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Clinic Asthma Control Test Based Control Assessment in Asthma Patients on Combined ICS and LABA

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ABSTRACT

BACKGROUND: Asthma is a chronic disease involving the inflammation of the air passages in the lungs and affects the sensitivity of the nerve endings in the airways, so they become easily irritated. Asthma attacks all age groups but often starts in childhood. Inhaled glucocorticoids and long-acting beta agonists (LABAs) have a well-established effectiveness for treating Asthma can be used as treatment option in severe persistent asthmatics with standard treatment guidelines. **OBJECTIVE:** The objective of the study was to evaluate the clinic asthma control test based control assessment in asthma patients on combined ICS and LABA in a patient population via observing the respective changes in lung volumes and capacities of individual patients by performing pulmonary function test. **METHODS:** The study is a prospective observational study within subject comparison carried out in a multi-speciality hospital, in the department of pulmonary medicine. Subjects enrolled based on the past diagnosis of asthma with FEV1 less than 80%, history of nighttime exacerbation. Patients were subjected pulmonary function test in order to obtain baseline FEV1 and PEFR the first visit and then in the second visit (after 12 weeks) SF in the dose 250mcg was prescribed as once daily inhalation of 2puffs(16mcg), FF in the dose 250mcg was prescribed as once daily inhalation of 2 puffs(16mcg). After 12 weeks of therapy in the third visit detail clinical and spirometric analysis were performed. The significant improvement in clinical as well as spirometric parameters is statistically analyzed to make conclusion. **RESULTS:** Out of 60 patients enrolled, Subjects (n=60) showed significant improvement in both clinical as well as spirometrical outcomes. FEV1 is improved with the use of Formoterol/Fluticasone and Salmeterol/Fluticasone, Mean difference of percentage predicted=11.083% and PEFR improved with the use of Formoterol/Fluticasone and Salmeterol/Fluticasone, Mean difference of percentage predicted=48.33%, with respect to baseline which is statistically significant (P<0.005). Clinically, the mean controlled score for group I subjects (Salmeterol/Fluticasone) was score 20. The mean controlled score for group II subjects (Formeterol/Fluticasone) was score 23. **CONCLUSION:** In patients with poorly controlled asthma despite the use of inhaled glucocorticoids and LABAs, the addition of FF in the dose of 250 mcg once daily via dry powder inhaler can result in 24 hour bronchodilation as well as with respect to Asthma control test was found to be more consistent compared to SF and resulted in sustained improvement for asthma.

INTRODUCTION

Asthma is defined as a chronic inflammatory disorder of airways in which many cells and cellular elements play a role in particular mast cells, eosinophils, T lymphocytes, macrophages, neutrophils and epithelial cells.[1] A combination of genetic and environmental factors can cause asthma or increase sensitivity to asthma triggers.[2] Asthma is considered severe persistent if without treatment any of the following are true: Symptoms Occur throughout each day, Severely limit daily physical activities, Nighttime symptoms occur often, sometimes every night, Lung function tests are abnormal (60% or less of expected value), and PEF varies more than 30% from morning to afternoon.[4]

In the early stages, when ventilation-perfusion mismatch results in hypoxia, hypercarbia is prevented by the ready diffusion of carbon dioxide across alveolar capillary membranes [3]. Thus, patients with asthma who are in the early stages of an acute episode have hypoxemia in the absence of carbon dioxide retention. Hyperventilation triggered by the hypoxic drive also causes a decrease in PaCO2[13]. An increase in alveolar ventilation in the early stages of an acute exacerbation prevents hypercarbia. With worsening obstruction and increasing ventilation-perfusion mismatch, carbon dioxide retention occurs. In the early stages of an acute episode, respiratory alkalosis results from hyperventilation[7]. Later, the increased work of breathing increases oxygen consumption and increases cardiac output result in metabolic acidosis. Respiratory failure leads to respiratory acidosis due to retention of carbon dioxide as alveolar ventilation decreases.[5]

Medications for asthma are Long term control medications used to achieve and maintain control of persistent asthma and quick relief medications used to treat acute symptoms and exacerbations such as Corticosteroids which are the most potent and effective anti-inflammatory medication currently available (evidence A) ICSs are used in the long term control of asthma[8]. Short courses of oral systemic corticosteroids are often used to gain prompt control of the disease when initiating long term therapy, long term oral systemic corticosteroids is used for severe persistent asthma.

Salmeterol and formoterol are bronchodilators that have duration of bronchodilators of at least 12 hours after a single dose – LABA are not to be used as monotherapy for long term control of asthma (evidence A).[9]

LABA are used in combination with ICSs for long term control and prevention of symptoms in moderate or severe persistent asthma (step 3 care or higher in children >/ 5 years of age and adults).[6]

Of the adjunctive therapies available LABA is the preferred therapy to combine with ICSs in youth >/12 years of age and adults.[11]

In the opinion of the expert panel, the beneficial effects of LABA in combination therapy for the great majority of patients who require more therapy than low dose (ICS alone to control asthma.[12]

LABA is used before exercise to prevent EIB (Evidence A). But duration of action does not exceeds 5 hours with chronic regular use. Frequent and chronic use of LABA for EIB is discouraged, because this use may disguise poorly controlled persistent asthma (evidence D).[13]

In the opinion of expert panel, the use of LABA for the treatment of acute symptoms of exacerbations is not currently recommended (evidence D).[7]

ASTHMA CONTROL TEST:

Asthma control test is a five-question survey used to measure asthma control in individuals 12 years of age and older. The survey measures the elements of asthma control as defined by the National Heart, Lung and Blood Institute (NHLBI).

Why to take asthma control test:

The asthma control test will provide a snapshot of how well asthma has been controlled over the last 4 weeks, giving a simple score out of 25. Asthma symptoms can vary from month to month, so it is worth keeping the test handy to see if score changes. [10]

OBJECTIVES

- To determine efficacy of combination therapy LABA+ICS.
- To determine the respective changes in the lung volumes and capacities of individual patients by performing PFT.
- Effects on Asthma exacerbations.

- To improve quality of life.

METHODOLOGY

A 6-month trial with 60 asthmatic patients were carefully selected with a typical history of asthma and documented significant reversibility, PEFR variability and hyperresponsiveness. Subjects were also enrolled based on the history of nighttime exacerbation. Patients were subjected to pulmonary function test in order to obtain baseline FEV1 and PEFR the first visit and then in the second visit(after 12 weeks) SF in the dose 250mcg was prescribed as once daily inhalation of 2puffs(16mcg), FF in the dose 250mcg was prescribed as once daily inhalation of 2 puffs(16mcg). After 12 weeks of therapy in the third visit detail clinical and spirometric analysis were performed. The significant improvement in clinical as well as spirometric parameters is statistically analyzed to make conclusion.

RESULTS

In our study of "clinic asthma control test based control assessment in asthma patients on combined ICS and LABA" we have enrolled 60 patients with severe persistent asthma following the inclusion criteria set up (n=60). Out of 60 enrolled patients (n=30), patients responded to SF i.e., Salmeterol and Fluticasone (50%), and the remaining n=30 patients have responded to the FF i.e., Fluticasone and Formoterol (50%)in the ongoing therapy of inhaled corticosteroids and long acting β- agonist. Thus, we have taken n=60 for our study and have calculated the results for n =60(changes in Pulmonary Function Test, PFT, and Peak Expiratory Flow Rate, PEFR,) and evaluated the efficacy of SF &FF based on the results on these 60 patients.

Table No. - 1 Classification of the patients enrolled in the study

SEX	MALE	FEMALE
No. of patients (%) SF	16 (53%)	14 (47%)
No. of patients (%) FF	14 (47%)	16 (53%)

Table No. - 2: classification based on age with SF

AGE (Yrs)	0-19	20-39	40-59	60-79
MALE	1	3	6	6
FEMALE	0	5	6	3

Table No. 3: classification based on age with FF

AGE (Yrs)	0-19	20-39	40-59	60-79
MALE	0	6	4	4
FEMALE	4	9	2	1

CALCULATIONS FOR CHANGES IN FEV1

The following FEV1 values are obtained after the addition of SF and FF to the ongoing therapy of ICS and LABA of severe persistent asthmatics, during a 6 months study period. The FEV1 values were taken after the use of SF and FF for a period of at least 12 weeks.

❖ **GRAPHICAL REPRESENTATION OF SF AND FF FEV_1 VALUES(**Fig 1) **:**

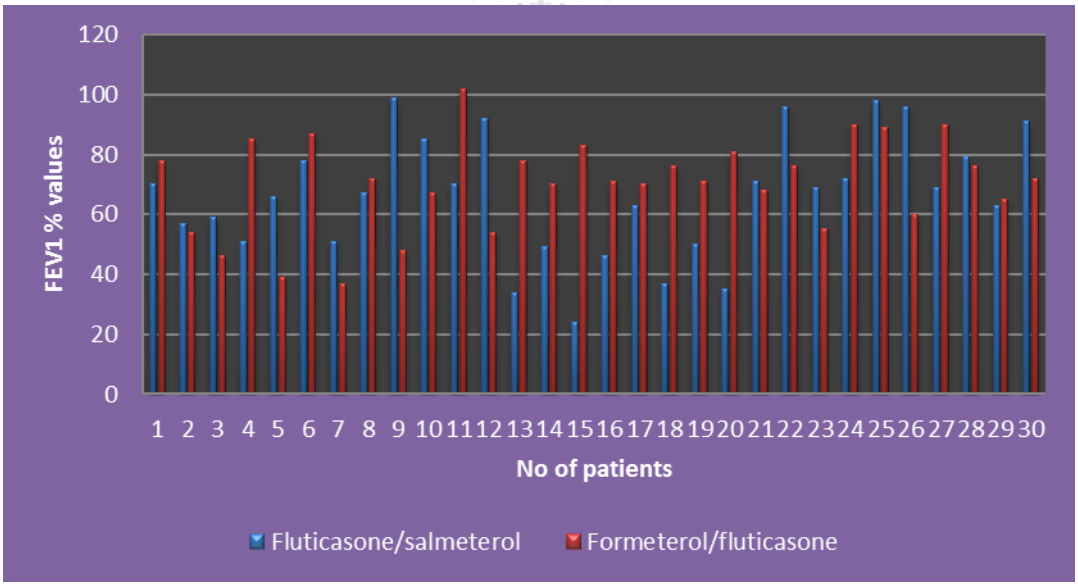

Fig No. 1 Improvement in FEV1 values with use of SF AND FF

❖ **GRAPHICAL REPRESENTATION OF DIFFERENCE OF FEV1 VALUES(**Fig 2)

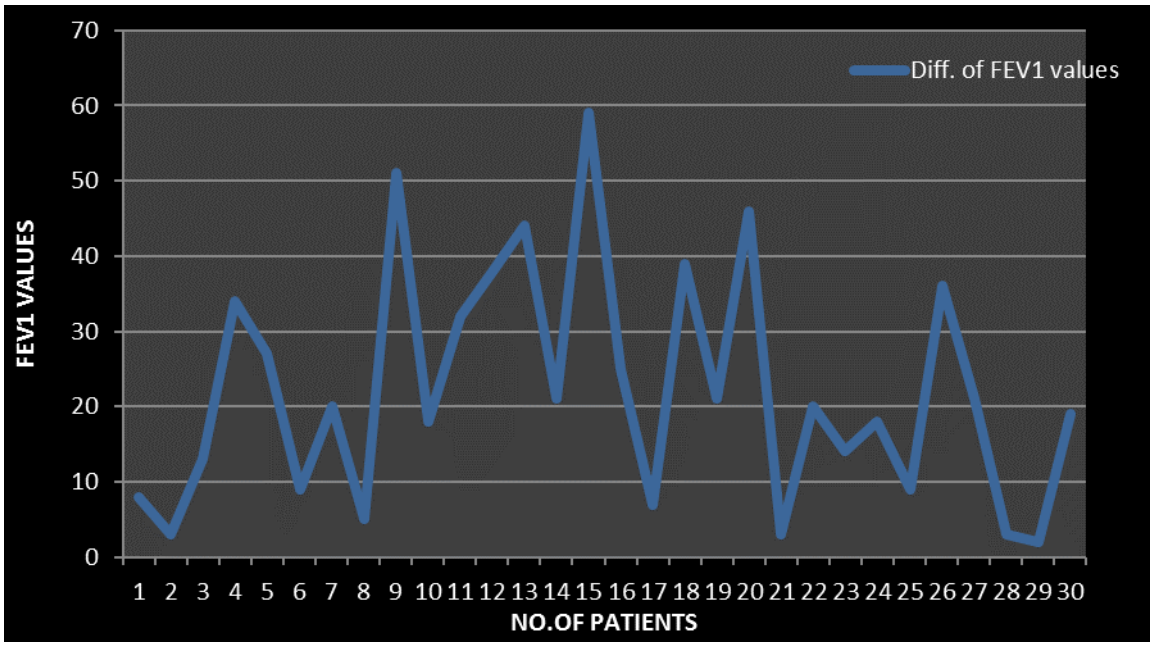

Fig No. 2 Difference of FEV1 values

The use of SF and FF in patients with asthma has shown a significant increase in the FEV1 value (shown above) with a mean of difference 11.0833**.**

CALCULATIONS FOR CHANGES IN PEFR

The PEFR values were taken after the use of SF and FF for a period of at least 12 weeks.

❖ **GRAPHICAL REPRESENTATION OF SF AND FF PEFR VALUES(**Fig 3)

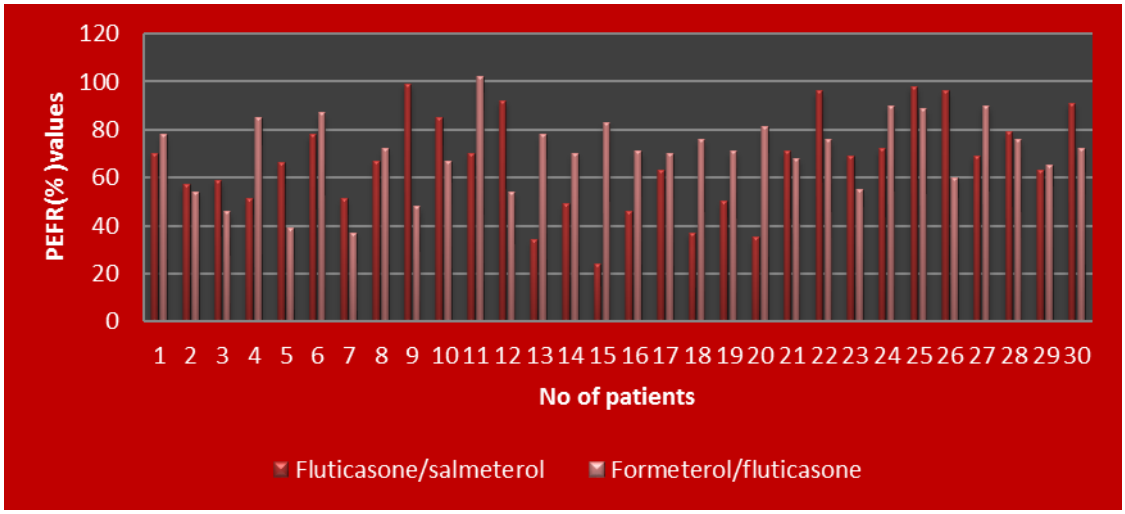

Fig No. 3: Improvement in PEFR values with use of SF AND FF.

❖ **GRAPHICAL REPRESENTATION OF DIFFERENCE OF PEFR VALUES(**Fig4)

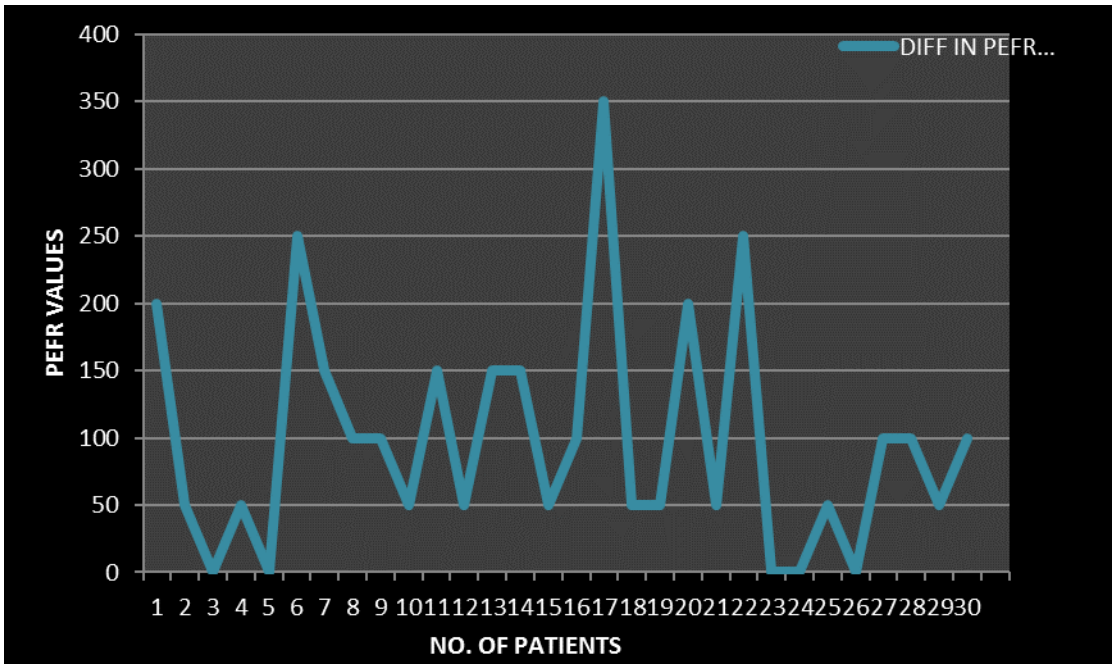

Fig No. 4: Difference of PEFR values

The use of SF and FF in patients with asthma has shown a significant increase in the PEFR value (shown above) with a mean of Difference 48.33.

• A total of 60 patients randomized for an equal distribution of 30 patients in each group ie group I (salmeterol/fluticasone), Group II (formoterol/fluticasone). The most common age group of patients who participated in the study, group I(salmeterol/fluticasone) was between 40-79years and group II(formoterol/fluticasone),was between 20-39years. Among 60 patients enrolled to study 30 were males, 30 females and some of them were smokers. Demographics data, spirometry and QOL scores of 2 groups were recorded using asthma control test questionnaire.

• The calculated student's paired ''t'' value for FEV1 and PEFR obtained from the data collected during the study period from the patient' pulmonary function test's reports peak expiratory flow meter readings is **6.28055** and **5.6312** respectively. Therefore, the null hypothesis can be rejected and the alternate hypothesis can be accepted for our study.

ASTHMA CONTROL TEST BASED QUALITY OF LIFE:

- The mean controlled score for group I subjects (Salmeterol/Fluticasone) was score 20.The mean controlled score for group II subjects (Formoterol/Fluticasone) was score 23.

- **SCORE 25: WELL DONE**: Asthma under control over the last 4 weeks

- **SCORE 20-24: ON TARGET:** Asthma reasonably well controlled during the last 4 weeks

- **SCORE LESS THAN 20: OFF TARGET:** Asthma not controlled during the last 4 weeks

CONCLUSION

This study documents a clear superiority of LABA+ICS (SF and FF) compared within asthmatic patients whose symptoms are not controlled in terms of primary and secondary spirometric endpoints at the end of 12 weeks of treatment. The observations were accompanied by better symptoms control and subjective global assessments by pulmonary function test. Significant decrease in each domains and total score as well as improvement in FEV1 ($P<0.005$) was observed in all study subjects. Maximum improvement was noted in patients receiving FF compared to SF with respect to Asthma control questionnaire and symptom treatment outcomes.

Subsequently, 2 combined ICS and bronchodilators showed similar improvement in lung functions and“Health Related Quality Of Life” throughout the study.

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