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Original Research Article

Spirometric Evaluation in Asthmatics Taking Formoterol/Budesonide V/S Salmeterol/Fluticasone

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Abstract: Asthma is 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. Formoterol is a long-acting (12 hours) beta2-agonist used in the management of asthma and/or chronic obstructive pulmonary disease (COPD). Inhaled formoterol works like other beta2-agonists, causing broncho dilatation through relaxation of the smooth muscle in the airway so as to treat the exacerbation of asthma. Budesonide is a glucocorticoid used in the management of asthma, the treatment of various skin disorders, and allergic rhinitis. The extended release oral tablet, marketed as Uceris, was FDA approved on January 14, 2013 for the management of ulcerative colitis. Budesonide is provided as a mixture of two epimers (22R and 22S). Interestingly, the 22R form is two times more active than the 22S epimer. Salmeterol is a long-acting β2 adrenergic receptor agonist (LABA) used in the maintenance and prevention of asthma symptoms and maintenance of chronic obstructive pulmonary disease (COPD) symptoms. Fluticasone is a synthetic glucocorticoid. It prevents the release of substances in the body that cause inflammation.
Keywords: LABA-Long acting β2 adrenergic receptor agonist (LABA), COPD -Chronic obstructive pulmonary disease, FEV1- Forced expiratory volume in 1 second, PEF-Peak expiratory flow rate, FVC-Forced vital capacity, ICS- Inhaled corticosteroids.

INTRODUCTION

Asthma is 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. Asthma is a common, chronic respiratory disease affecting 1–18% of the population in different countries.

Asthma is characterized by variable symptoms of wheeze, shortness of breath, chest tightness and/or cough, and by variable expiratory airflow limitation [1]. Both symptoms and airflow limitation characteristically vary over time and in intensity. These variations are often triggered by factors such as exercise, allergen or irritant exposure, change in weather, or viral respiratory infections.

Symptoms and airflow limitation may resolve spontaneously or in response to medication, and may sometimes be absent for weeks or months at a time. On the other hand, patients can experience episodic flare - ups (exacerbations) of asthma that may be life-threatening and carry a significant burden to patients and the community. Asthma is usually associated with airway hyper responsiveness to direct or indirect stimuli, and with chronic airway inflammation .

Asthma is characterized by variable expiratory airflow limitation, i.e. expiratory lung function varies over time and in magnitude to a greater extent than in healthy populations. In asthma, lung function may vary between completely normal and severely obstructed in the same patient.

Poorly controlled asthma is associated with greater variability in lung function than well-controlled asthma [2]. Lung function testing should be carried out

by well-trained operators with well-maintained and regularly calibrated equipment [3].

Forced expiratory volume in 1 second (FEV1) from spirometry is more reliable than peak expiratory flow (PEF).

If PEF is used, the same meter should be used each time, as measurements may differ from meter to meter by up to 20% [3].

A reduced FEV1may be found with many other lung diseases (or poor spirometric technique), but a reduced ratio of FEV1to FVC indicates airflow limitation. From population studies [4], the FEV1/FVC ratio is normally greater than 0.75 to 0.80,and usually greater than 0.90 in children. Any values less than these suggest airflow limitation. Many spirometers now include age-specific predicted values.

In clinical practice, once an obstructive defect has been confirmed, variation in airflow limitation is generally assessed from variation in FEV1or PEF. 'Variability' refers to improvement and/or deterioration in symptoms and lung function. Excessive variability may be identified over the course of one day (diurnal variability), from day to day, from visit to visit, or seasonally, or from a reversibility test.

'Reversibility' generally refers to rapid improvements in FEV1(or PEF), measured within minutes after inhalation of a rapid-acting bronchodilator such as 200–400 mcg salbutamol [5], or more sustained improvement over days or weeks after the introduction of effective controller treatment such as ICS [5]. Generally, in adults with respiratory symptoms typical of asthma, an increase or decrease in FEV1 of >12% and >200 mL from baseline, or (if spirometry is not available) a change in PEF of at least 20%, is accepted as being consistent with asthma.

Airflow limitation may be absent at the time of initial assessment in some patients. As documenting variable airflow limitation is a key part of establishing an asthma diagnosis, one option is to refer the patient for bronchial provocation testing to assess airway hyperresponsiveness. This is most often established with inhaled methacholine, but histamine, exercise [6] eucapnic voluntary hyperventilation or inhaled mannitol may also be used. These tests are moderately sensitive for a diagnosis of asthma but have limited specificity [7, 8] for example, airway hyper responsiveness to inhaled methacholine has been described in patients with allergic rhinitis [9], cystic fibrosis [10], bronchopulmonary dysplasia [11] and COPD [12].

MATERIALS & METHODS

This study was conducted on patients, who were either admitted or attended the outdoor in Department of Tuberculosis and Respiratory diseases at Govt. Medical College, Amritsar and were diagnosed as asthmatics. Patient were diagnosed as asthmatics on the basis of history of episodic breathlessness, early morning symptoms, night symptoms and post bronchodilator increase in FEV1 of more than 12%. Generally, in adults with respiratory symptomstypical of asthma, an increase or decrease in FEV1of >12% and >200 mL from baseline, or (if spirometry is not available) a change in PEF of at least 20%, is accepted as being consistent with asthma

For post bronchodilator test, patient is given 2 puffs of salbutamol 100 microgram each and lung function evaluation is done after 20 minutes. 12 % increase in FEV1 favors diagnosis of asthma. Patients showing 12% or more increase in FEV1 over baseline were included in the study. Then among patients diagnosed as asthmatics only the patients qualifying for step III of bronchial asthma according to GINA guidelines i.e.-

-Patients has symptoms of asthma daily
-Uses inhaled short acing beta-2 agonists daily
-Exacerbations affect activity
-Exacerbations at least twice weekly and may last for days
-Nocturnal symptoms more frequently than once weekly
-FEV1/PEFR exceeds 60 % but is less than 80 % of predicted or best
-PEFR variability > 20%

Fifty patients of Step III were included in the study. Routine investigations of every patient i.e. Hb, TLC, DLC, ESR, FBS, Chest x-ray was done. Patient were guided about the use of rotahaler in the prescribed manner .Only the patients who can generate proper flow rate from rotahaler were included in the study. Children under 6years of age were not included in this study as use of rotahaler is not recommended in them. As they cannot generate the proper flow rate of 6litre/minute from rotahaler. Prior to each study day, inhaled short-acting beta2 agonists was withheld for at least 8 hours prior to receiving the drug, Long-acting β2 agonist will be withheld for at least 72 hours & leukotriene antagonists and anticholinergics for at least 12 hours.

Patient were evaluated spirometrically in the department of Tuberculosis & Respiratory diseases at Govt. Medical College, Amritsar using spirometer which also gave the 'predicted values' of FEV1 & PEFR of each patient which depend on patients height, weight, age, sex & environmental temperature.

Patients were instructed to take a deep breath as deep as possible (upto total lung capacity) & then exhale into the mouth piece of spirometer with full force and speed till he can squeeze no more air out of

his lungs (upto residual volume) patients were instructed to seal their lips tightly around the mouth piece of spirometer to prevent leakage. Best of 3 readings was taken for record.

Patients were divided randomly in 2 groups of 25 each. Half the patients (25 out of 50) were advised to take inhaled salmeterol (50 µg BID) and inhaled fluticasone (100 µg BID) in combination & were assigned as group I. Remaining 25 will be advised to take inhaled formoterol (6 µg BID) and inhaled budesonide (200 µg BID),in combination & were assigned as group II. Drugs were in the form of Rotacaps, administered with the help of Rotahaler.
After using single dose of each drug i. e Salmeterol 50µg, Fluticasone 100 µg in combination and Formoterol 6 µg & budesonide 200µg. Spirometry was done again to see the onset of action. Serial measurement of FEV1 was done every 2 minute for 6 min and then every 5 minutes. In the first 6 minutes single value of FEV1 was taken, thereafter best of 3 values was taken. Improvement of 12% from the baseline was taken as onset of bronchodilation. Patients were followed up for a period of 1 month after giving single dose of each drug i. e Salmeterol 50µg, Fluticasone 100 µg in combination and Formoterol 6 µg & budesonide 200µg. Spirometry was done again to see the onset of action.

RESULTS & DISCUSSION

The present study was conducted on patients who qualify for step III of bronchial asthma according to GINA guidelines in Department of Tuberculosis & Respiratory disease, Amritsar. 50 patients were included in study following observations were made. Group I has total of 25 patients (16 males & 9 females) ,Group II has 25 patients (14 males & 11 females)

The table-1 shows that in patients of group 1 the onset of action is less than 15 minutes evidenced by improvement in FEV1 of more than 15 % following inhalation of single dose of salmeterol 50 µg and fluticasone 100 µg.

The table-2 shows that all patients in group 2 showed onset of action of less than 3 minutes evidenced by improvement in FEV1 of more than 15 % following inhalation of formoterol 6µg and Budesonide 200 µg.

Table 1: Improvement in FEV1 following inhalation of single dose of Salmeterol 50µg Fluticasone 100 µg in Group I

Sl no.	Pre-bronchodilator value of FEV1 in litres	Post-bronchodilator value of FEV1in litres	Improvement in FEV1 in %	Time of onset of action in minutes
1	1.29	1.63	26.4	15
2	1.28	1.58	23.4	15
3	1.40	1.69	20.7	15
4	1.32	1.58	19.7	15
5	1.44	1.69	17.4	15

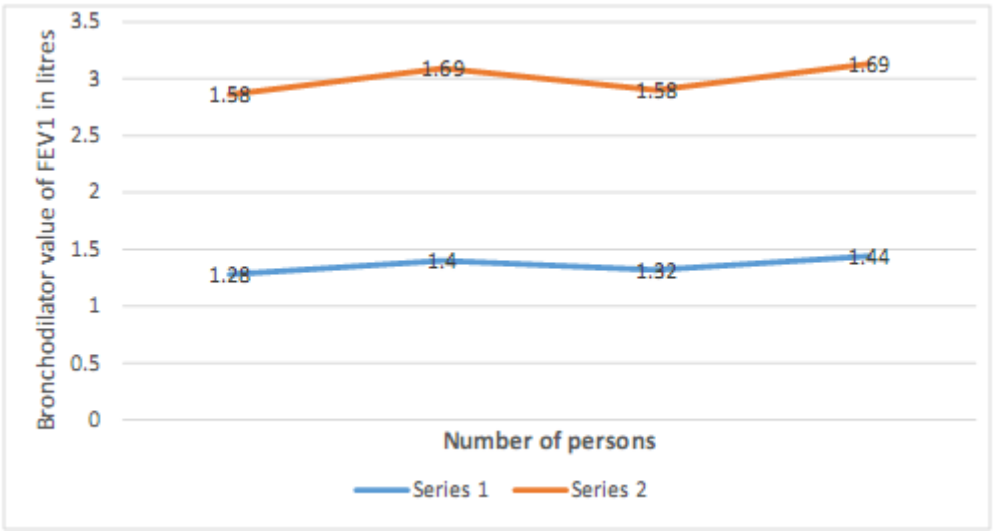

Fig-1: Graph showing improvement in FEV1 following inhalation of single dose of Salmeterol 50µg Fluticasone 100 µg in Group I

Table 2: Improvement in FEV1 following inhalation of single dose of Formoterol 6µg and Budesonide 200 µg in Group II

Sl no.	Pre-bronchodilator value of FEV1 in litres	Post-bronchodilator value of FEV1 in litres	Improvement of FEV1 in % age	Time of onset of action in minutes
1	1.06	1.36	28.3	3
2	1.11	1.32	20.1	3
3	1.20	1.31	21.1	3
4	1.40	1.28	18.2	3
5	1.06	1.31	27.1	3

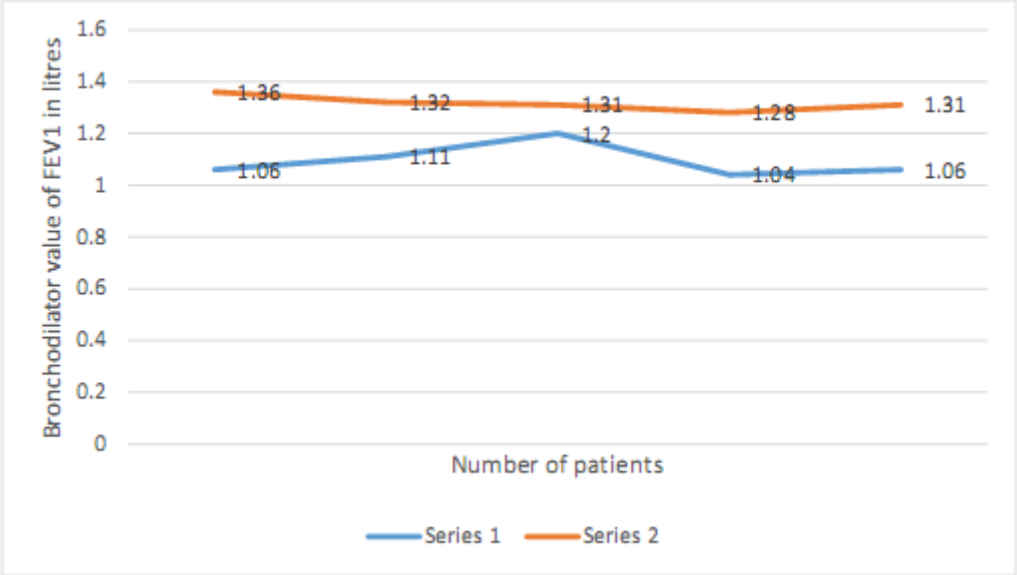

Fig-2: Graph showing improvement in FEV1 following inhalation of single dose of Formterol 6µg and Budesonide 200 µg in Group 2

All patients showed onset of action of less than 10 minutes evidenced by improvement in FEV1 of more than 15 % following inhalation of single dose of Salmeterol 50µg & fluticasone 100µg All patients showed onset of action of less than 3 minutes evidenced by improvement in FEV1 of more than 15 % following inhalation of single dose of formoterol 6 µg and budesonide 200 µg.

CONCLUSIONS

After using single dose of each drug i.e Salmeterol 50µg & fluticasone 100µg in combination & Formoterol 6 µg and budesonide 200 µg, spirometry was done to see the onset of action. Serial measurement of FEV1 was done every 5 minutes for 30min.Improvement of 12% from the baseline was taken as onset of bronchodilation & patients not responding even at 3 hour were taken as non-respondents.

The present study was conducted to see the onset of action of bronchodilation of salmeterol & formeterol. Time of onset of action of bronchodilation of formoterol proved to be faster than salmeterol in cases of formoterol being within 5 minutes while in cases of salmeterol being within 15 minutes. Both salmeterol & formeterol showed significant improvement at 1 month which was marginally but not significantly higher for formoterol. The results of the study were similar in both the sexes and all age groups.

So formeterol has rapid onset of action than salmeterol while their long term effects are same.

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