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Original Research Article

Comparative Efficacy and Safety between Combination Therapy of Salmeterol/Fluticasone and Formoterol/Budesonide in Moderate Persistent Asthma

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Conflict of interest: Nil

Abstract:

Background: Bronchial Asthma is a chronic inflammatory disorder of the airways in which many cells and cellular elements play a role. The chronic inflammation causes an associated increase in 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. It is a heterogeneous pulmonary disorder characterized by recurrent episodes of cough, breathlessness, and wheezing, which may resolve spontaneously or after the use of bronchodilator medication. The global prevalence of asthma is anticipated to be approximately 4.5 per cent. There are about 334 million patients with asthma affecting all age groups across the world5. The prevalence of asthma has increased over time and an additional 100 million people worldwide are expected to develop asthma by the year 2025.

Methods: The present prospective study has been done in Vizianagaram population in Maharajah`s institute of medical sciences to compare the efficacy and safety between combination therapy of salmeterol with fluticasone and formoterol with budesonide in moderate persistent asthma.

Results & Conclusion: Formoterol budesonide combination is better in comparison to the salmeterol fluticasone combination considering the lesser no of exacerbations and bronchodilator effect, both salmeterol and formoterol being long-acting bronchodilators.

Keywords: Bronchial Asthma, Formoterol, Budesonide, Salmeterol, Fluticasone.

Introduction

Bronchial Asthma is a chronic inflammatory disorder of the airways in which many cells and cellular elements play a role. The chronic inflammation causes an associated increase in 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] It is a heterogeneous pulmonary disorder characterized by recurrent episodes of cough, breathlessness, and wheezing, which may resolve spontaneously or after the use of bronchodilator medication[2]. The global prevalence of asthma is anticipated to be approximately 4.5 per cent [3,4]. There are about 334 million patients with asthma affecting all age groups across the world5. The prevalence of asthma has increased over time and an additional 100 million people worldwide are expected to develop asthma by the year 2025[5]. In the Indian study on epidemiology of asthma, respiratory symptoms, and chronic bronchitis in adults (INSEARCH), a survey conducted in two phases across 16 centers in India, the prevalence of asthma in adults was 2.05 per cent, with an estimated burden of 17.23 million6. A recent analysis using three different estimate models (INSEARCH, GINA and WHO survey) suggests that the prevalence of asthma in India varies between 2.05 to 3.5 per cent (17-30 million patients)7. The estimated cost of asthma treatment per year for the year 2015 has

been calculated to be approximately Rs 139.45 billion8. An estimated 15 million disability adjusted life years (DALYS) are lost due to asthma [4,9].

Materials and Methods

1. The present prospective study has been done in Vizianagaram population in Maharajah`s institute of medical sciences, Hospital.
2. To compare the efficacy and safety between combination therapy of salmeterol with fluticasone and formoterol with budesonide in moderate persistent asthma.

Study Design: Prospective, Single centre, Open Label, Comparative Design Study

Study Population: 100 Subjects

Setting: Vizianagaram Population

Place: MIMS Hospital in Vizianagaram

Materials

1. ROTAHALER available, the standard Rotahaler of Cipla Company available in the pharmacy.
2. Salmeterol + Fluticasone combination and Formoterol + Budesonide combination are available in the pharmacy of the same pharmaceutical company.
3. Each person was given 2 phials consisting of 30 capsules each so that it would last for 30 days.
4. All these people were taken within a radius of 5km away from the hospital so that in case of emergency they could rush to the hospital.

Methodology Data of 100 Subjects attending the Pulmonology OPD in MIMS from 2015 July to 2016 July were taken to study the relative Efficacy, Safety and Cost Effectiveness of Salmeterol with Fluticasone Combination (SFC) and Formoterol with Budesonide Combination (FBC) in Moderate Persistent Asthmatic Patients.

The Salmeterol/Fluticasone propionate combination contains Long-Acting Beta Agonist Salmeterol 50mcg and the Inhalational Corticosteroid Fluticasone Propionate 250mcg, 30 Capsules of (SFC)- Cost about Rs 240.

The Formoterol and Budesonide Combination contains the Long-Acting Beta Agonist Formoterol 6mcg and the Inhalational Corticosteroid Budesonide 200mcg (FORACORT200), 30 Capsules of (FBC) Cost about Rs 151.

Signs and symptoms must be classified at the initial and all following results because patients experience varied signs and symptoms. Initially and before treatment has been optimized. Clinical signs, symptoms and peak flow monitoring or spirometry are used to classify severity. After the condition is stable, severity is then classified according to the level of medication required to maintain treatment goals.

100 Subjects will be divided into half containing 50 each, one half will be given SFC and Another half will be given FBC. The dose will be given twice a day for about 4 weeks, Parameters of Spirometry (FEV1), PEFR and Asthma quality and Control Score of all the subjects will be obtained at the very beginning of the treatment course and after 4weeks.The Increase or decrease in the number of Acute Exacerbations while undergoing treatment will be noted. The Results outcome will be analyzed basing on the Parameters mentioned.

The improvement in FEV1 and PEFR will be observed based on (FEV1 predict % post treatment-FEV1predict % Pretreatment), Change % for each patient (i.e., Post best - Pre best/ Pre best x 100) and Mean percentage change will be calculated for each group. Improvement in Mean percentage change will be compared for both the groups (Sfc and fbc) for fev1 and pefr parameters respectively.
The Direct Costs include Medication i.e., FBC,30 Capsules of FBC Costs about Rs 151 per patient for 50 Subjects and SFC in another 50 Subjects Costing about Rs 240 for 30 Capsules per patient.
The pulmonary function tests are done free of cost as the hospital caters for poor patients.

Inclusion criteria

1. Male/Female above 16 yrs. of age,
2. Documented clinical history of Asthma with Broncho reversibility with 12% improvement in FEV1 with Salbutamol Nebulization (200-400ug) after 15mins.
3. Depending on the symptoms they are categorized into Mild, Moderate and Severe Persistent Asthma.
5. Moderate Persistent Asthmatic Cases are considered for the study. They must have normal chest skiagram, free from respiratory infections and normal blood count, certified by a clinician.

Moderate persistent asthma

Asthma is considered moderate persistent if without treatment any of the following are true:

1. Symptoms occur daily. Inhaled short-acting asthma medication is used every day.
2. Symptoms interfere with daily activities.
3. Night -time symptoms occur more than 1 time a week, but do not happen every day.
4. Lung function tests are abnormal (more than 60% to less than 80% of the expected value), and PEF varies more than 30% from morning to afternoon.

Exclusion criteria

1. Patients suffering with Upper /Lower Respira-

tory Tract Infection, as evidenced by fever, expectoration and running nose clinically.
2. Patients suffering with Acute Exacerbations of Asthma.
3. People who had a history of smoking for 10 pack years.
4. Patients who are on Oral Corticosteroids previously for 4 weeks before starting the study.

Ethical Issues History and examination

1. Institutional Ethics Committee approval was obtained before starting the study.
2. Informed consent was obtained from each study subject.
3. Confidentiality of the subject's information was maintained.

History and Examination

Of the patient like name, age, address, occupation was taken.

Detailed history was taken with special attention to following points:

1. Cough.
2. Expectoration.
3. Breathlessness.
4. Nocturnal awakening.
5. Hemoptysis.
6. Wheezing.
7. Chest pain.
8. Personal history-history of smoking and drinking.
9. Allergy history- food, house dust, pollen, traffic dust, perfumes, soaps, powders, hair dyes and others.
10. History:

a) History of similar complaints in the past.
b) History of chronic bronchitis, pulmonary tuberculosis, tropical pulmonary eosinophilia.
c) Diabetes mellitus, cardiac diseases, hypertension, chronic, renal failure.
d) Malignancy.

11. Family history: History of bronchial asthma among first degree relatives
12. Treatment history:

(a) History of bronchodilator therapy
(b) Corticosteroid therapy

After the history was taken, a detailed clinical examination was done. The following **investigations** were done:

(a) Routine blood tests
(b) Chest X-ray PA-view
(c) Pulmonary function tests

Patients with symptoms categorized under moderate persistent asthma were taken into consideration as per the inclusion criteria. Asthma is considered moderate persistent if without treatment any of the following are true:

(a) Symptoms occur daily. Inhaled short-acting asthma medication is used every day.
(b) Symptoms interfere with daily activities.
(c) Nighttime symptoms occur more than 1 time a week, but do not happen every day.
(d) Lung function tests are abnormal (more than 60% to less than 80% of the expected value), and PEF varies more than 30% from morning to afternoon.

Blood examination, Chest X-ray PA-view were done to exclude other conditions. A written informed consent was obtained from the patient. Patients were shown inhalational techniques with Rota halers, they were advised to rinse their mouth after each inhalation. They were followed up once a week for a period of 4 weeks. At each visit, they were clinically assessed. Pulmonary function tests as mentioned are done before and after treatment, FEV1, PEFR were assessed respectively.

Symptoms Severity Scoring

Patients' symptoms severity was assessed based on scoring done for following before and after treatment:

1. Cough
2. Wheeze
3. Breathlessness
4. Severity of nocturnal symptoms

Score for cough, wheeze, breathlessness, and severity of nocturnal symptoms.[10,11]

0 - No symptoms
1 - Mild
2- Moderate
3- Severe

Statical Analysis

The data would be presented as percentages. The comparison between the two groups was done using unpaired T test for FEV_1 and PEFR values. P value of <0.05 was considered as significant. The statistical analysis was done using SPSS software version 16.

Results

Demographic Data of Patients with Moderate Persistent Asthma

Table 1:

Group	No of Males	No of Females	Mean Age in Years
(Seroflo) Group 1	22	20	46
(Foracort) Group 2	24	18	44.9

Graph

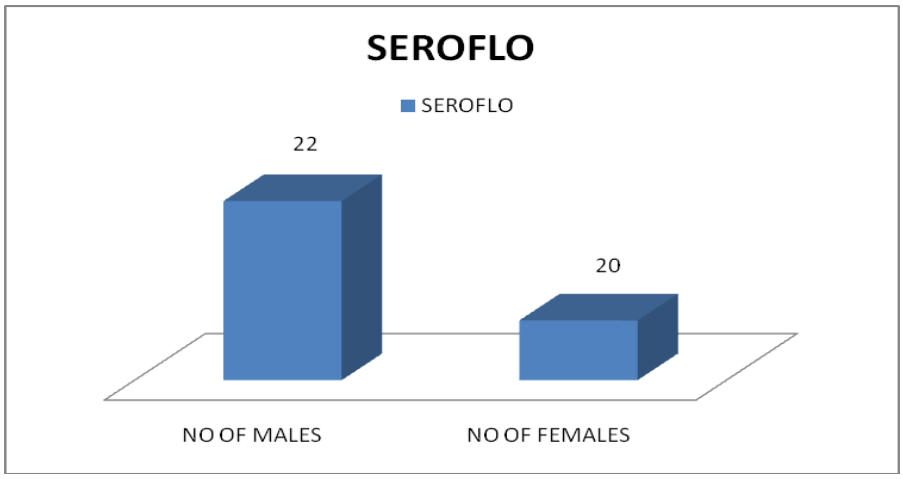

Figure 1: Corresponding Bar Diagram

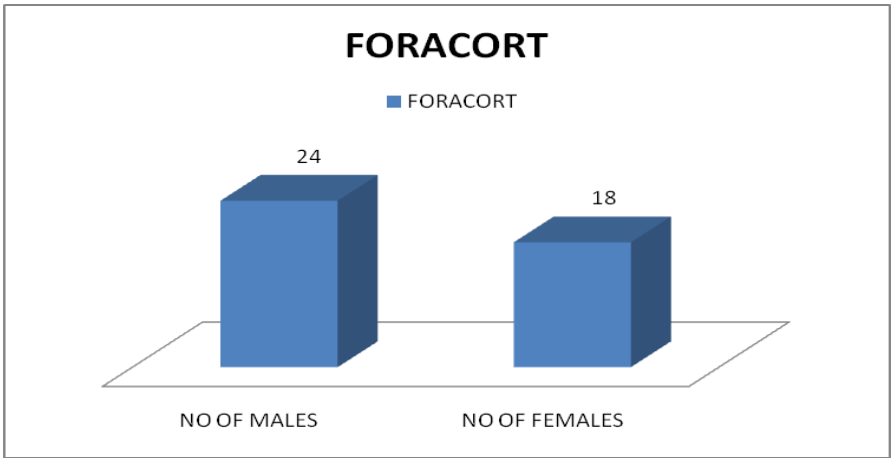

Figure 2: Corresponding Bar Diagram

The sample consisted of 22 Males and 20 Females with mean age of 46 in the SFC group. Similarly, in the FBC group there are 24 Males and 18 Females with mean age of 44.9. Thus, both are comparable.

Smokers Vs Nonsmokers

Table 2:

Group	Smokers	Non-Smokers
Seroflo (N=42)	19(45%)	23(55%)
Foracort(N=42)	17(41%)	25(59%)

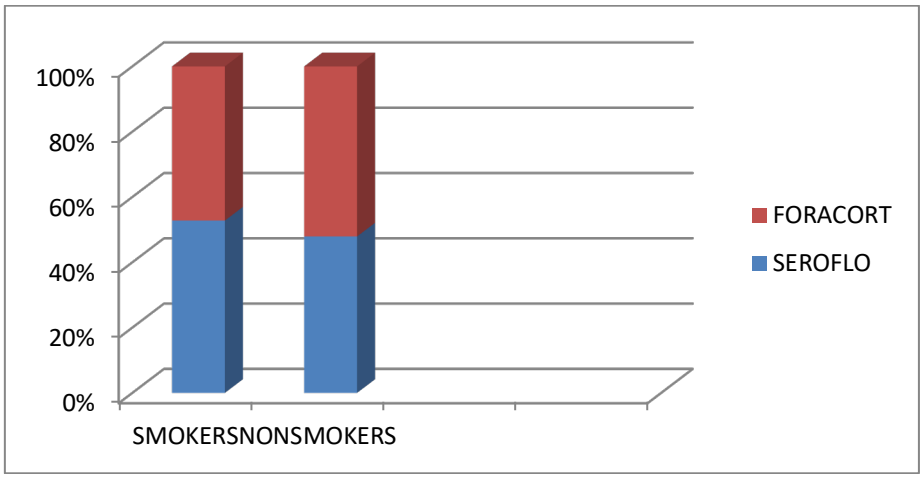

Figure 3: Corresponding Bar Diagram

Table -2 showed that there were 19(45%) smokers and 23(55%) nonsmokers in the SFC group. Whereas the FBC group showed 17(41%) smokers and 25(59%) non-smokers, thus in the SFC group the smokers were 4% more.

Analysis of Cough

Table 3:

Grading Of Cough	Seroflo Pre	Seroflo Post	Foracort Pre	Foracort Post
Nil-0	20(48%)	27(64%)	16(38%)	24(57%)
Mild - 1	5(12%)	13(31%)	13(31%)	18(43%)
Moderate -2	14(33%)	2(5%)	12(29%)	0
Severe -3	3(7%)	0	1(2%)	0

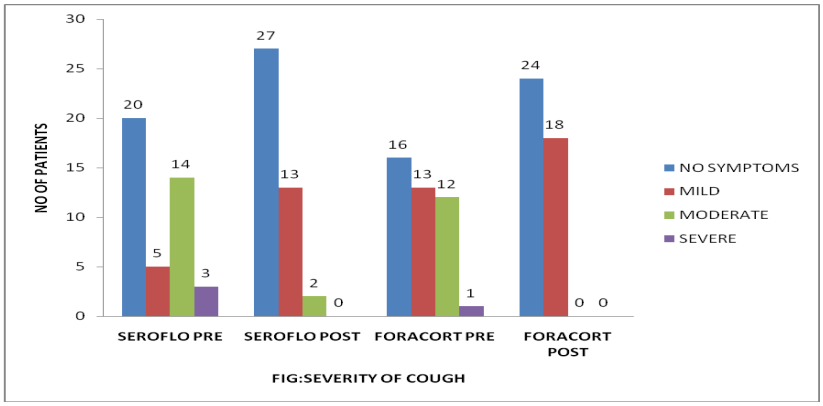

Figure 4: Corresponding Bar Diagram

Table-3 and corresponding bar diagram showed dry cough in 22 persons in the severity of mild (12%), moderate (33%), severe (7%). The Post treatment showed an improvement in all the four grades of severity, similarly the FBC Group revealed dry cough in the severity of mild (13%), moderate (29%), severe (2%). It is worth mentioning that post treatment showed vast improvement as compared to SFC Group, there was no cough in moderate and severe groups of FBC. Visavis SFC Group still had 5% of the patients in moderate and 31% in mild. Compared with the SFC, all the patients fell in the mild category (43%) post treatment in FBC.

Analysis of Wheeze

Table 4:

Grading Of Wheeze	Seroflo Pre	Seroflo Post	Foracort Pre	Foracort Post
Nil-0	4(10%)	16(38%)	9(21%)	22(52%)
Mild - 1	11(26%)	21(50%)	16(38%)	16(38%)
Moderate -2	25(60%)	5(12%)	13(31%)	4(10%)
Severe -3	2(4%)	0	4(10%)	0

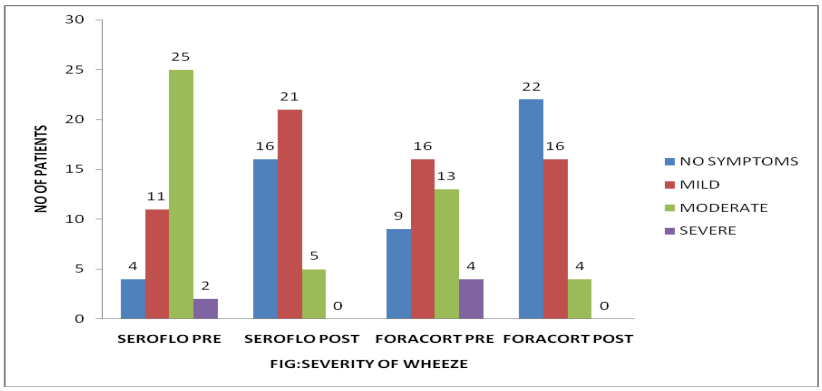

Figure 5: Corresponding Bar Diagram

Table 4 reveals the status of wheeze in the pre-treatment with SFC. There were 26%,60% and 4% of the sample group having mild, moderate, and severe wheeze respectively. Post treatment with SFC there were only 50% wheezers in mild, 12% in moderate and Nil in Severe category. It was obvi-

ous that treatment with SFC was beneficiated. FBC Group had 38%, 31% and 10% in mild, moderate, severe wheezing patients. Post treatment with FBC showed only 10% had moderate and the rest 38% mild and 52% had no wheeze which is noteworthy in comparison to SFC Group.

Analysis of Breathlessness

Table 5:

Grading of Breathlessness	Seroflo Pre	Seroflo Post	Foracort Pre	Foracort Post
Nil-0	1(2%)	20(48%)	10(24%)	26(62%)
Mild - 1	12(29%)	17(40%)	14(33%)	16(38%)
Moderate -2	23(55%)	5(12%)	14(33%)	0
Severe -3	6(14%)	0	4(10%)	0

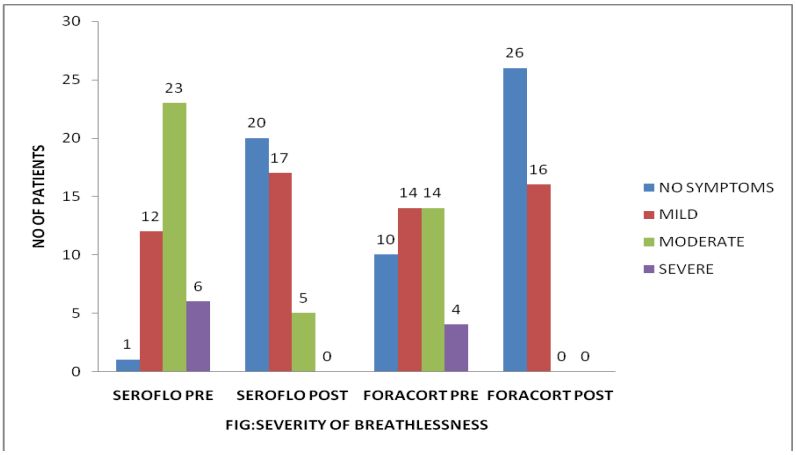

Figure 6: Corresponding Bar Diagram

Table -5 reveals SFC Group patients before treatment fall into mild, moderate severe categories - 29%,55% and 14% respectively. Post treatment showed no breathlessness in 48%, mild in 40%, moderate in 12%. Thus, there was global improvement in comparison FBC Group showed pretreatment breathlessness was not there in 24%, 33% each had mild and moderate type and 10% had severe breathlessness. Post treatment there was overall improvement. (62% Nil, 38% mild). This relief is striking in comparison to SFC Group.

Analysis of Nocturnal Symptoms

Table 6:

Grading of Nocturnal Symptoms	Seroflo Pre	Seroflo Post	Foracort Pre	Foracort Post
Nil-0	19(45%)	30(72%)	26(62%)	36(86%)
Mild – 1	13(31%)	11(26%)	7(17%)	6(14%)
Moderate -2	10(24%)	1(2%)	9(21%)	0
Severe -3	0	0	0	0

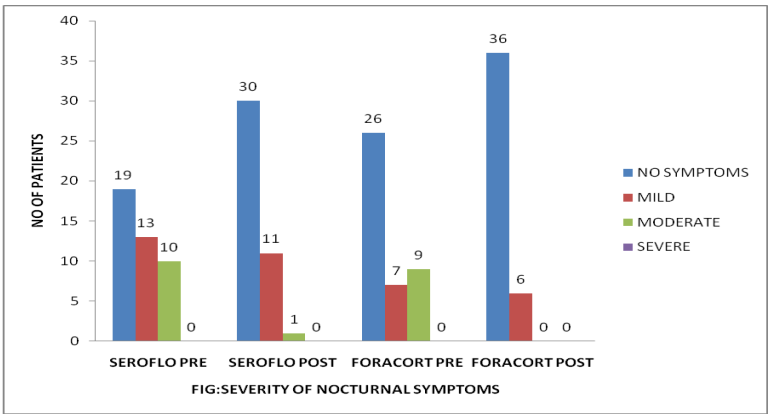

Figure 7: Corresponding Bar Diagram

Table-6 shows that 45% had no nocturnal dyspnea, 31% had mild and 24% moderate severity in SFC Group Post treatment a majority i.e., 72% had no nocturnal dyspnea only 26% had mild and 2% moderate dyspnea,

thus there was good improvement. In contrast, FBC pretreatment showed 62% without night symptoms, 21% moderate and 17% mild. The post treatment with FBC showed 86% were asymptomatic and only 14% had mild dyspnea. This shows an advantage with FBC Group.

Change in Fev1 Post Treatment in Both the Groups

Table 7:

	SFC PRE	SFC POST	FBC PRE	FBC POST
FEV1(60-70)	16(38%)	6(14.3%)	23(55)	1(2.4%)
FEV1(70-80)	26(62%)	3(7.2%)	18(43%)	3(7.2%)
FEV1(80-90)	0	19(45.2%)	1(2%)	22(52.4%)
FEV1(90-100)	0	14(33.3%)	0	16(38%)

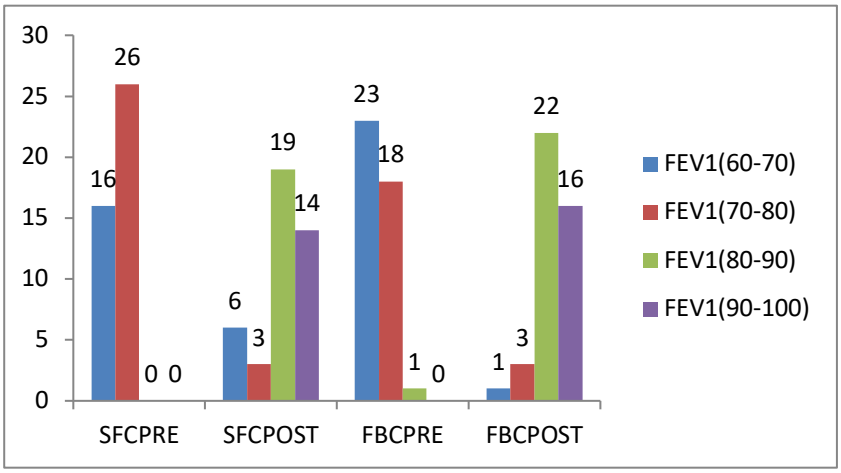

Figure 8: Corresponding Bar Diagram

The above table is the assessment by pulmonary function tests taking FEV1 into consideration. 90% of the SFC group had FEV1 between 60 -80%, all had improvement .78.5% had FEV1 between 80-90 and above. In the FBC Group 98% had FEV1 between 60 - 80 %. Post treatment 90.4% cases strikingly showed a hike in FEV1 to 80-90 and above. This is the contrasting objective difference between both groups.

Change in PEFR Post Treatment in Both the Groups

Table 8:

	SFC PRE	SFCPOST	FBC PRE	FBC POST
PEFR (10-30)	7(17%)	3(7%)	4(9%)	0
PEFR (30 -50)	14(33%)	12(29%)	11(26%)	7(17%)
PEFR (50-70)	14(33%)	10(24%)	20(48%)	11(26%)
PEFR (70 and above)	7(17%)	17(40%)	7(17%)	24(57%)

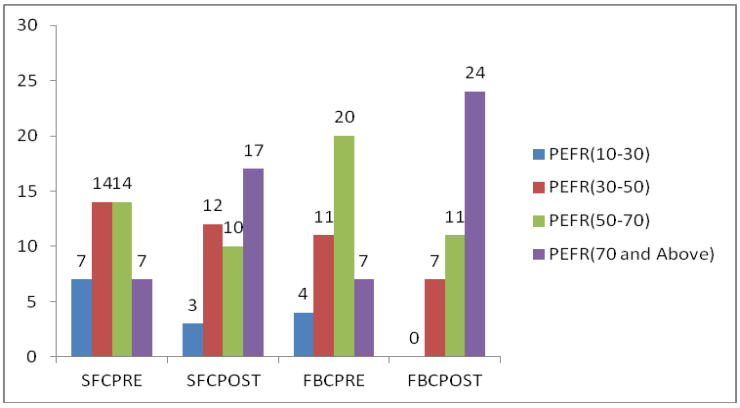

Figure 9: Corresponding Bar Diagram

The above table shows the peak flow ranging from 10% to above 70%.66% in the SFC Group had peak flow from 30 -70%. All had improvement in the post test and 40% of them had improvement above 70%. Similarly,

in the FBC Group 74% had peak flow ranging from 30 to 70%. After treatment there is improvement in all the subjects 57% of them had peak flow more than 70%. This is the contrasting difference.

Table 9: Assessment of Pulmonary Function Tests in Patients with Moderate Persistent Asthma

Group	Mean FEV1 Pre Pred%	Mean FEV1 Post Pred%	Mean FEV1 Change%	Mean PEFR Pre Pred%	Mean PEFR Post Pred%	Mean PEFR Change%
SFC(n=42)	71.12	84	18.50	49.83	60.09	21.98
FBC(n=42)	69.98	86.76	24.12	53.40	69.19	32.12

(FEV1 - P = 0.008) (PEFR - P = 0.003)

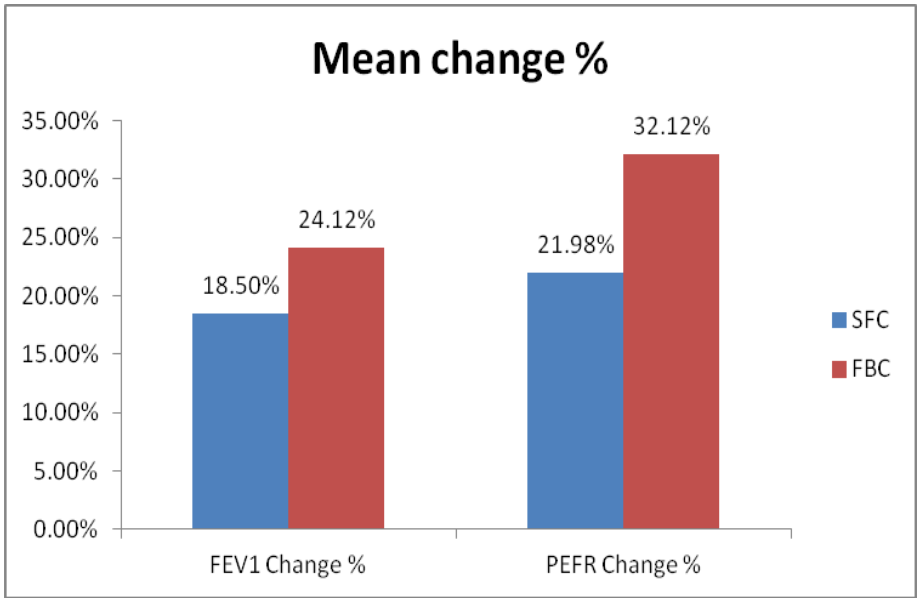

Figure 10: Corresponding Bar Diagram

A glance at the table showing FEV1 and PEFR changes in both the Groups of SFC and FBC there was global improvement of the bronchoconstriction however in the FBC Group the bronchodilator effect was significant (P = 0.008) for FEV1 and (P= 0.003) for PEFR.

Gina Assessment of Asthma Control in Adults, Adolescents and Children 6-11 Years [12]

Table 10:

Asthma Symptom Control		Level of Asthma Symptom Control
In the past 4 weeks, has the patient had	Well Controlled	Partly controlled Uncontrolled
1. Day time symptoms more than twice a week?	Yes No	
2. Any night waking due to Asthma?	Yes No	(None of these) (1 - 2 of these) (3 - 4 of these)
3. Reliever needed for symptoms more than twice a week?	Yes No	
4. Any activity limitation due to asthma?	Yes No	

Table 11: Level of Symptom Control, Post Treatment with Seroflo (SFC)

SFC Group (N= 42)	Well Controlled	Partially Controlled	Uncontrolled
	78.5% (33)	16.6% (7)	4.7% (2)

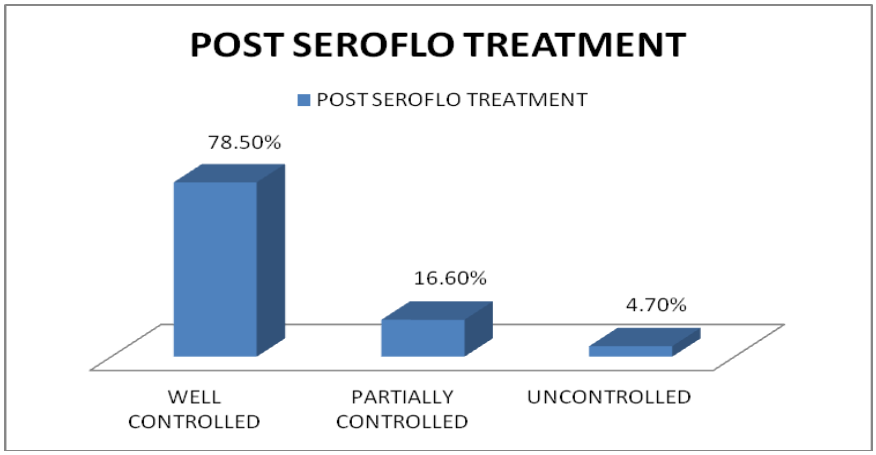

Figure 11: Its Corresponding Bar Diagram

Table 12: Level of Symptom Control, Post Treatment with Foracort (FBC)

FBC Group (N=42)	Well Controlled	Partially Controlled	Uncontrolled
	92.8% (39)	7.14% (3)	0% (Nil)

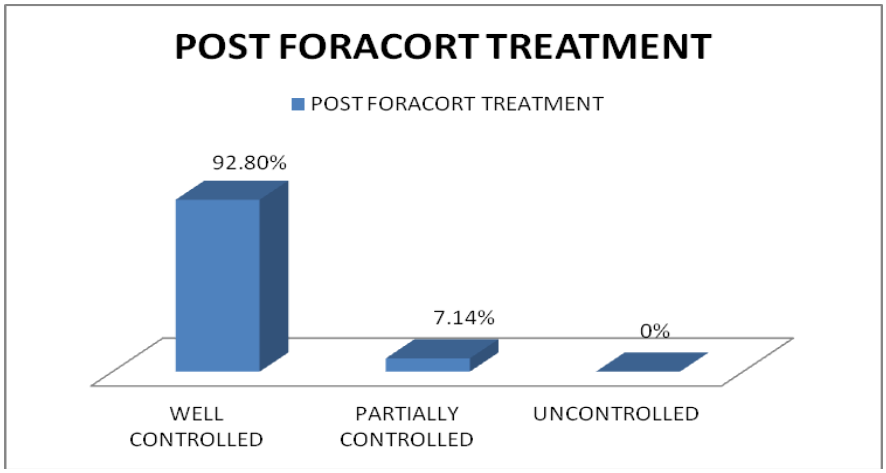

Figure 12: Its Corresponding Diagram

In the above tables, the SFC Group showed the status of Bronchospasm. In both the groups of SFC and FBC there was broncho dilatation for the sake of analysis subjectively they are classified into Well Controlled, partially controlled, uncontrolled. Thus, it was found that 78.5% of the subjects in SFC Group were well controlled. Whereas the FBC Group 92.8% were well controlled. Furthermore 4.70% were uncontrolled, contrastingly in the FBC Group none had this.

Discussion

The study was conducted in the department of pulmonology OPD in MIMS after clearance by the ethical committee and consent of the persons from July 2014 to July 2015.

This study consisted of 0f 100 subjects who fit in the inclusion criteria. They had been randomly allocated in two groups. SFC and FBC respectively, 50 in each group. After thorough history, clinical examination, Pulmonary function tests were done. Among 100 subjects, 11 patients did not come for the follow up and 5 patients were excluded from the study as they did not stick to the protocol.

The main objectives of the study were,

1) Compare the acceptability.
2) Better therapeutic efficacy
3) Cost effectiveness

As the persons having mild bronchospasm do have relief on their own, they are less likely to seek medical aid. As a corollary, subjects with acute bronchospasm will be necessarily treated as indoor patients. So, this study is confined to moderately persistent bronchial asthma as per GINA Guidelines. The subjects were included as per the inclusion and exclusion criteria. Many of the local people are nescient of the term bronchial asthma, culling us to develop an educative manual for the same and evolving a questionnaire for our study. This gave us an objective assessment of the symptom com-

plex along with the relief at the end of the study. The demographic analysis exhibited an identical intake of the sample. The SFC Group had 22 males and 20 females with mean age of 46 in SFC Group and the FBC Group had 24 males and 18 females with mean age of 44.9. This is in consonance with a similar study done by Jindal SK, et al.[13] Overall prevalence of asthma was respectively 2.05% (adults aged ≥15 years) and 3.49% (adults aged ≥35 years). Childhood asthma can reappear later in life precipitated with factors like atmospheric pollution habits and occupation.

There were 45% smokers in SFC Group and 41% in FBC Group with less than 10 pack years history. Albeit this tobacco habit may change bronchial asthma into asthma-COPD overlay, culminating in moderate persistent asthma. The classical symptom of bronchial asthma is Wheeze. Nevertheless, it may be a symptom complex with cough as a feature. According to GINA Guidelines moderate persistent asthma envisages Cough, Wheeze, Breathlessness and Nocturnal symptoms.

The subjects included in the study were clinically examined by the pulmonologist considering parameters of complete blood picture, chest X-ray and PFT besides thorough clinical examination. All these people had symptoms of dyspnea characterized by alar flare, purse lip breathing, accessory muscles overlay and rhonchi. The concomitant infection was ruled out by absence of expectoration, fever, and other toxic features. Furthermore, complete blood picture was normal in all these people. The chest skiagram was within normal limits and ruled out other co morbidities. Allowance was given for fidgety hyperinflation of the lungs, as is expected in this clinical sample. Dyspnea due to cardiac, renal, and hepatic causes was ruled out clinically. Both the groups had the symptom complex of cough, wheeze, breathlessness, and nocturnal dyspnea. A scrutiny of the therapeutic comparison revealed that the FBC Group fared better in comparison to the SFC Group as far as the symptom complex is concerned. Specifically, 86% did not have the irritating nocturnal dyspnea. The patients were explained how to take the Rota cap with rotahaler as this is the fundamental step in the effective relief from bronchospasm. It is noteworthy to recall that only 15 to 20% of the medication goes to the lower airways. Hence, the correct usage of the Rota haler with Rota cap was demonstrated to the patient. This consists of using a Rota cap with Rota haler of Cipla pharmaceuticals, The Rota haler consists of 2 parts, the upper part and lower part. The upper one has multiple sieves, a wide oral conduit through which the medicament is inhaled into the airways. There is also a small portal for the Rota cap. This can be smuggly fitted into the side portal, once the capsule is put the upper portion rotates, the capsule breakdown, because of a sharp partition in the upper portion. As a result, the capsule breakdown and the powder is released in the container after shaking this the person inhales through the conduit meant for the same, coinciding with the inspiration. Often only 15 to 20 % of the drug entrains the airways via larynx conversely, but much of this will also be sticking in the oropharynx so the user was instructed to rinse the mouth with water after the use. Frequently the failure of the treatment is due to improper usage of this implement with the drug. Adding insult to the injury, the entry of the drug depends on the patency of the oropharyngeal lumen.

The clinical examination showed signs of dyspnea such as alar flare, purse lip breathing, accessory muscles interaction along with audible rhonchi in the lungs. None of them had acute severe asthma. They also did not have any other comorbid conditions. Coming to the hematological investigations by enlarge were within normal limits. The chest skiagram in few cases showed mild hyperinflation otherwise there was no evidence of any active infection in terms of pneumonitis or Kochs lesions. The main crux of the investigations were pulmonary function tests. The Pre and Post FEV1 in SFC Group showed on an average 18.5 % reversibility whereas Ronald Dahl, et al.[14] found reversibility by 12% using accuhaler in series of 694 patients, their subjects had persistent asthma and currently receiving 1000 to 2000 micro grams per day of inhaled corticosteroids. However, this proves the utility of SFC that study was multicentric and they allowed ancillary medication as and when required. In our study they were excluded. Similarly, Akamatsu T, et al,[15] a Japanese study showed the efficacy of SFC in their series of 66 patients with mild to moderate asthma, with the usage of diskus and turbuhaler which are certainly costly in our setup. The same studies (ibid) conducted comparison of SFC versus FBC using different implements and strategy Akamatsu in his series of 61 patients switched from SFC to FBC after some time and found that it was useful, they attributed this to the particle size in the turbuhaler delivering FBC than the SFC Diskus particles. They propounded that with FBC Group the particles reached as far as small airways attributing it to the delivery by turbuhaler.

Ronald Dahl, et al.[14] compared FBC with SFC, it was a multicentric double-blind, double dummy, randomized 24 week study using accuhaler or Diskhaler, they opined that twice daily treatment with SFC and FBC over 6months significantly improved asthma symptoms, they concluded that SFC was found to be significantly superior to FBC However it was noteworthy they were persistent asthmatics with prior treatment of 1000 to 2000 micro grams per day of inhaled corticosteroids. This study was done in Denmark.

The study of Akamatsu in their study in Japan found relative improvement in the asthma control questionnaire when they switched to FBC from SFC after 8 weeks of usage of SFC.

The fixed dosage of SFC contained 50 / 250 micro grams of salmeterol and fluticasone. The FBC had 9/320 micro grams of formoterol and budesonide. Their study contained mild to moderate asthmatics, the asthma control questionnaire (ACQ5) Score consisted of Peak Expiratory Flow, Spirometry, FeNO, alveolar NO concentration (CANO) and maximal NO flux in the conducting airways. Based on this they concluded that FBC Group fared better than SFC Group although there was no improvement in the pulmonary function tests in asthma patients.

In the present study the previous treatment history was not considered as all of them had only SOS treatment from the local available sources. Over and above the Rota haler is much more cost effective compared to the sophisticated Disk haler, turbuhaler and accuhalers used elsewhere for the clinical sample included in included here. Another redeeming point is in our study the concentration of formoterol is 6 micro grams and budesonide 200 micrograms in comparison to that of Akamatsu FBC concentration. Thus, the present study seems to be better than both the studies of Akamatsu and Dahl as the FEV1 mean change percentage was 18% in SFC and 24% in FBC Group (P= 0.008) as regards the peak flow is concerned, the findings are parallel to that of FEV1.

The improvement in FEV1 for 84 subjects Post treatment was observed by reading the difference of Post treatment and Pretreatment FEV1 values and the Change percentage has been observed (Post best- Pre best / Pre best x 100) for each patient.

The mean percentage change was calculated for each group SFC and FBC respectively. As mentioned above, the mean improvement in FEV1 values i.e. (Post predicted minus pre predicted) and mean change % for FBC group revealed significant improvement when compared to the other group SFC group.

Tunceli and Williams, et al.[16] from USA published a retrospective, cohort, compared to effectiveness of FBC and SFC .Their series consisted of 3043 patients per cohort matched and balanced .They found during the 12 months following the initiation, the FBC Group had lower exacerbations per person per year versus SFC Cohort .They concluded that FBC was better in comparison to SFC taking into consideration of lower oral corticosteroid fill rates ,and fewer asthma related emergency. Though this was a retrospective study this highlighted the treatment of moderate to severe persistent asthma and concluded lesser exacerbations in the FBC Group. As a corollary ours is a prospective, comparative trial with a simple Rotahaler and lesser dosage of formoterol and budesonide.

From the above it is clear that formoterol budesonide combination is better in comparison to the salmeterol fluticasone combination considering the lesser no of exacerbations and bronchodilator effect, both salmeterol and formoterol being long-acting bronchodilators.

The Peak Expiratory Flow Rate for each subject has been calculated, the improvement in PEFR has been observed in the table- 9, the mean change percentage for SFC group was 21.98 whereas for FBC it was 32.12, the significant improvement in FBC was noted (P= 0.003). This improvement is parallel to the change in FEV1. These facts are in unison with the above studies, done elsewhere. The symptom-wise assessment was done consulting the questionnaire framed for the study. The symptom control wise as per the questionnaire, the assessment was done. This once again shows that vast majority (92.8%) had well controlled bronchospasm in comparison to 78.5% only in the SFC group, this subjective assessment has correlated with the objective assessment by FEV1 and Peak flow nonetheless there is global sense of improvement in the FBC group. Both the groups' acceptability of the drug was good as there were no reported side effects. The intake of the medicine was counter checked with the exhaustion of the Rota caps containers.

Thirty Rota caps of SFC cost INR 240/-. The total cost of the treatment is INR 480/- for thirty days. In comparison, 30 FBC Rota capscost INR 151/- and the total cost is INR 332/-, which is much less than the former. Probably, this may be the mainstay of treatment for these categories of patients. The ease of self-administration(bid), potability, and minimal side effects, such as tachycardia are the features of both SFC and FBC. However, the cost factor wise and the objective evidence of PFT tilt the favor towards the FBC.

Not only but also, the rank order of beta agonist potency was formoterol ≥ salmeterol ≥ clenbuterol >fenoterol = isoprenaline > terbutaline ≥ albuterol >quinprenaline. Another added advantage is that the onset of action of formoterol is quicker, thus giving the effect of a short acting bronchodilator.[17] In fact, SABA can be avoided, if these LABAS can control the bronchospasm. In this study, the dosage contained in the available preparation of FBC is less than the ones quoted in the earlier studies. Hence, in the present study, other aspects of the better therapeutic effect are also envisaged.

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