

COMPLIANCE, SYMPTOMATIC AND SPIROMETRIC IMPROVEMENT WITH DIFFERENT TYPES OF DRY POWDER INHALERS (DPIs) IN BRONCHIAL ASTHMA PATIENTS- A COMPARATIVE STUDY

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ABSTRACT

BACKGROUND

Asthma is a common and potentially serious disease that imposes a substantial burden on patients, their families and the community. It is one of the major non-communicable diseases of the world and in India the prevalence is about 2.38%. The disease is characterized by recurrent attacks of cough, breathlessness and wheeze following exposure to indoor and outdoor allergens. Effective inhaled bronchodilator and steroid therapy is the cornerstone of Asthma management. Inhaled therapy targets drugs directly into the lungs and allows a distinct therapeutic advantage over systemic therapy with less doses needed, more rapid action and few side effects. Among the different types of inhalers that are available – metered dose inhalers (pMDIs), dry powder inhalers (DPI), nebulizers and breath actuated inhalers, DPIs are the cheapest and universally available. This study is an attempt to understand the efficacy, safety and acceptability of three different types of DPIs each having a different chamber size and a different method of puncturing the drug capsule – with needles and small chamber (MACHALER) with a fin and a larger chamber (ROTAHALER) and a levered large chamber (REDIHALER).

The aim of the study is to assess the efficacy of different types of dry powder inhalers vis a vis compliance, symptomatic improvement and spirometric improvement.

MATERIALS AND METHODS

This is a prospective analytical study done in the Department of Pulmonary Medicine, SVRR Govt. General Hospital, Tirupathi between Nov. 2016 to April 2018, over a period of 1½ years. 90 asthmatics (63 males and 27 females) who were above 18 years of age, non-smokers, willing to participate in the study and whose spirometry was consistent with the diagnosis of asthma were recruited into the study. Patients were successively given the three different types of DPI, the needle puncture device (MACHALER), the fin breaking device (ROTAHALER) and the levered device (REDIHALER) along with Formoterol – Budesonide 400mg inhalant capsule (FORACORT 400 mcg) twice daily which is supplied by the institute. Where necessary oral bronchodilators like doxophylline, oral steroid, methyl prednisolone 1 mg/kg body weight for 3 to 5 days and a leukotriene antagonist montelukast-levocetirizine were added. The patients were followed up at 15 days, 1 month and 2 months and improvement in cough, breathlessness, wheeze and chest tightness noted. Predicted Forced Vital Capacity percentage (FVC), predicted forced expiratory volume in 1 second (FEV1) and predicted FEV1/FVC % and predicted peak flow rate (PEFR) were obtained spirometrically. Patient satisfaction was also enquired about.

RESULTS

Compliance was 100% with all the 3 devices. Cough, breathlessness and wheeze disappeared by 2 weeks of treatment with all the 3 devices but disappeared earlier with the MACHALER and ROTAHALER. FEV1 and PEFR doubled after 2 months treatment with MACHALER but the response was little less with ROTAHALER and lesser with REDIHALER. Even FEV1/FVC % was better with the MACHALER than with ROTAHALER and REDIHALER. No side effects were observed in any of the patients.

CONCLUSION

Symptomatic improvement and, compliance was same with all the 3 types of DPIs. However, spirometrically the small chambered needle containing device, the MACHALER showed doubling of predicted FEV1 %, predicted PEFR % and significant increase in FEV1/FVC % when compared to ROTAHALER and REDIHALER.

KEYWORDS

Bronchial Asthma, Dry Powder Inhalers, Symptomatic, Spirometry, Improvement, Compliance.

HOW TO CITE THIS ARTICLE: Yanamala SPR, Gorthi A. Compliance, symptomatic and spirometric improvement with different types of dry powder inhalers (DPIs) in bronchial asthma patients - a comparative study. J. Evid. Based Med. Healthc. 2018; 5(25), 1930-1935. DOI: 10.18410/jebmh/2018/402

BACKGROUND

The World Health Organization (WHO) estimates that about 235 million people currently suffer from Asthma and this figure is projected to rise to 400 million by year 2025.¹ 338,000 deaths were reported in 2015 and most deaths occur in older adults and 1.5 million disability life adjusted

years (DALYs) are lost annually due to Asthma.² It occurs in all countries irrespective of level of development. In India, a multicenter study by the Asthma Epidemiology Study Group of the Indian Council of Medical Research found the prevalence of Bronchial Asthma in Indian adults to be 2.38%.³

Financial or Other, Competing Interest: None.
Submission 25-05-2018, Peer Review 30-05-2018,
Acceptance 12-06-2018, Published 18-06-2018.
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 DOI: 10.18410/jebmh/2018/402



The disease is essentially familial, a genetic association has been described. The strongest risk factors for developing Asthma are exposure to indoor allergens such as house dust, mites in bedding, carpets and stuffed furniture, pollution and pet dander, outdoor allergens such as pollens and moulds.⁴ GINA defines "Asthma as a heterogeneous disease, 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."⁵

It is a complex inflammatory disease of the airways that involves many different cells (e.g., eosinophils, neutrophils, basophils, mast cells, macrophages, structural cells) and mediators (e.g., cytokines, chemokines, histamine, leukotrienes, reactive oxygen species, and thromboxanes). There is a general consensus that airway inflammation, hyperresponsiveness and remodelling are critical components of asthma. Furthermore, environmental exposures throughout life can modulate the expression of asthma susceptibility genes, making asthma a dynamic disease.⁶ Evidence from patients with asthma and animal models of bronchial hyperreactivity clearly explains the above.

Effective inhalational therapy is the cornerstone of Asthma management.⁵ Inhaled therapy delivers drug directly to the lungs very rapidly, with few side effects. There are several types of inhaler devices and drug delivery systems used in clinical practice for the management of Asthma and these include pressurized metered dose inhaler {pMDI}, with spacers, dry powder inhalers {DPIs}, nebulizers and breath actuated inhalers.⁷

Dry Powder Inhalers

Advantages- Compact and portable, easy to use, cost effective, no need of hand-mouth co-ordination, no need of spacer. Disadvantages: An inspiratory force of at least 60 L/Min is necessary, not possible in severely breathless patients, children, edentulous adults and very old patients.⁸ Only about 9-10% of drug is deposited into the lungs, the rest enters the stomach.⁹

There are potentially over 250 device drug combinations available and this leads to confusion in prescribing among healthcare practitioners. It has been shown that training and counselling patients in their inhalation technique can increase their adherence to device usage, and patients may

be assessed with respect to their suitability for a particular inhaler device.¹⁰

This study is a humble attempt to try to understand the clinical efficacy, safety, and acceptability of three different types of dry powder inhaler devices for the delivery of Formetrol – budesonide (400 mcg+12mcg) / dose twice daily⁸ in moderate persistent Asthma patients each having a different chamber size and a different method of puncturing the drug capsule - with needles and small chamber (MACHALER) with a fin and a larger chamber (ROTAHALER) and a levered large chamber (REDIHALER).

Aim

To assess the efficacy of different types of dry powder inhalers in Bronchial Asthma patients, by assessing the improvement in symptoms, by assessing the improvement in Spiro metric parameters, and by assessing the patient compliance.

MATERIALS AND METHODS

Study Design

A prospective analytical study was conducted among clinically diagnosed moderate persistent asthma patients from the Out-Patient Department & Wards of Department of Pulmonary Medicine, Sri Venkateswara Ram Narain Ruia Government General Hospital (SVRRGGH), TIRUPATHI.

Period of Study

November 2016 to April 2018 (1½ years).

Sample Size

90 patients (63 male, and 27 females) who satisfied the clinical and spirometric essential criteria, being FEV1 ≤80% with post bronchodilator reversibility of 12-20% or absolute value of FEV1 >200 ml after nebulisation with 200 mcg inhaled Salbutamol in a 15-minute period.

Criteria for Patient Selection

Inclusion Criteria

Patient age group of ≥18 years; willing to participate in this study; spirometric criteria satisfaction. No history of smoking.

Exclusion Criteria

Patients <18 years; Not willing to participate; Smokers; Co-morbidities like HIV, Diabetes Mellitus, Hypertension, and Pulmonary Tuberculosis (New and Old); Patients unable to perform PFT & Chest X- Ray showing abnormalities.

Patient Selection

Wheezing or whistling in the chest, Attacks of shortness of breath, no respiratory symptoms between the attacks, At least two provoking factors, Family history of Atopy, Patients with history of Eczema and Allergic rhinitis, Attacks having seasonal predilection.

Patients were successively given the three different types of DPI, the needle puncture device (MACHALER), the fin breaking device (ROTAHALER) and the levered device

(REDIHALER) along with Formoterol – Budesonide 400mcg inhalant capsule twice daily. Where necessary oral bronchodilators like doxophylline, oral steroid, Methyl prednisolone 1mg/kg body weight for 3 to 5 days and a leukotriene antagonist montelukast – levocetirizine were added. The brand of Formoterol – Budesonide 400 mcg used was FORACORT 400 mcg which is supplied by the institute.

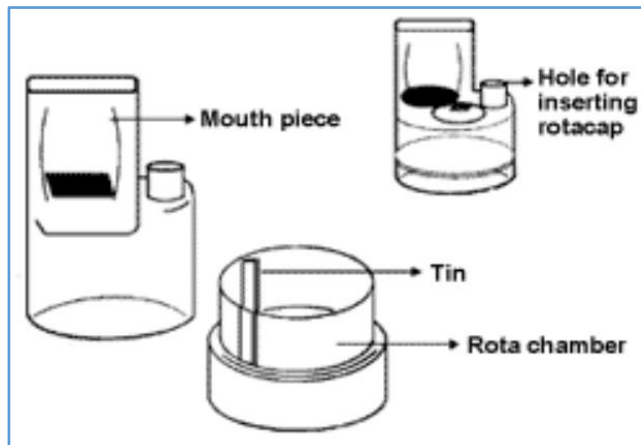


Figure 1. Rota Haler

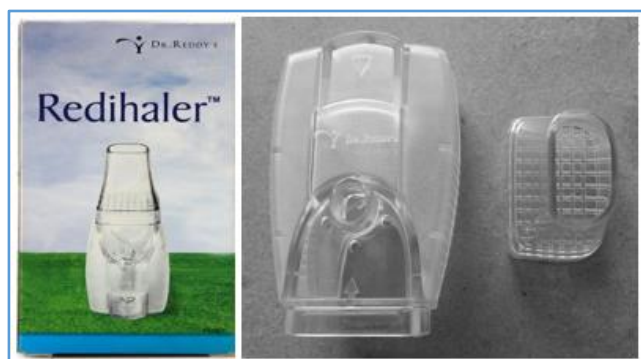


Figure 2. Redihaler

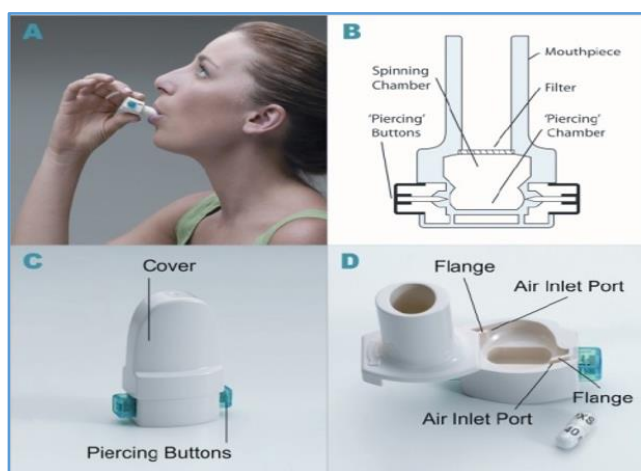


Figure 3. Machaler

Study Protocol

Data was collected on standardized proforma from all the subjects who were willing to participate in the study. Written consent was taken after explaining the procedure of Pulmonary Function Test and outcomes of the test.

PFT was done by a computerised spirometer Spirowin version 0.2. Each patient was asked to make three satisfactory curves. Best of the three was considered. After recording FEV1, salbutamol nebulisation with 200 mcg was done for 15 minutes and bronchodilator reversibility study of 12-20% improvement in FEV1 or 200 ml of base line FEV1 were considered as Asthma.

RESULTS

Total number of study subjects n= 90.
 Total number of males = 63.
 Total number of females = 27.

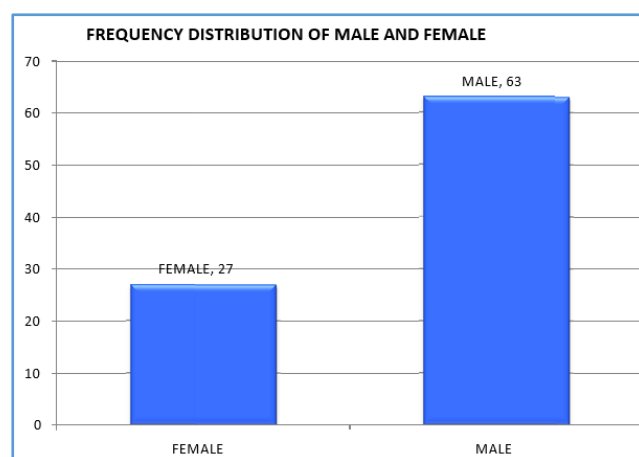


Figure 4. Frequency Distribution of Male and Female

Results with Machaler-

Total Number of Study Subjects n1= 30
 Symptomatic Improvement with Machaler
 Total Number of Patients n1 =30

No. of Patients with Symptoms	Before Treatment	After 15 Days	After 1 Month	After 2 Months
Cough	04	0	0	0
Breathlessness	30	0	0	0
Wheeze	30	0	0	0
Chest Tightness	05	0	0	0

Table 1. Symptomatic Improvement with MAC Haler

Spirometry Results with Machaler-

	Spirometric Parameters	Pre- Treatment Mean ± S.D.	After 15 Days Mean ± S.D.	After One Month Mean ± S.D.	After Two Months Mean ± S.D.
01	% FVC Predicted	52.42 ± 21.08	63.89 ± 21.41	69.83 ± 20.97	80.93 ± 14.76
02.	% FEV1 Predicted	41.78 ± 20.01	56.78 ± 21.64	64.11 ± 24.25	78.79 ± 16.83
03	% FEV1/FVC Predicted	80.99 ± 14.63	92.06 ± 10.81	94.05 ± 14.98	101.01 ± 9.48
04	% PEFR Predicted	29.82 ± 16.57	41.51 ± 17.30	45.00 ± 19.31	57.86 ± 19.72

Table 2. % Predicted Spirometric Values FVC, FEV1, FEV1/FVC, PEFR in patients using Machaler Device

MAC HALER-

Pre – Post Treatment Spirometric Values	t Value	p Value
% PRE FVC - % PRE FVC	6.583	.000
% PRE FEV1 - % PRE FEV1	9.239	.000
% PRE FEV1/FVC – % PRE FEV1/FVC	7.984	.000
% PRE PEFR - % PRE PEFR	8.492	M .000

Table 3. Paired Samples Test

P value is highly significant (p= 0.000) with all spirometric parameters.

i.e. % predicted FVC, FEV1, FEV1/FVC, PEFR.

Results with Redihaler

Total number of study subjects n2= 30

Symptomatic Improvement with Redihaler

Total Number of Patients- n1 =30

No. of Patients with Symptoms	Before Treatment	After 15 Days	After 1 Month	After 2 Months
Cough	02	0	0	0
Breathlessness	30	0	0	0
Wheeze	30	0	0	0
Chest Tightness	02	0	0	0

Table 4. Symptomatic Improvement with Redihaler

Redihaler

	Spirometric Parameters	Pre- Treatment Mean ± S.D.	After 15 Days Mean ± S.D.	After One Month Mean ± S.D.	After Two Months Mean ± S.D.
1	% FVC Predicted	60.31 ± 15.08	66.15 ± 17.82	71.48 ± 16.91	71.47 ± 18.67
2	% FEV1 Predicted	49.56 ± 13.59	58.61 ± 17.99	64.54 ± 17.76	69.35 ± 19.29
3	% FEV1/FVC Predicted	86.30 ± 11.08	91.78 ± 10.58	93.80 ± 8.53	95.60 ± 14.54
4	% PEFR Predicted	36.02 ± 13.24	38.11 ± 14.18	43.48 ± 13.82	50.96 ± 17.96

Table 5. Spirometry Results with Redihaler

Pre – Post Treatment Spirometric Values	t value	P value
% PRE FVC - %PRE FVC	2.568	0.016
% PRE FEV1 - %PRE FEV1	4.910	0.000
% PRE FEV1/FVC - %PRE FEV1/FVC	3.082	0.004
% PRE PEFR - %PRE PEFR	5.050	0.000

Table 6. Paired Samples Test

P value is highly significant (0.000) for FEV1, PEFR and significant with FVC, FEV1/FVC {P<0.01}.

Rotahaler

Total number of study subjects n2= 30.

Symptomatic Improvement with Rotahaler.

Total Number of Patients n1 =30.

Symptoms	No. of Patients			
	Before Treatment	After 15 Days	After 1 Month	After 2 Months
Cough	03	0	0	0
Breathlessness	30	0	0	0
Wheeze	30	0	0	0
Chest Tightness	04	0	0	0

Table 7. Symptomatic Improvement with Rotahaler

Sl. No.	Spirometric Parameters	Pre- Treatment Mean ± S.D.	After 15 Days Mean ± S.D.	After One Month Mean ± S.D.	After Two Months Mean ± S.D.
01	% FVC Predicted	57.86 ± 20.83	67.85 ± 17.55	68.81 ± 18.87	75.41 ± 19.19
02	% FEV1 Predicted	43.99 ± 18.60	62.11 ± 19.66	61.98 ± 21.71	72.30 ± 20.53
03	% FEV1/FVC Predicted	78.69 ± 13.82	92.08 ± 11.04	91.81 ± 11.12	97.70 ± 8.73
04	% PEFR Predicted	29.83 ± 15.33	40.86 ± 22.57	43.70 ± 18.74	53.09 ± 18.16

Table 8. Spirometry Results with Rotahaler

Pre - Post treatment spirometric values	t Value	P Value
% PRE FVC - % PRE FVC	4.103	0.000
% PRE FEV1 - % PRE FEV1	6.845	0.000
% PRE FEV1/FVC - % PRE FEV1/FVC	6.674	0.000
% PREPEFR - % PREPEFR	8.328	0.000

Table 9. Paired Samples Test

P value is highly significant (0.000) for all spirometric parameters with the Rotahaler.

DISCUSSION

This study is an attempt to analyse three different types of commonly used DPI devices-Machaler, Rotahaler and Redihaler. Minor differences in the design of the device have an impact on the compliance and clinical outcome.¹¹

The efficacy and safety of medication are important considerations when selecting a treatment for asthma. The effectiveness of treatment is also dependent on the patient using their inhaler correctly and as prescribed every time.¹² In addition, the choice of an inhaler device and the patient’s opinion on a particular device are also important factors in asthma patients.

In our study three different DPI devices were compared and results documented according to

- Symptomatic improvement
- Compliance
- Objective Spirometric findings

{FVC, FEV1, FEV1/FVC, PEFR}

The clinical picture at the end of 2 weeks of the treatment was same for all the three inhalers with cough, breathlessness and wheeze disappearing but with Machaler and Rotahaler symptoms came down even earlier.

The compliance was 100% with all three devices. This was probably because of regular motivation, follow up, and the dispensing of free medication to the patients.

The % FEV1 Predicted, % PEFR Predicted almost doubled after 2 months of treatment in patients using Mac haler.

This response was somewhat less marked with Rotahaler and < 25% with Redihaler.

The change in % predicted FEV1 / FVC was less dramatic with the Rotahaler FEV1 % predicted showed good response initially, but later the response was not very significant.

With the Redihaler % FEV1 predicted showed initially average response, the initial response was somewhat better with Rotahaler, but in both of these

devices the response was not as marked in the later phases. This may be attributed to large size of the chamber which encourages the sticking of the drug to the chamber wall itself, this could be appreciated by looking at the device itself.

Since the Machaler had a very small chamber, persistent and prolonged good response was observed with Machaler.

In our study, clinical and symptomatic improvement was good with all the three devices – Machaler, Rotahaler and Redihaler.

Machaler was superior to both Rotahaler and Redihaler as far as spirometric parameters were concerned. % predicted FEV1, % Predicted PEFR doubled by the end of two months. Even % predicted FEV1/FVC had significantly increased with Machaler. The Rotahaler was better than the Redihaler as far as the above parameters are concerned.

No side effects were observed in any of the patients.

CONCLUSION

- Symptomatic improvement in Bronchial Asthma Patients using Machaler, Redihaler and Rotahaler is comparable, with cough, breathlessness and wheeze subsiding with all the three devices, though patients using Machaler and Rotahaler seemed to have got rid of their symptoms earlier.
- Compliance was good with all the three devices; no patient was having any complaints about his/her device. All patients continued up to the end of the study.
- Spirometric values, especially % predicted FEV1, % Predicted PEFR doubled with Machaler by the end of two months. % predicted FEV1/FVC had reasonably improved with both the Machaler and Rotahaler.
- Our study concludes, that inspite of all the three DPIs being effective, spirometric parameters point to Machaler being superior to Rotahaler which is a little better than the Redihaler.

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