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A Successful Case of Persistent Asthma in the Treatment of Inhalation Corticosteroid Combination Therapy of Budesonide/Folmoterol and Ciclesonide

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Abstract

A-60 years old woman has been observed in our outpatient clinic for several years. She has been uncontrolled for her asthma despite multi-drug therapy; [Fluticazone (FP) 800 μg/day+Salmeterol(SM l00 μg+Montelukast 10 mg+Theophilline 200 mg/day], presenting asthma control test (ACT) score as 13. We added Ciclesonide (CIC) to her therapy and replaced FP and SM with BFC. As a result, her pulmonary function and ACT score improved. The counts of eosinophils in induced sputum decreased significantly. Furthermore, during an observation period of 9 months, she had neither had an emergency visit nor an asthma exacerbation.

While some physicians previously reported efficacy of Inhaled corticosteroids (ICS) combination therapy of FP and Beclomethasone (BDP), there are no reports concerning the efficacy and tolerability of ICS combination therapy of Budesonide/Folmoterol combination (BFC) and Ciclesonide-hydrofluoroalkane (CIC-HFA). This is the first case report of a persistent asthma patient succesfully treated by the ICS combination therapy of BFC and CIC-HFA.

Keywords: Asthma; Inhalation corticosteroid combination therapy; Budesonide/Folmoterol combination; Ciclesonide

Introduction

It is commonly known that the inflammation in asthma involves both central and peripheral airways [1]. Some suggest that early closure of these distal airways, smaller than 2 mm in diameter due to uncontrolled inflammation, results in patients being characterized as "difficult to control asthma" [2-5]. There are several types of Inhaled corticosteroids (ICS) such as Fluticazone (FP), Budesonide, Beclomethasone or Ciclesonide (CIC), which are commonly used for asthmatics [6]. They are different in size of device or particles from each other. Aerosol consensus statement demonstrates that aerosol particles with a Mass Median Aerodynamic Diameter (MMAD) of 0.8-5.0 μm are ideal for deposition in the lung. Especially, aerosols with MMADs between 0.8-3.0 μm are considered suitable for drug delivery to the parenchyma. Glover et al. reported that the lung deposition of dry powder aerosols depended on their particle size. The deposition of the smaller particles was seen as more peripheral [7]. It has also been documented that CIC-HFA as well as BDP-HFA deposited at a higher rate in peripheral airways compared to FP because particles in CIC and BDP are smaller than those in FP. Therefore, it is quite important to choose drugs with adequate delivery potential to distal airways in controlling asthma and prevention of its exacerbation. We present a successfully treated case of persistent asthmatics by ICS combination therapy; added CIC on Budesonide/Folmoterol Combination (BFC). Some physicians previously reported efficacy of ICS combination therapy of FP and BDP [8,9]. However, there are no reports that concerning the efficacy and tolerability of ICS combination therapy of BFC and CIC-HPA. This is the first case report of a persistent asthma patient successfully treated by the ICS combination therapy of BFC and CIC-HPA. Pulmonologists should know that ICS combination therapy would be one of the effective tools in the treatment of persistent asthma despite multiple-drug therapy with acceptable toxicities.

Case Report

A-60 years old woman has been observed in our outpatient clinic for several years. She had past history of childhood bronchial asthma, which required no medication. Her family history revealed asthma in her father and brother. She has been uncontrolled for her asthma despite multi-drug therapy;

(FP800 μg/day+Salmeterol (SM) l00 μg+Montelukast 10 mg+Theophilline 200 mg/day), presenting Asthma Control Test (ACT) score as 13. The total IgE level was 80 IU/ml and allergen-specific IgE of house dust and mite were positive.

She had an emergency room visits due to mild to moderate asthma exacerbations once a month in spite of inhaler technique training and frequent house cleaning a week. Then, we added CIC to her therapy. Pulmonary functions, especially $\dot{V}25$ and $\dot{V}25$/height improved. We administered BFC instead of FP and SM. After that, her ACT, pulmonary functions, PEF, $\dot{V}25$ and $\dot{V}50$ improved (Tables 1 and 2). The counts of eosinophils in induced sputum decreased dramatically. During an observation period of 9 months, she had neither had an emergency visit nor an asthma exacerbation as shown in Table 2. No adverse effect was seen in this therapy.

Discussion

Some physicians documented the efficacy of ICS combination therapy of FP and BDP-HFA in the treatment of persistent asthmatics [8,9]. However, efficacy of ICS therapy of BFC and CIC-HPA has never been reported. In terms of medication compliance, CIC-HPA which needs inhalation once per day is much better than BDP-HPA which needs twice inhalation per day. In addition, Folmoterol (FM) shows

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Date Variables	2010.7.28 FP+SM	2010.9.15 FP+SM+CIC	2011.2.1 BFC+CIC
PEF	3.46	3.74	5.35
FVC	2.47	2.95	3.40
$FEV_{1.0}$	1.38	1.54	2.08
$FEV_{1.0\%}$	55.9	52.2	61.2
V25	0.12	0.19	0.25
V25/HT	0.07	0.13	0.15

*Theophilline 200 mg and Montelukast 10 mg were administered in all terms.
FP: Fluticazone; SM: Salmeterol; CIC: Ciclesonide; BFC: Budesonide/Folmoterol Combination; PEF: Peak Expiratory Flow; FVC: Forced Vital Capacity; FEV1.0: Forced Expiratory Volume in one second; FEV1.0%: one second Forced Expiratory Volume rate

Table 1: Pulmonary function after administering CIC and BFC.

Variables	FP+SM	FP+SM+CIC	BFC+CIC
ACT	13	20	25
Emergency visits	12 times/year	0	0
Severe attacks	2	0	0

ICS: Inhaled Corticosteroids; FP: Fluticazone; SM: Salmeterol; CIC: Ciclesonide; BFC: Budesonide/Folmoterol Combination; ACT: Asthma Control Test

Table 2: Relationship between ICS combination therapy and asthma control.

effectiveness of bronchodilation depending on the degree of the dose escalation and the efficacy appears more rapidly than SM. That is why BFC is superior to SFC for persistent asthmatics [10].

Eoshinophilic inflammation in peripheral airways results in difficulty in controlling asthma [2,4]. It is very important to deliver drugs in both central and distal airways for controlling persistent asthma and prevention of its exacerbation. The depth of penetration of an aerosol into the bronchial tree decreases as particle sizes increase. In general, aerosol particles with Mass Median Aerodynamic Diameters (MMADs) between 2-5 μm are considered optimal for delivery to the airways, and aerosols with MMADs between 0.8-3.0 μm are considered suitable for drug delivery to the parenchyma [2-5]. BFC when their MMAD is 2.4 μm, deposit mainly in large and intermediate airways, whereas CIC-HFA can reach distal airways (<2 mm diameter). In this case, it is thought that CIC affected peripheral airways favorably as patient's $\dot{V}25$ and $\dot{V}25$/height improved after administration of CIC (Table 1). Moreover, BFC was effective in improvement of central airways. It is very reasonable that combination therapy of BFC and CIC in the treatment of persistent asthma is considered to be effective, compared with conventional therapy. While cost-effectiveness or adverse effects in combination ICS therapy could possibly be problematic, this therapy would be one of the effective tools for persistent asthmatics.

In conclusion, we suggest that combination therapy of BFC and CIC-HPA would be one of the effective tools in the treatment of asthmatics. Physicians should choose ICS depending on the targeting airways in asthmatics.

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