

**Comparative efficacy of inhaled ciclesonide, budesonide, and fluticasone in mild to moderately persistent bronchial asthma****Tamoghna Maiti<sup>1\*</sup>, Syed Mohammed Naser<sup>1</sup>, Amrita Panda<sup>2</sup>, Sekhar Mandal<sup>1</sup>, Sonai Mandal<sup>1</sup>, Tanmoy Gangopadhyay<sup>1</sup>, Parvin Banu<sup>3</sup>**

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**ABSTRACT**

**Background:** Bronchodilators and glucocorticoids have been proven to be very effective and safe in asthma treatment, which recommend the use of steroids and  $\beta_2$ -agonist (long or short acting) as the first line of treatment in of asthma. This study was aimed to compare the efficacy of three different inhaled corticosteroids ciclesonide, budesonide, and fluticasone in bronchial asthma.

**Methods:** A total of 30 patients with mild to moderately persistent bronchial asthma was selected as per the NAEP classification in the expert panel report (EPR) update 2002, NHLBL USA 2003. They were randomly divided into 3 groups of 10 patients each, and they were given 3 different steroid inhalers (ciclesonide or budesonide or fluticasone). Baseline and post-therapy spirometry were performed on day 1 and after 2 months and 6 months of treatment. Data were analyzed using SPSS software.

**Results:** It was observed that most of the cases (43.3%) were between 26 and 35 years of age with female preponderance (56.6%). Significant symptomatic improvement was observed in all 3 groups. The percentage of improvement in mean peak expiratory flow rate was 17%, 18%, and 18% in ciclesonide, budesonide, and fluticasone group, respectively. The percentage improvement of forced expiratory volume in 1 second (FEV1)/forced vital capacity after bronchodilatation was 18%, 18%, and 19% in ciclesonide, budesonide, and fluticasone group, respectively. The improvement in mean FEV1% predicted was 20%, 19%, and 21% in three groups, respectively.

**Conclusion:** Steroid therapy along with  $\beta_2$ -agonists showed a significant improvement in symptoms. There was no difference among the three different types of steroids.

**Keywords:** Ciclesonide, Budesonide, Fluticasone, Asthma, Spirometry

**INTRODUCTION**

Asthma meaning “panting or short-drawn breath” in Greek has been a known disease since antiquity. According to the international consensus and the global strategy for asthma management, asthma is defined as “asthma is a chronic inflammatory disorder of the airways in which many cells and cellular elements play a role. The chronic inflammation is 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 within the lung that is often reversible either spontaneously or with treatment.”<sup>1</sup>

Asthma is a problem worldwide, with an estimated 300 million affected individuals.<sup>2</sup> India has an estimated 15-20 million asthmatics in 2013.<sup>3</sup> Both mortality and morbidity due to asthma are on the rise due to increase in smoking, pollution, and occupational factors.<sup>4</sup>

Bronchodilators (long or short acting  $\beta_2$ -agonist), glucocorticoids (systemic and inhaled like beclomethasone, budesonide, flunisonide, ciclesonide triamcinolone, and

fluticasone) and anti-inflammatory agents have been proven to be very effective and safe in asthma treatment which recommend the use of steroids and  $\beta_2$ -agonist (long or short acting) as the first line of treatment in of asthma these are often very under used in the treatment of asthma particularly by the primary care physicians' world over.

### **Aims and objectives**

The aim of the study was to observe the comparative efficacy of three different Inhaled corticosteroids ciclesonide, budesonide, and fluticasone combined with long acting  $\beta_2$ -agonist, at their estimated comparative daily dose, on patients with mild to moderately persistent bronchial asthma selected from the outpatient department (OPD) and indoor patient departments (IPD).

### **METHODS**

The study included three groups of asthmatics selected from the OPD and IPD of the department of Medicine of the Bankura Sammilani Medical College. Asthmatics with mild to moderately persistent asthma as per the NAEP classification in the EPR update 2002, NHLBL, USA 2003 were included in the study. The study was conducted in the period of March 2011-April 2012.

After taking a detail history and performing general examination and systemic examination, routine investigations of blood, urine, stool and chest X-ray posterior-anterior view, sputum cytology, culture; sensitivity, sputum for acid-fast bacilli, and spirometry forced expiratory volume in 1 second (FEV1), forced vital capacity (FVC), peak expiratory flow rate (PEFR) was performed on all the subjects (30 patients). Base line spirometry and post-bronchodilatation spirometry were performed on the day of initial presentation and after 2 months and 6 months of use of a particular steroid inhaler with the equivalent dose of long acting  $\beta_2$ -agonist. Each group of patients was being put on one type of inhaled glucocorticosteroid, long acting  $\beta_2$ -agonist (salmeterol) combination (by pressurized metered-dose inhaler or rotahaler) at its comparative daily doses with the other two types of steroids used in this study (i.e., one among fluticasone propionate, budesonide). After 6 months, data were analyzed, and conclusions were drawn as to their relative clinical efficacy in the management of mild persistent and moderate persistent bronchial asthma. All the combinations were being given in twice daily dose (early morning and evening).

### **Selection criteria**

Mild to moderately persistent bronchial asthmatics without any other respiratory disease were being selected from the Department of Medicine of Bankura Sammilani Medical College Hospital. They were selected after they filled into the classification to either mild to moderately persistent type as per the NAEP classification in the EPR update 2002, NHLBL, USA 2003.<sup>5</sup>

<b>Mild persistent</b>	<b>Moderate persistent</b>
Exacerbations of cough and sneezing less than 1-2/week	Exacerbations more than 2/week
No/few signs and symptoms in between exacerbations	Cough and low grade wheezing in between exacerbations
Nocturnal asthma not more than 1-2 times/month	More than 1/week
PEFR more than or equal to 80% predicted	PEFR 60-80% predicted
PEFR variability 20-30%	More than 30%
Normal/minimal airway obstruction	Airway obstruction evident
Normal expiratory flow volume curve	Reduced expiratory flow at low volumes
Normal lung volumes	Lung volumes increased

### **RESULTS**

From the total number of 30 cases taken in the study, age distribution shows the maximum number of cases (13) to be in the age group of 26-35 years. In the study, sex distribution shows that there was a female preponderance, i.e., 17 out of 30 cases (56.6%) were female and 13 cases (43.3%) were males.

Of 30 patients, 70% had a positive family history of asthma, and 46.6% had a positive history of atopy, there is no family history of asthma in 43.3%. This finding goes well along with the fact that asthma runs in families.

The symptoms evaluated for were wheezing, breathlessness, cough, sputum production, and nocturnal symptoms. The group put on ciclesonide, showed a gradual decrease in wheeze (60→10%), cough (50→20%) with the use of the drugs. In the case of breathlessness and nocturnal symptom, the symptoms totally abolished at the end of 6 month treatment. In the case of budesonide group, it has been seen that cough (50→20%) and breathlessness (50→10%) improve gradually with the use of drugs like the ciclesonide but in case of wheeze (80→10%) and nocturnal symptoms (80→0%) it showed quite good result than the ciclesonide group. Fluticasone group showed some similar result with that of the budesonide group. In all the three groups, equivalent number of patients had sputum production which was relieved at the end of the month, and the patients

were free from these symptoms thereafter.

The mean pretreatment PEFr observed was 66.81%, 67.1%, and 67.9% of predicted for the groups put on ciclesonide, budesonide, and fluticasone, respectively. At the end of 2 months of treatment with steroid inhaler and  $\beta_2$ -agonist, the mean PEFr values was 76.3% for ciclesonide, 74.3% for budesonide, and 75.9% for fluticasone compared to pre-treatment values of 66.81%, 67.1%, and 67.9%, respectively. At the end of 6 months of treatment with steroids, the mean PEFr observed was 77.2%, 75.1%, and 76.3% for ciclesonide, budesonide, and fluticasone groups, respectively. The mean FEV1 observed was 1.33, 1.17, and 1.65, and the mean FEV1% predicted was 64.1%, 60.1%, and 60%, respectively, and the percentage of improvement after bronchodilatation was 20%, 19%, and 21% for beclomethasone, budesonide, and fluticasone in that order.

The mean percentage FEV1/FVC predicted was 77.3%, 74.1%, and 77.9% for ciclesonide, budesonide, and fluticasone, respectively, and the percentage improvement after bronchodilatation was 18%, 18%, and 19% in that order.

The mean percentage predicted FEV1/FVC was 77.3%, 80.0%, and 78.5% for the 3 groups in that order after 2 months which was improved to 79.7%, 80.9%, and 79.4% for ciclesonide, budesonide, and fluticasone, respectively, at the end of 6 months.

## DISCUSSION

Asthma remains a common and troublesome problem affecting a substantial proportion of our childhood and adult population worldwide. Epidemiological surveys have confirmed that the incidence and the prevalence of this disease and that this increase is real and associated with significant morbidity at a time when morbidity and mortality due to other disease are declining, suggesting that this condition is not adequately treated in some patients. Increased westernization and effects of modern civilization have contributed to these trends. Glucocorticoids have been used to treat a variety of airway diseases, now a days both oral and inhaled steroids have evolved into important useful drugs currently available to treat asthma. Initial studies evaluating the efficacy of inhaled corticosteroids in asthma were performed in patients with moderate to severe disease at the time of their introduction to clinical practice in the early 1970s and for many years after this, their use was mainly limited to patients who had persistent symptoms despite oral or inhaled bronchodilators. The increased application in 1980s of the role of airway inflammation in the pathogenesis of asthma provided a rationale for the earlier introduction of inhaled steroids to reduce airway inflammation and improve some of the structural abnormalities.

The study was done to compare the efficacy of three types of inhaled corticosteroids, ciclesonide, budesonide, and fluticasone

in the management of bronchial asthma. The patients included were mildly persistent and moderately persistent bronchial asthmatics without any additional diseases who presented at the OPD of TB/CD Department and the Medicine Department in the Bankura Sammilani Medical College and Hospital.

All patients after clinical assessment were given same dose of long acting  $\beta_2$ -agonist through inhalation route.

Three groups of 10 subjects each were given a different type of steroid inhaler such as ciclesonide or budesonide or fluticasone along with long acting  $\beta_2$ -agonist. From the analysis, it was seen that maximum number of cases was between 26 and 35 years with female preponderance. Among the all cases, (70%) had family history of asthma with 46.6% positive history of atopy.<sup>6-8</sup>

Symptoms evaluated for, were wheezing, breathlessness, cough, sputum production, and nocturnal symptoms showed significant improvement at the end of 2<sup>nd</sup> month and further improvement at the end of 6<sup>th</sup> month.  $\beta_2$ -agonist has been known to relax airway smooth muscle and enhance mucociliary clearance and decrease vascular permeability and modulate mediator release as well. Thereby, they decrease the wheezing, cough, sputum, and nocturnal symptoms. The long acting  $\beta_2$ -agonist administered in the treatment account for the improvement of symptoms. Corticosteroids have been known to reduce bronchial inflammation and hyperresponsiveness and reduce symptoms also account for the clinical improvement.

The mean pretreatment, PEFr was (66.81%), (67.1%), and (67.9%), respectively, for the group put on ciclesonide, budesonide, and fluticasone. The percentage of improvement of PEFr after bronchodilatation was 17%, 18%, and 18%, respectively, in three groups. But at the end of 6<sup>th</sup> month, there was a marked improvement in PEFr seen in all the three groups.<sup>9-12</sup>

Initially, the mean FEV1% predicted was 64.1%, 60.1%, and 60.5% for the groups put on ciclesonide, budesonide, and fluticasone, respectively, and the percentage of improvement after bronchodilatation was 20%, 19%, and 21%, respectively, which markedly improved after 6-month treatment and is comparable to the study under taken by Burke et al. 1991.<sup>13</sup> Thus, showing significant improvement in the mean values at the end of the treatment, which is comparable to the study by Buhl et al. (2006).<sup>9</sup>

### FEV1/FVC

The mean percentage predicted FEV1/FVC recorded in the three groups was 77.3, 74.1, and 77.9 (Table 1), respectively, at the pre-treatment level, and the percentage improvement after bronchodilatation was 18, 18, and 19, respectively. And there was a significant increase in the FEV1/FVC ratio at the end of 6 months.

Though according to Auffarth (1991)<sup>14</sup> steroid therapy

**Table 1: Spirometric values in mean percentage predicted during 6 months.**

Group	PEFR (mean % p)			FEV1 (mean % p)			FEV1/FVC (mean % p)		
	0 month	2 months	6 months	0 month	2 months	6 months	0 month	2 months	6 months
Budesonid E-400 mcg	67.1	74.3	75.1	60.1	74.3	75.4	74.1	80.0	80.9
Fluticason E-200 mcg	67.9	75.9	76.3	60.5	70.4	71.3	77.9	78.5	79.4
Ciclesonid E-400 mcg	66.81	76.3	77.2	64.1	72.6	72.9	77.3	77.3	79.7

FEV1: Forced expiratory volume in 1 second, FVC: Forced vital capacity, PEFR: Peak expiratory flow rate

caused no significant changes in spirometric values. Our study was in comparison with the result of Chiu et al. (2014)<sup>15</sup> who showed significant improvement in PEFR, FEV1, and FVC values at 3 and 6 weeks but with no significant difference between the different steroids used.

## CONCLUSIONS

The mean percentage predicted FEV1/FVC like the mean percentage predicted PEFR and mean percentage predicted FEV1, also showed steady and continuous improvement at the end of 2<sup>nd</sup> month and 6<sup>th</sup> month and the improvement was similar in all the three groups.

From the above study, it was concluded that steroid therapy along with  $\beta_2$ -agonists showed a significant improvement in symptoms by the end of 2 months, and it was well-maintained till the end of 6 months. There was no difference among the three different types of steroids used in the study, i.e., ciclesonide, budesonide, fluticasone. And both the spirometric values and clinical improvement were similar in all three groups.

The spirometric value such as PFR, FEV1, and FEV1/FVC all showed significant improvement at the end of 2<sup>nd</sup> month and 6<sup>th</sup> month.

Once again, the comparison between the three drugs used in the study, ciclesonide, budesonide, and fluticasone, showed that all of them were equally effective in the management of asthma at their estimated daily comparative dosages.

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