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 FEV1 may be found with many other lung diseases (or poor spirometric technique), but a reduced ratio of FEV1/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 FEV1 or 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.

 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 acting 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 instructed to take a deep breath and speed till he can squeeze no more air out of

 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 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.

 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 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.

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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 50µg 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

<table>
<thead>
<tr>
<th>Sl no.</th>
<th>Pre-bronchodilator value of FEV1 in litres</th>
<th>Post-bronchodilator value of FEV1 in litres</th>
<th>Improvement in FEV1 in %</th>
<th>Time of onset of action in minutes</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1.29</td>
<td>1.63</td>
<td>26.4</td>
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<td>1.58</td>
<td>23.4</td>
<td>15</td>
</tr>
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<td>3</td>
<td>1.40</td>
<td>1.69</td>
<td>20.7</td>
<td>15</td>
</tr>
<tr>
<td>4</td>
<td>1.32</td>
<td>1.58</td>
<td>19.7</td>
<td>15</td>
</tr>
<tr>
<td>5</td>
<td>1.44</td>
<td>1.69</td>
<td>17.4</td>
<td>15</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Sl no.</th>
<th>Pre-bronchodilator value of FEV1 in litres</th>
<th>Post-bronchodilator value of FEV1 in litres</th>
<th>Improvement of FEV1 in % age</th>
<th>Time of onset of action in minutes</th>
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<tbody>
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<td>1.36</td>
<td>28.3</td>
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<td>3</td>
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<td>3</td>
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<td>4</td>
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<td>1.28</td>
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<td>3</td>
</tr>
<tr>
<td>5</td>
<td>1.06</td>
<td>1.31</td>
<td>27.1</td>
<td>3</td>
</tr>
</tbody>
</table>

![Graph](Image)

**Fig-2: Graph showing improvement in FEV1 following inhalation of single dose of Formoterol 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.

**CONCLUSION**

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

**REFERENCES**


2. Reddel H, Ware S, Marks G, Salome C, Jenkins C, Woolcock A; Differences between asthma exacerbations and poor asthma control. erratum in Lancet, 1999; 353:758.


