DP Rastogi Central Research Institute, Noida, National Homeopathy Research Institute for Mental Health, Kottayam, Regional Research Institutes (Homoeopathy), Puri and Guwahati, Clinical Research Units, Puducherry, Chennai and Tirupati*. The study protocol was prepared in accordance with Helsinki declaration [19] on human experimentation and necessary ethical clearance was obtained from the ethical committee of the Council and trial was registered at Clinical trials Registry-India (CTRI/2011/09/001994). The Investigators having an institutional qualification in Homoeopathy as per the regulations of Central Council of Homoeopathy, a statutory body for education and practice under Ministry of AYUSH, Govt. of India, and with more than 10 years of experience of homeopathic practice were responsible for prescribing homeopathic medicines, collecting data and for follow up for 2 years. All the investigators were trained in the protocol before initiation of the study. Doctors with speciality in Medicine were engaged as consultants at respective study centres for screening, enrolment and follow up of the study patients throughout. All patients gave written informed consent.

Study Participants

Inclusion criteria: Participants fulfilling the following inclusion criteria were enrolled in the study.

- Both genders and age between 20 and 50 years
- Patients presenting with chronic cough with excessive mucopurulent expectoration for at least 3 months in a year for more than two consecutive years
- Recurrent attacks of chronic cough usually in winter months which steadily increases in severity and duration.
- Patients who are not, on any other treatment, including homoeopathy
- Patients residing within approachable distance.

- FEV₁ > 80% predicted.
- Patients willing to participate in the study
- Patients who match the prescribing criteria for any of the 14 pre-defined medicines.

Exclusion criteria

- Patients suffering from central airflow obstruction, emphysema, cor-pulmonale, bronchial asthma, active pulmonary tuberculosis, broncho-pulmonary mycosis, acute bronchitis, pulmonary thromboembolism, pulmonary hypertension.
- Persons require hospitalization with other co-morbid conditions.
- Persons requiring oxygen therapy and hospitalization;
- FEV₁ < 80% predicted
- FEV₁ / FVC < 0.7
- Patients who did not match the prescribing criteria for any of the 14 pre-defined medicines.

Homeopathic treatment

The patients were screened in the Outpatient department (OPD) as per the inclusion and exclusion criteria mentioned above. A detailed case taking as per homeopathic methods was done after patient fulfilled the inclusion criteria. Those who were not fulfilling the inclusion criteria, were excluded and treated in the General OPD.

Selection of pre-defined trial medicines, first prescription and follow up

The selection of pre-defined trial medicines was done by repertorizing the 21 disease symptoms of CB (Table 1). Repertorisation was done using the Complete Repertory from CARA Professional software [20] (Table 2). Considering the fact that the study pertains to CB, the drugs given in the first grade (3 points) followed by those in the second grade (2 points) mentioned against the rubric 'chronic cough' were short-listed through an elimination method. The 14 pre-defined medicines identified in the order of their high score were, *Stannum metallicum*, *Arsenicum album*, *Silicea*, *Phosphorus*, *Lycopodium*, *Pulsatilla nigricans*, *Calcarea carbonica*, *Sulphur*, *Hepar sulphur*, *Bryonia alba*, *Ipecacuanha*, *Antimonium tartaricum*, *Carbo vegetalis* and *Spongia tosta*. These medicines were procured from M/S Sharda Boiron Laboratory Pvt. Ltd. Sahibabad, (U.P.) India.

Selection of the specific medicine for each patient was done on basis of the highest score on repertorization of the presenting signs and symptoms of the patient which was further guided by the characteristic mental/emotional and physical attributes of the patient, finally verified by the Materia Medica. The investigator was free to change prescription up to three times including first prescription. However, if the selected medicine was out of the group of pre-defined trial medicines then the patient was not included in the study but was treated in the general OPD. Throughout the study period each enrolled patient was prescribed one of these trial medicines only.

The prescription of the selected medicine started with 30CH potency, in a single dose (four pills of globule No. 30) followed by placebo (four pills of unmedicated globules No. 30), daily. Follow up was weekly for the 1st month, fortnightly for the next 2 months and monthly for the remaining period until completion of 24 months. On each of these visits, clinical assessment was done by the investigator. Spirometry was performed at the time of enrollment, at every 3rd month till 24 months.

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Table1 - List of 21 symptoms of chronic bronchitis considered for repertorization

1.Chest; inflammation; Bronchial tubes	2.Cough; chronic
3.Expectoration; copious; chronically	4.Cough, winter
5.Expectoration; constant, almost day and evening	6.Expectoration; copious; paroxysmal cough, after
7.Expectoration; frequent	8.Respiration; difficult; cough; with
9.Expectoration; mucous	10.Expectoration; mucous; translucent
11.Expectoration; frothy	12.Expectoration; easy
13.Expectoration; transparent	14.Expectoration, white
15.Expectoration; purulent	16.Expectoration; difficult
17.Expectoration; yellow	18.Expectoration; thick
19.Expectoration; lumpy	20.Expectoration; balls, in shape of
21.Respiration; difficult; exertion, after	

The prescription of the selected medicine started with 30CH potency, in a single dose (four pills of globule No. 30) followed by placebo (four pills of unmedicated globules No. 30), daily. Follow up was weekly for the 1st month, fortnightly for the next 2 months and monthly for the remaining period until completion of 24 months. On each of these visits, clinical assessment was done by the investigator. Spirometry was performed at the time of enrollment, at every 3rd month till 24 months.

In case there was no perceptible change after one week of administration of the indicated medicine, one more dose of the same medicine was repeated in higher potency. If no improvement was found even after adequate repetition of the medicine in higher potencies, the investigator was allowed to change the prescription. All patients were advised for avoidance of smoking, dust and air pollution. Patients were advised for intake of nutritious diet and to do routine physical exercise as a part of general management. Patients were free to report at any time during adverse events or emergency situations. Any change (improvement/deterioration) triggered by administration of placebo or change in potency (from 30C to 200C or 1M) or change in remedy was managed by following the guidelines of Hahnemann [21] and Kent [22]. The guidelines were:

- i. If improvement continues (score is reduced) → Placebo to continue.
- ii. If improvement stops (same score) → repeat the medicine (first prescription) in the same potency.

- iii. If no further amelioration occurs even after medicine is given in same potency or improvement lasts for a very short period → to give higher potency of same medicine.
- iv. If amelioration of presenting complaints is accompanied by appearance of old symptoms → to continue placebo, till the improvement continues.
- v. If old symptoms come back to stay → same medicine in same potency to be repeated and then followed as in (iii) above. In case there was no perceptible improvement after adequate repetition of medicine in different potencies, change of medicine was to be considered.

In case of acute exacerbation of CB or any other acute disease condition, the medicine selected was either a continuation of the pre-selected medicine, or one of the better indicated trial medicines. This medicine was prescribed repeatedly as per intensity of the acute exacerbation.

Outcome assessment

The symptoms and signs of the enrolled patients were rated by the investigators using Chronic Bronchitis Symptom Scale (CBSS) at baseline and follow-up visits at every 3 months up to 2 years (Table 3). This scale was developed by the Council and approved by a group of experts for its content and consistency to assess the symptoms of enrolled patients. Evaluation of each subjective symptom in terms of score was done by attributing "0" score to no symptom, and 1, 2, 3, 4, ranking was made for different degrees of intensity of each symptom. The intensity of the disease at baseline was classified and graded into 3 categories. Mild (CBS score 10 to 15); Moderate (CBS score 16 to 31) and Severe (CBS score 32 to 40). The FEV₁ and FEV₁/ FVC ratio was also estimated at baseline and at time points of 3, 6, 9, 12, 15, 18, 21, and 24 months.

Further outcome in terms of percentage was also calculated as follows:

$$\text{Outcome} = \frac{\text{Baseline score} - \text{Score at end}}{\text{Baseline score}} \times 100$$

Changes were graded as:

- Marked improvement (75% to < 100%),
- Moderate improvement (50% to < 75%),
- Mild improvement (25% to < 50%),
- Not significant improvement (< 25%),
- Static (no change), and
- worse (increase in CBSS).

Statistical analysis

Statistical analysis was done using IBM Statistical Package for Social Sciences, version 20, based on intention to treat approach: The last value for those patients who dropped out, was carried forward for analysis. Data were analyzed using parametric/non-parametric statistical tools depending on the nature of the data. Therefore, dispersion is represented with mean ± SD, mean change (SE) with 95% CI. Repeated measure of ANOVA was used to assess the outcome at different time points up to 24 months. Standardized effects (d) were calculated by dividing Treatment effects as estimated above by baseline Standard deviations. They were classified: as |d| > 0.8, large; |d| > 0.5, medium; |d| > 0.2, small [23]. P value < 0.05 was considered as significant.

Table 2 - Repertorization chart (using complete repertory)

Drug	Stann	Ars	Sil	Phos	Lyc	Puls	Calc	Sulph	Hep	Ip	Bry	Caust	Ant-t	Carb-v	Dulc	Spong	Dros	Chin
Score	40/ 16	36 / 15	35 / 17	34/ 14	29 / 14	29/ 14	25/ 11	24/ 18	22/ 11	20 / 12	20 / 11	20/ 9	19/ 12	19/ 11	17/ 10	17/ 9	17/ 8	16/ 8
01	3	3	3	3	3	3	2	2	3	3	3	2	3	2	2	3	3	3
02	0	0	1	2	1	1	0	1	0	0	0	0	2	0	1	2	2	0
03	3	3	3	3	1	0	3	3	0	0	2	3	0	3	3	0	0	0
04	2	1	0	0	0	0	0	0	0	1	1	0	1	0	1	0	0	0
05	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
06	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0
07	2	0	1	0	1	2	0	1	1	0	0	0	0	0	0	0	0	0
08	3	3	2	3	2	0	1	1	2	3	1	2	3	2	0	1	3	1
09	3	3	3	3	3	3	3	1	3	1	3	3	2	2	3	2	3	3
10	0	3	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	3
11	0	3	1	2	0	2	1	1	1	1	1	0	1	0	0	0	1	0
12	3	0	1	0	0	2	0	1	1	1	0	0	1	1	1	0	0	0
13	2	2	2	3	0	1	0	1	0	0	1	2	1	0	0	0	0	1
14	2	2	1	3	3	2	2	2	0	1	1	2	1	2	1	2	0	1
15	2	2	3	3	3	2	3	1	1	1	1	0	2	1	1	0	2	3
16	3	2	0	2	2	3	2	1	2	3	1	3	1	0	2	1	1	1
17	3	2	3	3	3	3	3	2	3	1	2	1	0	2	0	2	2	0
18	2	2	3	1	2	2	2	1	3	1	1	2	1	1	2	0	0	0
19	2	2	3	1	1	1	0	1	2	0	1	0	0	1	0	1	0	0
20	3	0	2	0	1	0	0	1	0	0	0	0	0	0	0	0	0	0
21	2	3	2	2	3	2	3	2	0	3	0	0	0	2	0	3	0	0

Table 3 - The chronic bronchitis symptom scale(CBSS)

Symptoms	Score				
	0	1	2	3	4
Chronic Cough	Absent		Present		
Severity		Mild (irritating)	Moderate (distressing)		Severe (spasmodic)
Paroxysms [duration]	Nil	1 hour to less than 6 hours	6 hours to less than 12 hours	12 hours to less than 18 hours	18 hours to less than 24 hours
Expectoration					
Expectoration	Absent	1 hr. to 6 hrs.	6 hrs. to 12 hrs.	12 hrs. to 18 hrs.	18 hrs. to 24 hrs.
Difficulty in raising		Easy		Difficult	
Quantity		Scanty		Copious	
Quality		Thin		Thick	Lumpy / in shape of balls
Quality-1		Mucoid	Frothy		Purulent
Quality-2		Transparent / Translucent	White	Yellow	Greenish
Difficult respiration	Absent		Present		
	Absent	Heavy exertion		Mild exertion	With cough
Crackles	Absent		Present		
Total					
Total of symptom score: ----[10-40]					
Intensity of disease - MILD: 10 to 15 MODERATE: 16 to 31 SEVERE: 32 to 40					

Results

A total of 597 patients were enrolled in the study from seven centres . Out of these, 109 patients were lost to follow up at different time points. Data of 65 patients who dropped out could not be traced. Therefore this paper reflects the ITT analysis of 532 patients suffering from SMCB. Figure 1 shows the flow of patients throughout the study. The study population (n= 532) consisted of 321 males, 211 females with average age of 34.1 years $\pm$ 8.6 years. Out of 321 males, 60 (11%) were smokers. The baseline characteristics of the patients are given in table 4.

Figure 1 - Flow of patients throughout the study

Table 4 - Baseline information of 532 analyzed patients

Baseline data	n (%) / Mean $\pm$ sd
Chennai	174 (32.7)
Puducherry	159 (29.9)
Guwahati	24 (4.5)
Kottayam	24 (4.5)
Noida	24 (4.5)
Age in Yrs.	34.1 $\pm$ 8.6
Male	321 (60.3), 34.01 $\pm$ 8.3
Female	211 (39.7), 34.44 $\pm$ 8.5
Smoking present	60(11)
Cough severity	
Mild	41 (7.7)
Moderate	133 (25)
Severe	358 (67.3)
Paroxysms	
1 hour to 6 hours	152(28.6)
6 hours to 12 hours	250(47)
12 hours to 18 hours	88(16.5)
18 hours to 24 hours	32(6)
raising	
Easy	118 (22.2)
Difficult	414 (77.8)
expectoration(Quantity)	
scanty	93 (17.5)
copious	439 (82.5)
sputum(Quality)	
Thin	44 (8.3)
Thick	285 (52.6)
Lumpy/In Shape of Balls	203 (38.2)
Sputum - (Quality)	
Mucoid	170 (32)
Frothy	139 (26.1)
Purulent	223 (41.9)
Sputum Quality-(color)	
Transparent	11 (2.1)
White	234 (44)
Yellow	257(48.3)
Greenish	30 (5.6)
Difficult Respiration	527 (99.1)
Crackles Present	526 (98.9)
CBSS	29.8 $\pm$ 4.5

CBSS gradation	
Mild	1(0.2)
Moderate	297 (55.8);
Severe	234(44)
FEV1	94.12±13.6
FEV1/FVC ratio	1.64±0.92

Effect on SMCB symptoms

The mean CBS score at baseline was 29.86 ± 4.5 and reduced to 12.33 ± 7.6 at completion of 2 years. Repeated measures ANOVA, during the two-year treatment period, at time points 0(baseline), 3, 6, 9, 12, 15, 18, 21 and 24 months, showed significant reduction in CBS scores [Wilk's Lambda 0.104, $F=564$, $df\ 524$; $p=00001$]. Figure 2 shows the trend in scores at different time points. Post hoc paired t test also showed significant difference at 24 months compared to baseline. The Effect size as mentioned by cohen was calculated. There is a significant effect of homeopathic medicines on SMCB patients at 3 months ($Mdn = 4$, $Z = 20.2$, $r = 0.6$, $P < 0.001$) which was maintained up to 24th month ($Mdn = 3$, $Z = 20.32$, $r = 0.6$, $P < 0.001$ (Table 5). It was observed that homeopathic treatment based on individualization has large effect size which was maintained upto 24th month of treatment. Most of the patients belonged to moderate (55.8%) and severe intensity (44%) of CB as per the CBSS at baseline. Overall, marked improvement was observed in 176 patients (33.1%), moderate improvement in 213 patients (40%), mild improvement in 63 patients (11.8%), no significant improvement in 52 patients (9.8%), status quo in 20(3.8%), and worsening in 8(1.5%) patients. The category wise outcome as per the CBS score is given in figure 3.

Figure 2 - Trend line showing mean CBS scores at different time points with 95% Error bars

Table 5 - Outcome at different time points of 24 months

Variable	At baseline (0 month)	3 months	6 months	12 months	24 months	0-3	0-6	0-12	0-24
		Mean change (SE);95% CI				Cohen's d			
Total CBSS	29.9±4.5	11.4(0.3); 10-8, 12.0	13.9(0.3); 13.2, 14.5	17.1(0.3); 16.5, 17.7	17.5(0.3); 16.8, 18.2	1.84	2.24	3.04	2.81
• Mild (n=1)*	15.0± 0.0	-	-	-	-				-
• Moderate (n=297)	26.9±3.6	10.8 (0.4); 10.0, 11.5	12.8 (0.4); 12.0, 13.7	15.6 (0.4); 14.8, 16.4	15.9 (0.4); 15.1, 16.7	2.10	2.39	3.23	3.07
• Severe (n=234)	33.7±1.6	12.3 (0.5); 11.3, 13.4	15.4 (0.5); 14.3, 16.4	19.2 (0.5); 18.3, 20.1	19.7 (0.6); 18.6, 20.8	2.08	2.65	3.73	3.17
FEV ₁	94.13±13.61	1.6 (0.5); 0.6, 2.6	2.3 (0.7); 1.0, 3.6	0.5 (0.7); -0.9, 1.8	-2.5 (0.8); -4.0, -1.0	0.11	0.14	0.03	0.16
FEV ₁ /FVC ratio	1.65±0.93	0.01 (0.004); -0.0003, 0.02	-0.006 (0.02); -0.04, 0.02	-0.05 (0.02); -0.09, -0.01	-0.07 (0.01); -0.10, -0.04	0.011	0.010	0.050	0.07

*only one patient was in mild category, so no analysis could be performed.

Figure 3 - Outcome of patients according to severity as per the gradation of total CBS score.

Effect on spirometry test

The mean FEV_1/FVC of 1.6 ± 0.9 at baseline was maintained at time points 3, 6, 9, 12, 15, 18, 21 and 24 months respectively. A scattered plot drawn depicting difference of total CBS scores (0 -24 months) and difference of FEV_1 , FEV_1/FVC (24 -0 months) showed statistically significant positive correlation (Figure 4, 5). The FEV_1 and FEV_1/FVC was maintained within normal limits throughout the study period showing effect of homeopathic medicines in SMCB.

Figure 4 - Correlation CBS score and FEV_1

Figure 5 - Correlation CBS score and FEV_1/FVC

Homeopathic medicines prescribed

The 14 pre defined medicines, which were prescribed as per the descending order are: *Lycopodium* (n=168; 31.6%), *Arsenicum album* (n=93; 17.5%), *Pulsatilla* (n=83; 15.6%), *Phosphorus* (n=53; 10.05%), *Stannum metallicum* (n=41; 7.7%), *Calcarea carbonica* (n=24; 4.5%), *Silicea* (n=19; 3.6%), *Bryonia* (n=12; 2.3%), *Antimonium tartaricum* (n=9; 1.7%), *Sulphur* (n=8; 1.5%), *Hepar sulph.* (n=7; 1.3%), *Spongia* (n=7; 1.3%), *Ipecacuanha* (n=6; 1.1%), *Carbo vegetabilis* (n=2; 0.4%).

Discussion

This is a cohort study with two years follow up wherein patients in early years of chronic bronchitis without any pathological changes i.e. changes in the FEV₁ and FEV₁/FVC ratio, were evaluated to assess symptomatic improvement with pre-defined homeopathic medicines. Data of 532 patients with SMCB was analyzed. Using the 14 pre-defined homeopathic medicines, the results showed a positive role of homeopathic medicines in the management of symptoms of SMCB and maintaining the levels of FEV₁/FVC within normal limits. The mean CBS score of 29.75 was reduced to 12.3 during 24 months of treatment.

The males were predominantly affected than the females. This is consistent with epidemiological data on chronic bronchitis showing predilection in males compared to females [24].

86% of the prescriptions were covered by the 6 high scoring trial medicines *Lycopodium*, *Arsenicum album*, *Pulsatilla*, *Phosphorus*, *Stannum metallicum*, and *Calcarea carbonica*. Frass *et al* [17] had conducted a study on 50 critically ill patients of COPD with a history of tobacco use. Their primary outcome was on the amount of tenacious, stringy tracheal secretions. The intervention group was given Potassium dichromate 30C (*Kali bichromicum* 30C). The amount of tracheal secretions was reduced significantly in intervention group ($p < 0.0001$). Extubation could be performed significantly earlier in group 1 ($p < 0.0001$). Further, in the said study length of stay was significantly shorter in intervention group (4.20 ± 1.61 days vs 7.68 ± 3.60 days, $p < 0.0001$ [mean $\pm$ SD]). However, *Kali bichromicum* was not prescribed in our study as this drug was not enlisted under 14 pre- defined medicines.

There is still no consensus definition of “early” COPD. Therefore, the treatment of early COPD with inhalers is also questionable. Enright in his paper [25] quoted that “There is limited and conflicting evidence of health benefits from initiation of inhaled bronchodilators (anticholinergics or long-acting beta-agonists) in symptomatic patients with FEV₁ between 60% - 80% predicted as documented by spirometry”. However, GOLD statement [1] clearly mentions that use of short acting bronchodilators is not recommended. Further the same statement also conveys that there is no conclusive clinical trial evidence that any existing medications for COPD modify the long-term decline in lung function. Homeopathic intervention if used as per the outcomes observed in this study may help in managing the symptoms of SMCB in its early years and with no side effects.

In the absence of control arm, there is always chance of over-estimation of treatment effect sizes. This may be attributable to placebo effect; regression effect to the mean. Another, limitation was the absence of pre-validated scale to measure the improvement. We developed a scoring scale (CBSS), however, its validity and reliability remained untested. Though our study has several biases, it has

scope too. This present study describes patients with varying lifestyles and socio-economic background, with high degree of external validity that extends to usual medical practice. These results certainly contribute to the growing evidence that homeopathy is a safe and beneficial treatment strategy for chronic diseases in primary care settings.

Conclusion

The results of this study show beneficial effects of homeopathic medicines using a treatment plan with 14 pre-selected homeopathic medicines in patients of simple and muco-purulent chronic bronchitis. There was a positive correlation between CBS score and spirometry findings up to two years. Further studies with controlled study designs under different setting are warranted.

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Conflict of interest - We declare no conflict of interest.

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