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Original Research Article

Comparison of clinical outcomes of inhaled formoterol or fluticasone versus formoterol or mometasone in the patients of bronchial asthma

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ABSTRACT

Background: This study was undertaken because of paucity of literature regarding outcomes of inhaled formeterol/fluticasone versus formoterol/mometasone in asthmatic patients.
Methods: Fifty newly (male/female) recruited cases of bronchial asthma were diagnosed on the basis of spirometry. The patients were allocated to two groups viz group A and B. Group-A received mometasone furoate/formoterol (200/10 µg OD) and Group-B received fluticasone/formoterol (200/10 µg OD) respectively. The drugs were administered through metered-dose inhaler (MDI).
Results: The mean FEV1/FVC ratio recorded (64.40±9.01) before starting the treatment has significantly changed to (68.92±8.58) after starting the treatment. Mean forced expiratory volume (47.56±14.73%) noted before the use of bronchodilator also changed to mean FEV1 63.98±15.17. Mean forced expiratory volume recorded before treatment (55.02±5.01) in a group who were treated with formoterol/mometasone combination changed to (72.06±5.86) after treatment. However, the mean forced expiratory volume recorded before treatment 54.92±4.47 in a group who were treated with formoterol/fluticasone combination changed to 75.48±5.03 after the treatment. While comparing the two treatment regimens, it is evident from the results that there is no significant difference in FEV1 between the groups. However, the post bronchodilator FEV1 was significantly ($p<0.001$) higher among the patient group which were treated with fluticasone/formoterol combination than the group who were treated with mometasone/formoterol combination. No significant adverse effect of either of two regimens was observed thus showing that both the combinations are comparatively safe for use.
Conclusions: This study reveals that both the treatment regimens showed a significant improvement in lung functions without any significant adverse event.

Keywords: Fluticasone/Formoterol, Mometasone/formoterol, FEV1, Bronchial asthma

INTRODUCTION

Bronchial Asthma is a chronic inflammatory disorder of the airways associated with airway hyper-responsiveness that leads to recurrent episodes of wheezing, breathlessness, chest tightness and coughing particularly at night or in the early morning. These episodes are usually associated with widespread but variable airflow obstruction that is often reversible either spontaneously or with treatment.[1]

The prevalence of asthma is reported to range from 1.2 to 6.3% adults in most countries.[2] There is very limited data on asthma epidemiology from the developing world,

including India. However, India is a vast country with immense geographical, economical, racial, religious and socio-political diversity. There are obvious differences in prevalence of disease and approach to management of health problems.[3] In a recent multi-centric study, prevalence of asthma in India has been reported to be 2.05%.[4] Inhalers are being used for management of asthma for quite some long since the introduction of first pressurized metered-dose inhaler (pMDI) in 1956 using rapidly acting nonselective β-agonists (i.e., isoprenaline and epinephrine) followed by selective short-acting β2-adrenergic agonist (SABA) salbutamol and inhaled corticosteroids and leukotriene modifiers.[5]

Moreover, studies demonstrated that monotherapy with a long-acting β2-adrenergic agonist (LABA) was insufficient to control asthma.[6,7] Concerns regarding the safety of high-dose inhaled corticosteroids (ICS) (e.g., rare cases of adrenal suppression) and findings from randomized, controlled trials showing a more effective reduction in symptoms and exacerbations with a reduced ICS dose and a LABA (e.g., salmeterol or formoterol) compared with high-dose ICS alone eventually cemented the role of LABA in the therapeutic armamentarium.5 Indeed, contemporary asthma treatment guidelines recommend add-on LABA to ICS therapy for those patients who do not respond optimally to low- to medium-dose ICS.[5,8,9]

Formoterol is a LABA which has been used for treatment of asthma in monotherapy for quite long. Mometasone furoate and fluticasone are synthetic glucocorticoids that have shown efficacy in treatment of asthma either alone or in combination with LABA drugs.[10,11] However, there is limited literature available on evaluation of efficacy of formoterol/mometasone and formoterol/fluticasone combinations in management of bronchial asthma. Hence, the objective of this study was to evaluate and compare the safety and efficacy of inhaled formoterol/mometasone versus formoterol/fluticasone combination in patients of bronchial asthma in order to fill this gap.

METHODS

This study was carried out in the department of Pharmacology, ELMC and Hospital, for a period from January 2012 to September 2012. The bronchial asthma patients diagnosed on the basis of spirometry were recruited and included into the study. The asthma patients of either sex aged between 18-60 year were included after their formal consent. However, the patients who were in acute exacerbation of bronchial asthma and patients above age of 60 year were excluded. In addition, the patients with renal, cardiac and liver diseases were also excluded. Each patient participating in the study was subjected to the detailed history and clinical examination with history related to asthma was noted before starting the treatment. Written, informed consent of all the patients and approval of institutional ethics committee (IEC) was taken before starting the study. This study was a prospective open label randomized controlled trial carried out on bronchial asthma patients. It enrolled a total of 45 bronchial asthma patients who were randomly allocated to two groups viz group A and group B respectively. Group A received a fixed dose combination of formoterol and fluticasone in a dose of 200/10µg once daily. While as group B received a fixed dose combination of formoterol and mometasone in a dose of 200/10µg once daily respectively. Following the American thoracic society criteria, the spirometry was done in each patient by measuring forced vital capacity (FVC), forced expired volume FEV1 and a ratio of FEV1/FVC was evaluated. Each patient in either group was followed and continuously assessed for clinical outcomes for a period of three months from the date of start of treatment.

A proforma was developed for collecting the data required for this study. Face to face interview technique was employed for interviewing the patients and/or their closest attendants. The patient sample for this study was calculated as per the incidence of bronchial asthma in the projected area. Paired t-test was employed for statistical analysis of the data. Statistical analysis was done by SPSS version 10.0 statistical software. A probability value of less than 0.05 ($p<0.05$) was considered to be statistically significant.

RESULTS

In present study age of enrolled patient population ranged from 8 to 38 years (Table 1). Maximum number of patients (n=23; 46%) were aged 21-30 years followed by those aged 11-20 years (32%). There were only 2 (4%) patients who were <10 years of age and 9 (18%) patients aged 31-40 years. Mean age of patients was 22.38±7.46 years. The age profile of patients in present study is similar to that reported in a study which also found majority of their patients to be aged between 21 to 40 years. It was recorded that majority of patients were males (68%). Male to female ratio of patients was 2.13:1.

Table 1: Demographic variables.

Variable	Attribute	Number (N)	Percentage (%)
Sex	Male	34	68.0
	Female	16	32.0
Age group (in years)	≤10	2	4.0
	11-20	16	32.0
	21-30	23	46.0
	31-40	9	18.0
Occupation	Farmer	10	20.0
	Laborer	8	16.0
	Service	7	14.0
	Shopkeeper	3	6.0
	Student	18	36.0
	Worker	4	8.0

The male predominance may be related to a greater degree of bronchial lability in males. This finding correlates with the finding of other studies.[36,37] It was also noted that maximum number of patients were students (n=18; 36%) followed by farmers (n=10; 20%), labourers (n=8; 16%), those in service (n=7; 14%), domestic workers (n=4; 8%) and shopkeepers (n=4; 8%).

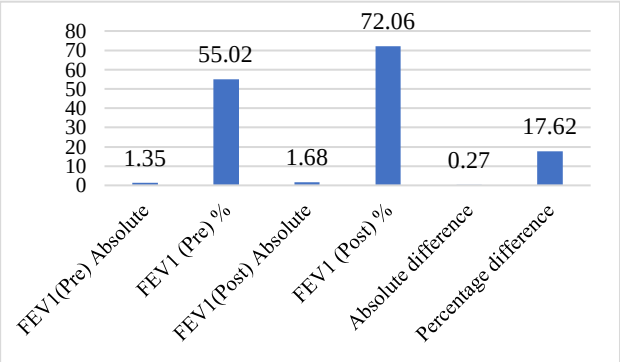

Figure 1: Pulmonary function tests after intervention in group I (formoterol/mometasone).

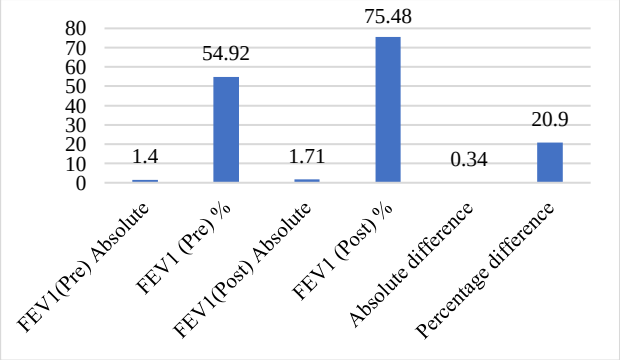

Figure 2: Pulmonary function tests after intervention in group II (formoterol/fluticasone).

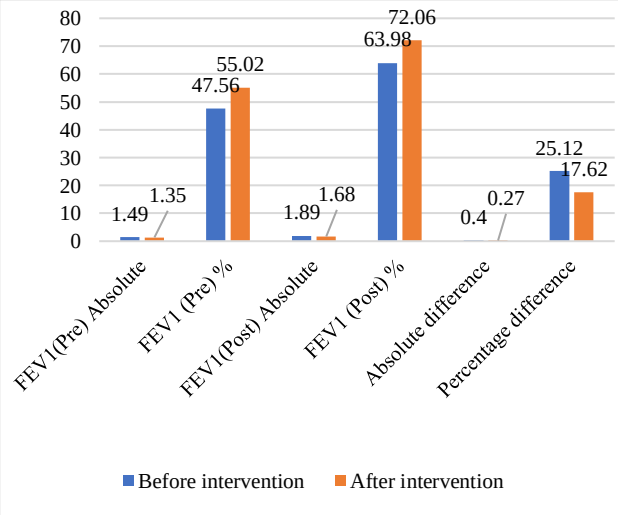

Figure 3: Comparison pulmonary function in group I, before and after intervention.

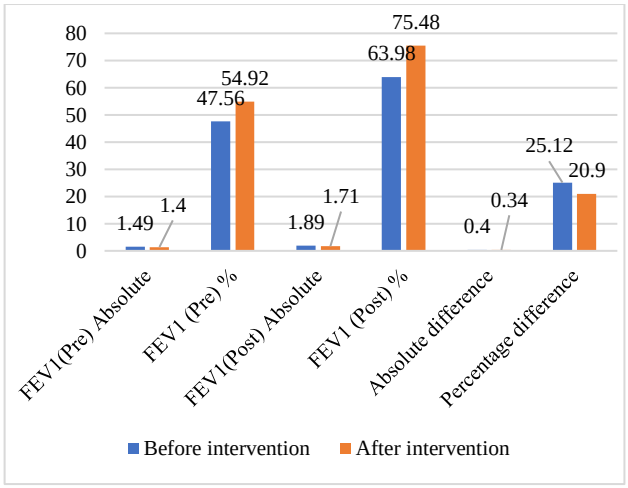

Figure 4: Comparison pulmonary function in group II, before and after intervention.

While comparing the FEV1/FVC ratios a statistically significant difference was noted in mean FEV1/FVC ratio before (64.40±9.01) and after (68.92±8.58) the use of bronchodilator (Figure 1). The FEV1/FVC ratios recorded before the use of bronchodilator varied from 46-82% which changed to 55-92% after the use of bronchodilator. However, the Forced expiratory volume in 1 sec ranged from 21-91% before the use of bronchodilator which changed to 26 to 102% after the use of bronchodilator. This difference in mean FEV1 recorded before (47.56±14.73) and after (63.98±15.17) use of bronchodilator was statistically significant. Similarly, a statistically significant difference was noted in mean FEV1 to be 54.92±4.47% before the use of bronchodilator which changed to reach at 75.48±5.03% after treatment in Formoterol/Fluticasone group (Figure 2). On comparing the two regimens under investigation, post- intervention forced expiratory volume in 1 sec was significantly higher in fluticasone/formoterol combination group as compared to mometasone/formoterol combination group (Figure 3).

DISCUSSION

Bronchial asthma is a chronic inflammatory disorder of the airways associated with airway hyperresponsiveness. Many drugs are employed for its treatment but the introduction of long acting β2 agonists has brought a new dimension to symptomatic treatment. The long-acting β2 agonists in combination with inhaled glucocorticosteroids are the mainstay of treatment in severe persistent asthma.[12] Its long-lasting bronchodilating effect and twice a day application results in increased patient compliance.[13,14] Formoterol is a one such drug with a bronchodilator effect lasting 12 hours.[15] In adult patients with asthma, it is currently recommended as an alternative to increasing moderate doses of inhaled corticosteroids or as an adjunct to high doses of inhaled corticosteroids.[16,12] Mometasone is a common glucocorticosteroid being used as an adjunct to Formoterol and has shown promising results in the management of bronchial asthma.[17-26]

Fluticasone is another glucocorticosteroid, use of which has recently been started as an adjunct to long acting beta agonist formoterol and has also shown good response.[27-35] Despite being same class of drugs, there are few comparative studies comparing the efficacy of mometasone and fluticasone as an adjunct to formoterol and virtually there is gap of knowledge regarding the relative superiority of either of two combinations. Hence, it was found worthwhile to study and compare the clinical outcomes of formoterol in combination with glucocorticosteroids in bronchial asthmatic patients.

Following use of formoterol/mometasone combination, a significant difference was noted in mean FEV1 before and after starting the treatment (Figure 1). The forced expiratory volume in 1 sec ranged from 46-65% before starting the treatment which changed to 60-81% after starting the treatment. Although, mean values did not show a categorical shift, however, comparison of mean change during the period showed a significant improvement in both before and after use of the combination. A number of studies in variable intervention protocols have reported variable efficacy yet an incremental effect on forced expiratory volume. The results are in accordance with a study mentioning an intervention with MF/F-MDI was found to show a significant improvement in FEV1.[20] Another study mentioning using a 26-week protocol, also showed that combined corticosteroid mometasone and formoterol show a significant improvement in lung function.[21] Similar observations for efficacy of formoterol/ mometasone in improving lung function has also been reported in other studies too.[26] Similarly, a statistically significant difference was noted in mean FEV1 to be 54.92±4.47% before the use of bronchodilator which changed to reach at 75.48±5.03% after treatment in Formoterol/Fluticasone group (Figure 2). The forced expiratory volume in 1 sec ranged from 46 - 65% before starting the treatment changed to 61 to 85% after the treatment. The nature of change observed in present study is similar to study which investigated the efficacy and tolerability of combination of fluticasone propionate and formoterol- fumarate for treatment of bronchial asthma and found it to be both safe and efficacious at a dose schedule used by them or that in present study.[27] Similar results in terms of improvement in lung functional ability of fluticasone/formoterol were also observed in other studies.[28-30,32,34] Comparing the two regimens post-intervention forced expiratory volume in 1 sec was significantly higher in fluticasone/formoterol combination group as compared to mometasone/formoterol combination group (Figure 3). Some studies have attempted to compare the mometasone/formoterol against fluticasone/salmeterol and have shown similar results or relatively superior results of fluticasone/salmeterol combination.[38,20] This study found fluticasone/formoterol combination to be similar with respect to pre-dilation FEV1, however, with respect to post-dilation FEV1, the outcome was significantly better in fluticasone/formoterol group. The relatively better effect of fluticasone/formoterol group in present study could be attributed to maintenance of higher plasma cortisol levels in fluticasone adjunct group as observed in a study.[25] The results are in support of study comparing the use of fluticasone against mometasone monotherapy which mentioned that mometasone to be more effective against treatment of mild asthma, however, another study found that mometasone (MF) is a less specific glucocorticoid than fluticasone propionate (FP).[39,40] In another study it noted that fluticasone and mometasone did not show a significant difference in symptomatic improvement in cases of perennial rhinitis when used as aqueous nasal sprays.[41] Relatively higher specificity of fluticasone might be responsible for a better improvement in post-dilation FEV1 as observed in present study. This study has not observed any significant adverse effect of either of two regimens. The major limitations of the study were time and financial constraints. Considering the fact that present study was a short-term study, further long-term studies are required to explore the difference in clinical outcomes.

CONCLUSION

The results of this study reveal that both the treatment regimens showed a significant improvement in lung function in bronchial asthmatic patients without any significant adverse effect. Fluticasone/formeterol showed a relatively higher FEV1 following dilatation.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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