ROLE OF HOMOEOPATHY IN THE MANAGEMENT OF BRONCHIAL ASTHMA: AN OPEN-LABEL INTERVENTIONAL UNCONTROLLED STUDY BASED ON SPIROMETRY EVIDENCE

Sharma Vanija[1*], Master Farokh J.[2], Jain Tarkeshwar[3] and Jaiswal Prastuti[4]

[1]Principal Investigator, Assistant Prof., Dept. of Materia Medica and Dy. Ph.D. Co-Ordinator, Homoeopathy University, Jaipur, Rajasthan, India.

[2]Ph.D. Research Supervisor, Visiting Prof., Dept. of Materia Medica, Homoeopathy University, Jaipur, Rajasthan, India.

[3]Ph.D. Research Co-Supervisor, HOD of Materia Medica and Registrar, Homoeopathy University, Jaipur, Rajasthan, India.

[4]PG Resident, Dept. of Materia Medica, Homoeopathy University, Jaipur, Rajasthan, India.

*Corresponding Author
Dr. Vanija Sharma
Principal Investigator,
Assistant Prof., Dept. of
Materia Medica and Dy.
Ph.D. Co-Ordinator,
Homoeopathy University,
Jaipur, Rajasthan, India.

ABSTRACT

Asthma is a common, chronic respiratory disease affecting 1-18% of the population in different countries, defined by the history of respiratory symptoms such as wheeze, shortness of breath, chest tightness and cough that vary over time and in intensity, together with variable expiratory airflow limitation. This was an open-label experimental uncontrolled evidence based study conducted over 45 patients for period of one and half year at outpatient department of Homoeopathy University, Jaipur. Change in Spirometry values (FEV1) was used as the major evidence for assessing the effect of Homoeopathic remedies. Observing the no. of patients shifting from off- target cases to on- target cases through analyzing the ACT score was another measure to assess the effectiveness of treatment used.

After statistical analysis of data it was found that $p = 0.000$ and Effect size "r" (Cliff's delta) = 0.617 for the average changes in the Asthma Control Test after individualized homoeopathic treatment where 100% were off-target before treatment and only 40% after treatment, consequently 0% on-target before treatment and 60% after treatment. Statistically significant difference in FEV1 on an average is 20.11 ± 11.53 with a change in SD from 8.34 before treatment to 15.77 after treatment. One Way ANOVA shows p value 2.77E-11.

Cohen's $f2$ value is 0.459 reflects large and consistent effect on improvement of FEV1 clinically as well. The value of Spearman's Rho Coefficient (r) which is 0.83 representing the positive correlation between FEV1 and Asthma Control Test Score. Out of 45 patients, 27 observed marked improvement in Spirometry readings and ACT score. Life functioning and quality was much better after treatment. Study reveals positive role of Constitutional medicines and intercurrent remedies in the difficult cases of asthma and also the constraints of the study e.g. being a short duration trial in the OPD of rural area it lacks the information regarding socio-economic status associated with asthma, more important remedies with their specific potencies in asthma treatment, remedies for managing acute exacerbations, etc.

KEYWORDS: Bronchial asthma, Homoeopathy, Spirometry, Asthma Control Test, $FEV_{1.}$

INTRODUCTION

Asthma is a common, chronic respiratory disease affecting 1-18% of the population in different countries. More recently, studies of the epidemiology, natural history, and pathogenesis have clearly demonstrated that asthma is a heterogeneous disease, with multiple etiologies and contributing cofactors, complex pathobiologic mechanisms, and different molecular phenotypes usually characterized by chronic airway inflammation. It is defined by the history of respiratory symptoms such as wheeze, shortness of breath, chest tightness and cough that vary over time and in intensity, together with variable expiratory airflow limitation.[1,2]

Since asthma is a chronic condition, in conventional system of medicine, it usually requires continuous medical care. Patients with moderate to severe asthma have to take long-term medication daily (for example, anti-inflammatory drugs) to control the underlying inflammation and prevent symptoms and attacks or, short-term medications (inhaled short-acting beta2-agonists) are used to relieve them. It is also important to avoid asthma triggers - stimuli that irritate and inflame the airways.[3]

According to GINA (Global initiative for asthma), there is a limited role of complementary and alternative medicine in which they also include Homoeopathy, for the treatment of asthma because the approaches have been insufficiently researched and effectiveness is largely unproven.[4] Homoeopathy is lacking in an evidence based clinical trial in this field, but the proving records of Homoeopathic medicines in source books and many recent researches published in Homoeopathic journals provide a firm background that Homoeopathy

has a better answer for asthma treatment. This study was taken with intent to affirm the efficiency of Homoeopathic intervention on the basis of universally accepted criteria in the management of Bronchial Asthma using Spirometry evidence before, during and after the treatment and self-assessment of asthma status by applying Asthma Control Test (ACT). ACT is a commonly used Numerical asthma control tool in clinical research which provides sores and cut points to distinguish different levels of symptom control, validated against health care provider assessment.[1] It is a patient self-administered tool for identifying those with poorly controlled asthma. Five items, with 4-week recall (on symptoms and daily functioning). ACT assesses the frequency of shortness of breath and general asthma symptoms, use of rescue medications, the effect of asthma on daily functioning, and overall self-assessment of asthma control. The scores range from 5 (poor control of asthma) to 25 (complete control of asthma), with higher scores reflecting greater asthma control.[1]

Spirometry is a physiological test that measures how an individual inhales or exhales volumes of air as a function of time. The primary signal measured in spirometry may be volume or flow. The FEV1, derived from spirometry, is the most reproducible pulmonary function parameter and is linearly related to the severity of airways obstruction.[5] The post-bronchodilator FEV1 measures the best lung function that can be achieved by bronchodilator therapy on the day of the visit and therefore is a more stable measure in asthmatics than comparing visit-to-visit baseline FEV1 a positive acute response to bronchodilator helps to confirm the diagnosis of asthma.[6]

MATERIALS AND METHODS

Study Setting: Study was conducted at OPD of Homoeopathy University, Saipura-Sanganer, Jaipur.. Medicines were dispensed from OPD dispensary. Investigations (spirometry, blood analysis etc.) have been done by the technically latest equipments e.g. computerized spirometer available in the laboratory of OPD by trained staff.

Study Duration: Duration of the study was from March, 2014 to November, 2015 i.e. 21 months including 3 months for data analysis and interpretation of results. All the patients were instructed to report at the project site after every 15 days interval during the treatment for follow-up visit.

Study Design: Interventional, Single arm, open -label study.

Selection of samples: Total 67 patients of every age (except children up to 6 years of age), gender, locality and socio-economic status were enrolled for the study out of which 45 were randomly selected for the analysis of observations.

Inclusion Criteria

- Cases of every age (except children below 6 years of age), both sexes and different occupations have been included in the study.

- Already diagnosed cases on the basis of family/medical history (allergic disorder), sign and symptoms of asthma, Spirometry and blood analysis (eosinophil count) who are taking treatment from other system of medicine with no relief and seeking for Homoeopathic treatment.

- Undiagnosed cases of suspected asthma having specific medical/family history along with signs and symptoms of asthma (dyspnoea, night waking due to difficult breathing, chest tightness, wheezing respiration, cough and wheezing sounds on auscultation) advised for investigation; seeking for Homoeopathic treatment.

Exclusion Criteria

Patients with negative results of advised investigations for confirmation of asthma instead having other respiratory/pulmonary ailment, patients who do not continue with treatment up to 4-6 visits will be dropped out of the study, patients with acute severe asthma or status asthmaticus, patients with cardiac, pulmonary or any other systemic diseases and pregnant ladies, patients below 6 years of age have not been included in study, patients who do not gave consent for the study were excluded from the study.

Diagnostic Criteria: Clinical / physical examination revealing relevant medical or family history with most common symptoms of asthma(dyspnoea, night waking due to difficult breathing, chest tightness, wheezing sounds while breathing, cough etc.) and wheezing sounds on auscultation. Laboratory investigations- Diagnostic Spirometry (FEV1< 80% of predicted value and positive reversibility test i.e. increase in 12% pred or more after Short acting beta 2 agonist (SABA) administration. Blood analysis (blood count) if necessary.[1]

Criteria for Results of Treatment/Outcome Assessment

Fixed parameters for the asthma control assessment are employed i.e.:

- ACT (Asthma Control Test) score before, during and after treatment with a minimum interval of 4 weeks between two tests. A self assessment questionnaire form is attached

with each case taking proforma to calculate the ACT score subsequently the change in score after treatment.

- Measurement of Lung functions- FEV1 (Spirometry) before, during and after treatment at a minimum interval of 30 days to assess the change in reading.

Statistically authenticated changes in ACT score in synchronization with changes in FEV1 readings are the basis of assessing the effectiveness of Homoeopathic intervention.[1]

Intervention: Medicines were selected on the basis of proper analysis and evaluation of the case, framing the totality of symptoms which indicate the individuality of the patient. Selection of dose and potency was according to susceptibility of the patient. Medicines of authentic pharmacies i.e. RW/WSI/SBL have been dispensed from the OPD of the University, which are manufacturing medicines under GMP regulations.

Data Collection and assessment: A case taking proforma is especially designed for the study according to Homoeopathic system with special reference to ACT. The whole data were kept confidential stored in the win zip programme of RADAR repertorisation software (Radar Opus version 1.35, Build: 11; Archibel, Belgium. Last Updated: Jan 2014) Data-sheet have been made on the Microsoft office excel worksheet for further analysis.

Data Analysis: Analysis has been done by data sorting method, classification by tabulation and presentation by histograms. Statistical methods such as calculation of mean, Standard Deviation, Standard error of mean and various statistical tests like Wilcoxon Signed Rank Test, One Way ANOVA etc. have been employed to find out the Significance.

Ethical Clearance: Informed consent form was specially designed to obtain the consent of patients for participation in the study. Ethical clearance was obtained from the Institutional Ethics Committee of the University.

RESULTS

Study was conducted for a period of 21 months at the outpatient department of Homoeopathy University. A total number of 67 patients were enrolled out of which 45 patients were randomly selected for the analysis who were in accordance to pre-defined inclusion and exclusion criteria. This study has patient enrollment from the age as low as 8 years to highest age of 76 years. As evident from Table 1, mean age group of male patients suffering from bronchial asthma is 41.62 (SD=19.89) while mean age group of female patient suffering from

Asthma is 30.09 (SD=19.86). Maximum number of patients were in the age group of 41-50 years that is 22%. Mean duration in male patients suffering from asthma was 7.14 (SD=9.65) while in females it was 5 (SD= 7.07). The average spirometry FEV1 in male patients was 49.88 ± 8.55 while in female patients it was 49.90 ± 7.63; the distribution pattern is normal. The median ACT score is 16 before treatment. For the Assumption for Homoscedasticity the Welch''s t-test and Levene's t-test were applied and significant p values were observed which means in this study we can apply the results on both genders equally. Study includes 24% female and 76% male population suffering from bronchial asthma.

Table 1: Showing gender wise distribution pattern.

	Male (n = 34)		Female (n = 11)		Assumption for Homoscedasticity
	Mean ($\bar{x}$)	SD (s)	Mean ($\bar{x}$)	SD (s)	
Age (In years)	41.61	19.89	30.09	19.86	$p = 0.11*$
Duration of Asthma (In years)	7.14	9.65	5	6.07	$p = 0.39*$
Spirometry (FEV$_1$)	49.88	8.55	49.90	7.63	$p = 0.99*$
	Median		Median		
ACT Total Score	16		14		$p = 0.59**$

*Welch''s t – test applied. Significant if $p < 0.05$

**Levene''s test applied. Significant if $p < 0.05$

Table. 2 shows the average change in ACT after individualized Homoeopathic treatment shows that ACT score before treatment was 689 which increased significantly to the level of 887 remarking the change in score 198. On statistical application of Wilcoxon Signed - Ranked test, significant p value was observed. Median ACT score before treatment was 16 which increased to 21 post treatment. Patient's asthma status was 24% improved. [Effect size "r"(Cliff delta) = 0.617] which shows that Homoeopathic effect was large and consistent.

Table 2: Average changes in the Asthma Control Test after individualized homoeopathic treatment.

ASTHMA CONTROL TEST SCORE	BEFORE Rx	AFTER Rx	CHANGE IN SCORE	STATISTICALLY SIGNIFICANT
Total Score	689	887	-198	$p = 0.000*$
Median	16	21	-5	

*Wilcoxon Signed – Rank test applied. Significant if $p < 0.05$

In Figure 1, a box plot shows that before treatment 2/3 area of the box was with ACT score range 14-16 which was enhanced after treatment up to 3/4 area with ACT score range 18-21. It may be considered as a positive shift after Homoeopathic treatment.
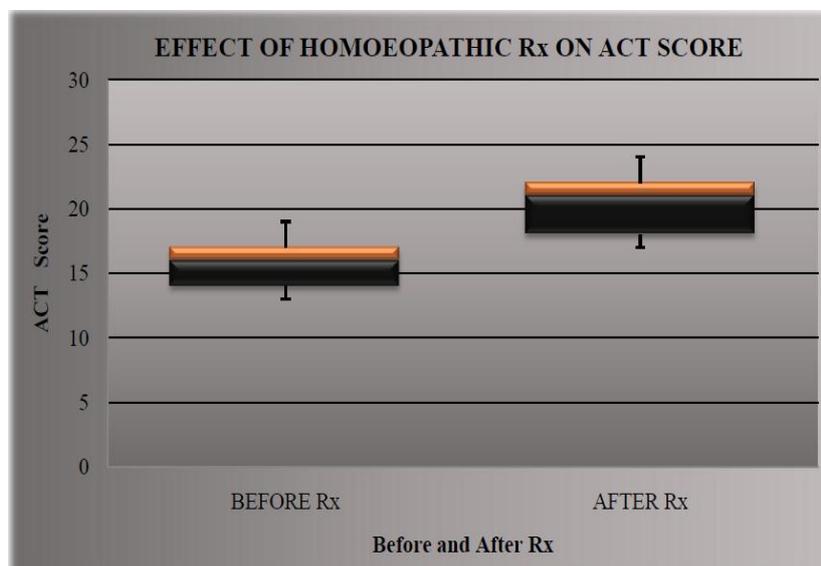
Fig.1. Box plot representing the effect of Homoeopathic Rx on Overall Asthma Control.

Table 3 represents the effect of individualized Homoeopathic treatment on overall asthma control. 100% were off-target before treatment and only 40% after treatment, consequently 0% on-target before treatment and 60% after treatment which means out of 45 patients, 27 patients (60%) experienced significant control on their asthma symptoms while 18 patients (40%) were either partially controlled or remained uncontrolled.

Table 3: Table representing the effect of individualized Homoeopathic Rx on Overall Asthma Control.

	OFF Target (Partially controlled or Uncontrolled)	ON Target (Well Control)
Before Treatment	45 (100%)	0
After Treatment	18 (40%)	27 (60%)

Out of 45 patients, 34 patients (76%) had change in ACT score more than 3 points while only 11 patients (24%) had change in ACT score less than 3. Recalling the fact that a minimum change of 3 points in the ACT score is considered to be clinically significant, we may assume

that a large no. of patients (76%) are benefitted while 24% did not show any significant change after treatment.

Daily functioning, shortness of breath, general asthma symptoms, use of rescue medicines and overall self-assessment of Asthma control were the main parameters of ACT.
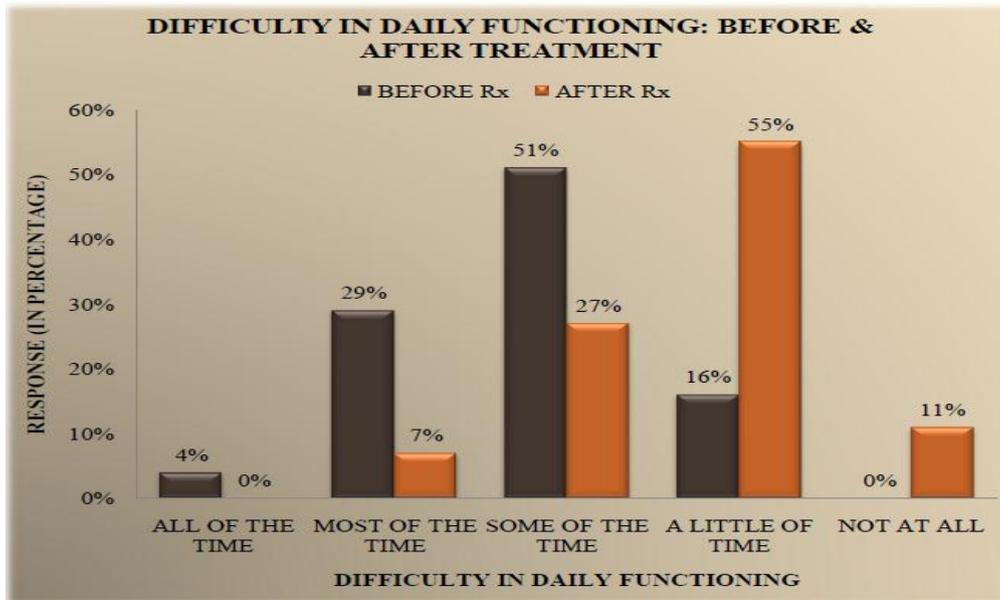

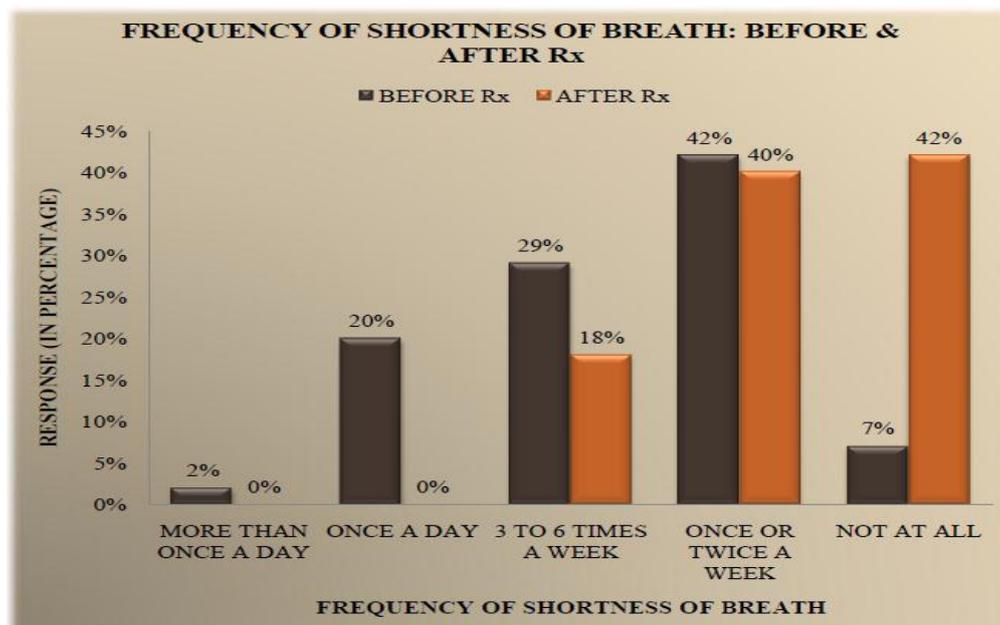**Figure 2: Comparative Bar Graph represents the effect of Homoeopathic Rx on difficulty in Daily Functioning.**

Figure 3: Comparative Bar Graph represents the effect of Homoeopathic Rx on frequency of shortness of breath.
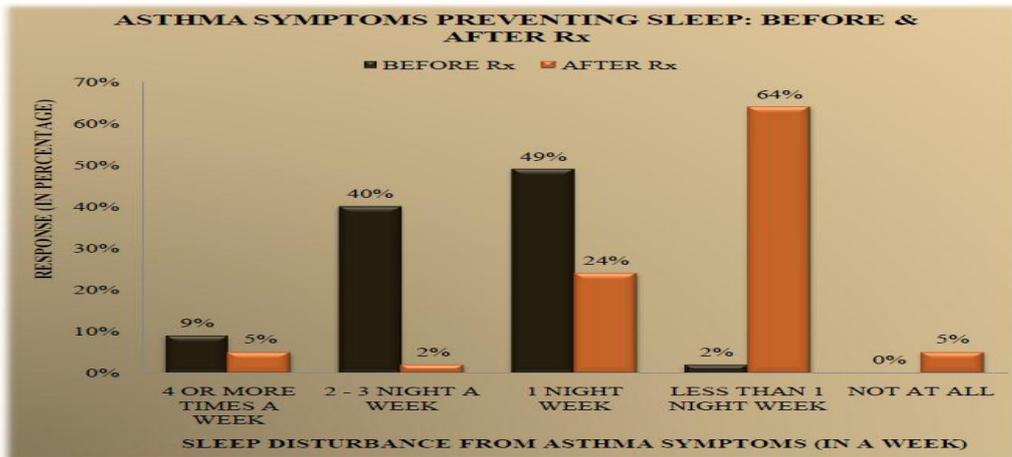
Figure 4: Comparative Bar Graph represents the effect of Homoeopathic Rx on Asthma symptoms preventing sleep.
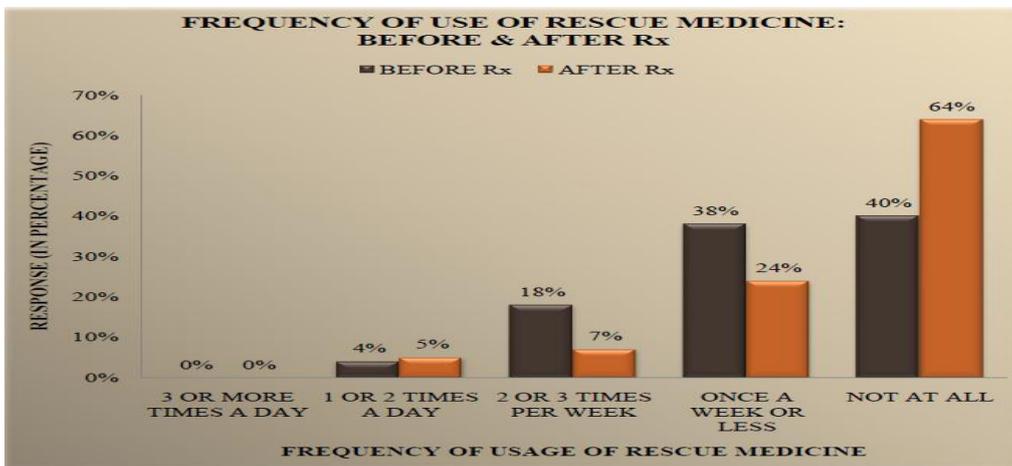

Figure 5: Comparative Bar Graph represents the effect of Homoeopathic Rx on Use of rescue medications during course of Homoeopathic Rx.
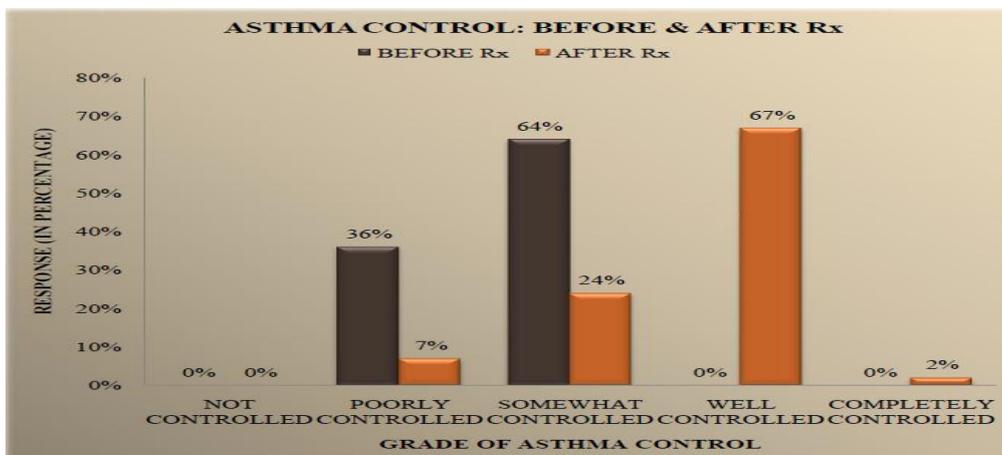

Figure 6: Comparative Bar Graph represents the effect of Homoeopathic Rx on Asthma control (Self assessment by patient).

After application of Homoeopathic remedies, 11% patients had no difficulty at all in their daily functioning (Fig.2) 55% patients experienced a little of difficulty in functioning while only 16% patients were there in this category before treatment, 51% patients were experiencing difficult functioning some of time before treatment and the number reduced to 27% post treatment, 29% patients had difficulty most of the time while only 7% patients were there in this segment after treatment, no patient was with difficult functioning all of the time. 42% patients had no shortness of breath (Fig.3) at all after treatment in comparison to just 7% patients in this category before treatment. 40% experienced once or twice after treatment while 42% patients were earlier in this category. 18% had shortness of breath 3 to 6 times a week in comparison to 29% patients earlier in this category before treatment. 20% patients experienced shortness of breath once a day while 2% were having this problem more than once a day. After treatment, 5% patient had no sleep disturbance (Fig.4) at all, while 64% woke up less than one night a week due to asthma attack, 24% woke once a week which was 49% before the treatment, 40% were having disturbed sleep 2-3 times a night before treatment which remained only 2% after treatment, 5% had disturbed sleep 4 or more times a week and earlier this percentage was 9%. There was significant shift in the frequency of using rescue measures (Fig.5) before and after homoeopathy. 64% patient required no rescue measures while earlier percentage in this category was 40%. There were only 24% patients in the category of once a week or less in comparison to before treatment group of 38%. Only 7% required rescue measures 2 or 3 time per week while earlier this percentage was 18%. There was little change in the percentage of 1 or two times day as earlier also it was 4% and after treatment it was 5%. Fig.6 represents the patient self-assessment on effect of Homoeopathic medicine for controlling asthma. 2% patients reported of total control on asthma while 67% informed about well control on asthma symptoms. Percentile value in somewhat controlled and poorly controlled also decreased from 64% to 24% and 36% to 7% respectively. There was no patient in No control category.

Table 4: Average changes in the Asthma Control Test parameters after individualized homoeopathic treatment.

SR. NO.	DOMAIN	BEFORE Rx (Median)	AFTER Rx (Median)	STATISTICAL INTERPRETATION
1	Daily Functioning	3	4	$p = 0.000*$
2	Shortness of Breath	3	4	$p = 0.000*$
3	General Asthma Symptoms	3	4	$p = 0.000*$
4	Use of Rescue Medicine	4	5	$p = 0.00044*$
5	Over all self assessment of Asthma control	3	4	$p = 0.000*$

Wilcoxon signed- rank test displayed significant p values denoting the remarkable positive changes after application of individualized Homoeopathic treatment which is also visible by the mean values of each parameter in Table 4 before and after treatment.

Table 5: Tabular representation shows the qualitative changes in the Asthma Control Test before & after individualized homoeopathic treatment.

SR. NO.	DOMAIN	DETERIORATE IN GRADE	SAME GRADE	IMPROVED IN GRADE
1	Difficulty in Daily Functioning	0	10 (22%)	35 (78%)
2	Frequency of Shortness of Breath	0	14 (31%)	31 (69%)
3	Frequency of Asthma Symptoms	0	7 (16%)	38 (84%)
4	Frequency of usage of rescue medication	0	29 (64%)	16 (36%)
5	Asthma control	0	10 (22%)	35 (78%)

Table 5 represents the qualitative changes in the asthma control test before and after individualized Homoeopathic treatment. It was observed that 78% had improvement in difficulty in daily functioning while only 22% remained same, 69% had improved in shortness of breath in while in 31% problem still persisted, frequency of asthma symptoms preventing sleep was better in 84% patients in comparison to 16% in whom problem remained same, in 36% patients need for rescue medication reduced in comparison to 64% patients who still required rescue medication, asthma control was effective in 78% patients while 22% patients remained in status quo category.

Mean FEV1 before treatment was 49.82, during treatment it was 60.73 while after treatment it has increased to the level of 69.93. Standard deviation before treatment was 8.34, during treatment it was 12.13 and after treatment it was 15.77. Fig. 7 shows the positive changes in

FEV1 before, during and after Homoeopathic treatment. It is clearly perceptible that after individualized Homoeopathic treatment, average FEV1 increases from 49.82 to 69.93.
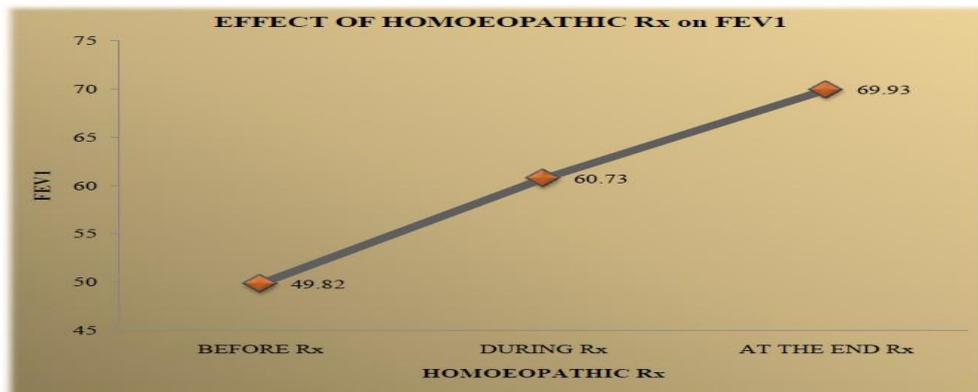
Fig.7: Frequency Polygon representing the effect of Individualized Homoeopathic Rx on Spirometry – FEV1.

One Way ANOVA shows p value 2.77E-11. The calculated F value (29.38) is more than F critical value (3.06). This shows that Individualized Homoeopathic treatment has produced statistically significant difference in FEV1. The improvement in FEV1 on an average is 20.11 ± 11.53. Cohen's $f2$ = 0.459 shows that Homoeopathic Intervention has produced large and consistent effect on improvement of FEV1 clinically as well.
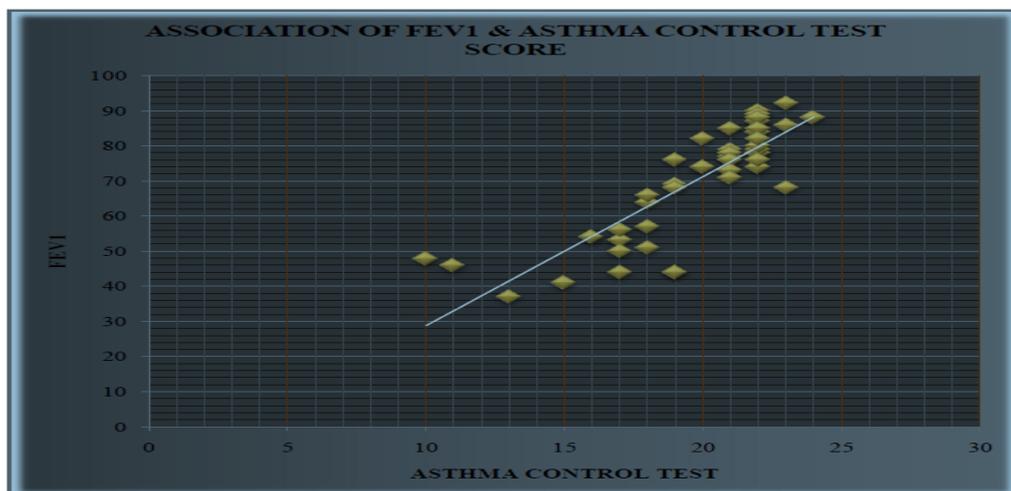
Fig. 8: Scatter plot represents the association between Asthma control test score & Spirometry – FEV1 after Individualized Homoeopathic Rx.

Spearman's Rho Coefficient (r) = 0.83. This represents the positive correlation between FEV1 and Asthma Control Test Score. This interprets that controlled Asthma symptomatically shows improvement in FEV1.

Homoeopathic remedies were applied in all the cases on the basis of symptom similarity. Constitutional remedies used in treatment were Kali Carbonicum (27%), Arsenic Album (13%), Pulsatilla (13%), Nux vomica (11%), Phosphorus (9%), Merc solubulis (9%), Natrium Muriaticum (7%) Spongia (7%) and Calcarea Phosphoricum in (4%) cases. Out of 45 cases, 38 cases (84%) were prescribed only constitutional remedies while in 7 cases (16%), both constitutional and intercurrent remedies were used. Intercurrent remedies were also used in cases where treatment was not furthering or indicated remedies were not giving desirable result. Out of 7 cases Sulphur was used maximally as an intercurrent remedy (43%), Thuja was used in 29% cases, Psorinum was used in 14% cases and Tuberculinum was used in 14% cases.

DISCUSSION

This was an open – label evidence based experimental study conducted over 45 patients out of which maximum number of patients were in the age group of 41-50 years comprising which 76% were male while only 24% females. Out of 45 patients, 27 patients (60%) experienced significant control on their asthma symptoms. In a patient pool of 45, 34 patients (76%) had change in ACT score more than 3 points. Most patients observed significant improvement in daily functioning after treatment. Shortness of breath was minimized as much as 42% patients had no problem at all. 5% patients has no sleep disturbance at all while 64% patients woke less than one night in a week time,. 64% patients required no rescue measures at all after treatment. 2% patients reported total control on their asthma symptoms while 64% patients reported of significant control on their asthma symptoms. There was a positive correlation between Asthma Control Test score and Spirometry readings (FEV1).

Homoeopathic remedies were used on the basis of symptom similarity. Constitutional remedies used in treatment, among which Kali carb was maximally used followed by Ars alb and Pulsatilla. Few intercurrent remedies were also required in difficult cases, Sulphur was used maximally followed by Thuja as intercurrent.

Application of Homoeopathic remedies and their corresponding results reciprocate the literature value of Materia medica and Repertory. In this study, Kali carb was found to be most effective remedy confirming the anecdote of Kent that Kali carb is the most important anti psoric remedy for lung affections.[7,9] If we go through the repertory and Materia medica, Kali carb is a remedy for dry cold weather, hitherto affirming the results as the prevalence area where the research was conducted is mostly dry area with pronounced cold. Similarly for

Arsenic Alb which is the second most used remedy in research also confirms the Materia medica references as this is also a dry cold weather remedy and sensitive to various allergens too. Homoeopathic Materia medica also point out about the time modality of both the drugs which is mostly night/midnight aggravation, in synchronicity of common mode of asthma presentation where sleep disturbance is highly opulent in asthmatics.[7,8,9,10,11]

According to the CCRH report, while Homoeopathic remedies are quiet effective in controlling future risk by ensuring absence of asthma exacerbation, no side effect from medication and prevention of accelerated decline in lung function over time; but unavailability of multicentric, controlled and evidence based studies hinders the path of systematic establishment of efficacy of Homoeopathic intervention. This report also states that most of the studies are observational and based on the symptomatology of the patients but the pathological parameters including PFTs, clinical scores and Quality of Life scores were lacking.[12] This vacuum abridged in our study where an attempt has been made to verify the Homoeopathic effect by taking in consideration the pre, during and post Spirometry (FEV1) readings and changes in ACT (Asthma Control Test) score showing the changes in quality of life in asthmatics. A vital limitation pointed out by CCRH report is genuinely addressed in our study hence raising this study one step ahead from existing work done in the field.

Limitation of the study: It is difficult to draw a fair verdict in terms occupation, social background and habitation of patients suffering from Bronchial asthma. A multi-centric study with inclusion of patients from all segments of society shall be more informative and sharply targeted. In some cases, few acute remedies were also used on emergent situation of cases after predefined follow up period of three month or 6 visits but their results are not included in this study and the specific potencies of the medicines used are also not included in making the analysis and final results because the orientation of this study was to produce the evidences either in favor of or denying the hypothesis. Time span taken for the presented study was sufficient only to generate the pre, during and post Homoeopathic treatment ACT scores and FEV1 readings but not for deriving more specific/precise conclusions about the potencies of medicines used for the treatment.

CONCLUSION

As the present study is a tiny initiative effort in the direction of evidence based studies dealing with Bronchial Asthma through Homoeopathy; the aforesaid summarized detail is

fairly helpful in establishing the significant role of Homoeopathic remedies in managing cases of Bronchial Asthma. Out of 45 cases, 27 (60%) cases experienced much better control of their Asthma symptoms. There was notably positive changes in Asthma Control test parameters (improved ACT score) marking the better life functioning of patients. Spirometry was the main assessment tool for result. FEV1 values significantly increased during and post treatment. It can be safely concluded that Homoeopathy plays an important role in treating chronic and seemingly difficult condition like asthma with minimizing the future risk. Though the obtained results are quite encouraging, more concrete opinion about effectiveness of Homoeopathy can be established if study can be furthered for longer time and on large patient pool to generate large data size and consequently more accurate results with minimal error. Moreover the study should be controlled and multicentric to overcome the limitations of this study.

Finally, this study also establishes harmony with the expert statement of GINA report-2015, "However, an overarching principle in the new GINA report is the importance of individualizing patient management not only by using genomics or proteomics, but also with "humanomics", taking into account the behavioural, social and cultural factors that shape outcomes for individual patients" as Homoeopathy itself is the science of individualization with an holistic approach.[1]

Conflict of Interest

There are no conflicts of interest.

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