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Clinical benefits of switching to an inhaled corticosteroid extrafine aerosol; a case series

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Abstract. – **Hydrofluoroalkane beclomethasone dipropionate (HFA-BDP) extrafine aerosol is the first in a new generation of inhaled corticosteroid (ICS) formulations that have an improved deposition profile in comparison with conventional ICS preparations. This reformulation offers potential benefits to patients with asthma in terms of improved symptom control and reduced oropharyngeal adverse effects, such as dysphonia and candidiasis. This article presents four cases that illustrate the clinical benefits that can be obtained following a switch from conventional ICS preparations to treatment with HFA-BDP extrafine aerosol. The patients described were experiencing significant exacerbations of their asthma and increasing asthma symptoms and/or oropharyngeal adverse effects during treatment with conventional ICS preparations. On switching to HFA-BDP extrafine aerosol, the patients experienced an improvement in their asthma control and resolution of any oropharyngeal adverse effects.**

Key Words:

Asthma; Inhaled corticosteroid; HFA-BDP; Beclomethasone dipropionate; Qvar™.

Introduction

Inhaled corticosteroids (ICS) have been used effectively for many years in the treatment of asthma, and are considered by national and international therapeutic guidelines to be first-line therapy[1]. Of the available ICS, beclomethasone dipropionate (BDP) is frequently prescribed and has been in clinical use for almost 30 years as asthma medication. A new formulation of BDP, which uses hydrofluoroalkane-134a (HFA) as propellant instead of chlorofluorocarbons (CFCs), has been developed (HFA-BDP; QVAR™; 3M Pharmaceuticals), in response to the Montreal Protocol on substances that deplete the ozone layer[3]. This reformulation, combined with improvements in inhaler technology, delivers an extrafine aerosol of BDP.

HFA-BDP extrafine aerosol delivers up to 60% of the active drug to the lungs[4-6]. This contrasts with CFC-BDP, and fluticasone and budesonide pressurized metered-dose inhalers (pMDIs), which typically deliver no more than 15% of the inhaled drug to the lungs even with optimal use[4-8]. Additionally, while drug deposition with conventional pMDIs is mostly confined to the central airways, inhalation of HFA-BDP extrafine aerosol results in drug deposition in the large, intermediate and peripheral airways[4,5,8].

The improved deposition profile of HFA-BDP extrafine aerosol offers potential benefits to patients in terms of improved symptom control and reduced oropharyngeal adverse effects. In this article we present four case reports that illustrate the clinical benefits that can be obtained in patients with asthma following a switch from conventional ICS preparations to treatment with HFA-BDP extrafine aerosol.

Case Reports

Case 1

This case involved an 81-year-old woman with at least a 10-year history of asthma, nasal polyps, allergic rhinitis, aspirin hypersensitivity and gastroesophageal reflux disease (GERD). Treatment with inhaled flunisolide, albuterol and an anticholinergic

combination product were only mildly successful in preventing exacerbations of her aspirin sensitivity. Aspirin desensitisation was discontinued after approximately 1 year due to persistent bruising on her extremities. The patient continued to experience repeated asthma exacerbations requiring several prednisone bursts each year. The patient also suffered from frequent sinusitis, which appeared to be associated with her asthma exacerbations.

Over the past 2 years, the patient had been on inhaled fluticasone 440 µg twice daily. After she reported the onset of persistent hoarseness, the dose was decreased to 220 µg twice daily. Subsequently the patient discontinued fluticasone treatment of her own accord and restarted flunisolide treatment, two puffs twice daily. However, numerous corticosteroid bursts and antibiotics were required because of persistent sinusitis. In late 1999, the patient was switched to budesonide, two puffs twice daily, and her symptoms appeared to stabilize temporarily. Several months later, she again reverted to flunisolide with poor asthma control. The addition of zafirlukast, a leukotriene receptor antagonist, did not result in a significant improvement in her condition and subsequent addition of salmeterol failed to reduce symptoms of shortness of breath and wheezing. She was then switched to albuterol plus ipatropium bromide and the dose of flunisolide was increased to four puffs twice daily. Her symptoms stabilized briefly. Six weeks later she had an asthma exacerbation requiring treatment with prednisone and an antibiotic.

At the end of October 2000, the patient experienced increasing asthma symptoms, namely cough and nocturnal wheezing. At that point, treatment with HFA-BDP (80 µg/puff, 2 puffs twice daily) was initiated, with HFA-albuterol twice daily and as needed. After 14 days, the patient was no longer suffering from nocturnal asthma, sleep disturbance, or shortness of breath and she was able to decrease her daily HFA-albuterol rescue use. Oral corticosteroids have not been required since that time. The dose of HFA-BDP was reduced from 320 µg/day to 160 µg/day after the patient developed some hoarseness. The patient now reports no significant impairment of her daily activities and she is able to exercise regularly.

Case 2

The second case involved an 83-year-old white woman who presented to the clinic 2 years ago with sinusitis, shortness of breath, wheezing, chest tightness and recurrent bronchitis. Skin-prick tests revealed that she was sensitized to tree, grass and weed pollen, cat hair, and house dust. Pulmonary function tests performed over the previous few years revealed decreased mid-expiratory flow rates indicating airway obstruction.

Initially, the patient was prescribed inhaled fluticasone 440 µg daily plus salmeterol twice daily, but she continued to experience asthma exacerbations. As a result, in September 2000 she was switched to treatment with HFA-BDP (80 µg/puff, 2 puffs twice daily) whilst continuing with her regular salmeterol regimen. She noticed a gradual improvement in her asthma control. She experienced asthma exacerbations in March 2001, which were treated with prednisone. After this time, no further treatment with oral corticosteroids was required.

Since then, the patient's peak flow has been maintained at between 280 and 380 L/min and there has been no evidence of thrush or dysphonia. She has experienced a moist cough secondary to postnasal drip intermittently, which has been responsive to symptomatic therapy. She has also receivied zafirlukast and nasal budesonide aqueous solution. Overall her progress has been excellent and she is clinically stable with regard to her asthma control. Over the past 6 months she has been able to play golf regularly and to perform her normal daily activities without difficulty.

Case 3

This case involved a 66-year-old African-American woman with at least a 30-year history of severe asthma. For the past 15 years, the patient had achieved reasonable asthma control with a long-acting β-agonist and high-dose ICS. During this time, she did not require emergency room treatment or hospitalisation but she was treated two- to three-times a year for asthma exacerbations with short courses of oral corticosteroids. During asthma exacerbations, her symptoms included shortness of breath, chest tightness and wheezing, which worsened with exertion, cold air, viral respiratory infections, dust and

a spectrum of irritants such as smoke and car exhaust. She was allergic to dust mites and mold spores.

The patient presented to the clinic with an increasing shortness of breath on exertion and decreasing peak flow. She had no recent viral infection or other environmental exposures that could precipitate her symptoms. She was not experiencing nocturnal symptoms but reported that she had been using her short-acting β-agonist more frequently during the day, especially after physical exertion. She mentioned a slight but chronic hoarseness, which worsened if she spoke for long periods of time. The increased symptoms made it very difficult for her to complete her daily assignments at work.

Her peak expiratory flow rate was 180 L/min compared with a baseline value of 230 L/min. Spirometry revealed a forced expiratory volume in one second (FEV_1) of 1.5 L (54% predicted, down from 2.0 L one year previously), a forced vital capacity (FVC) of 1.8 L (60% predicted) and a forced expiratory flow rate over the 25% to 75% of exhalation (25-75% FEF) of 2.2 L/min (32% predicted). Her FEV_1 post-bronchodilator response improved by 16%.

Given the gradual deterioration of the patient's asthma, it was decided to modify her treatment regimen by replacing her existing ICS with an equivalent dose of HFA-BDP (80 µg/puff, 2 puffs twice daily). At follow-up evaluation 4 weeks later, her peak flow had returned to the baseline value of 230 L/min and her shortness of breath on exertion had resolved. She felt the change in her medication had really made a difference in her ability to carry out her daily responsibilities. She also noticed that she was no longer hoarse even after she had been talking on the telephone for an extended period of time. It was decided to leave her on HFA-BDP after a successful 3 months follow-up in to reassess her overall status.

Case 4

The fourth case involved a 52-year-old white man with a history of chronic sinusitis, GERD and chronic cough who presented in the clinic as a new patient. He had undergone two previous sinus surgeries to remove nasal polyps and open his osteomeatal complexes, which had provided temporary relief. His GERD had been diagnosed by pH probe and was being effectively managed with a proton pump inhibitor by a gastroenterologist. His cough did not appear to be related to increased GERD symptoms. He associated the onset of the cough with having experienced a viral respiratory infection 2 years previously. Since that time he has been treated with antibiotics and antitussives four- to five-times a year by his primary care doctor. The cough was becoming a nuisance, interfering with both his work and personal life. He was taking no other medications and had no symptoms of post-nasal drainage and was otherwise healthy. There were no obvious environmental factors at home or work that seem to make his symptoms worse. There was no family history of asthma or allergies, and the patient had no history of drug allergies.

Spirometry revealed a normal FEV_1 with a 25-75% slightly diminished FEF. There was no reversal of his FEV_1 post-bronchodilator inhalation. A subsequent methacholine challenge test was performed which revealed a 20PD of 0.56 mg/mL (20PD is the provocative dose of inhaled methacholine required to produce a 20% fall in FEV_1 from baseline). When skin tested, he was not sensitized to selected seasonal and perennial aeroallergens.

The patient was initially treated with high-dose ICS plus a course of oral corticosteroids to reduce his airway hyperresponsiveness and cough. After two weeks of treatment, his cough had completely resolved, although he noticed more hoarseness of his throat after using the inhaler, even after rinsing his mouth. It was decided to switch his ICS to HFA-BDP (80 µg/puff, 2 puffs twice daily). He was seen for follow-up evaluation 4 weeks later. At that time he was not experiencing a cough or any other respiratory symptoms. He noticed that, after 2 weeks on HFA-BDP, his hoarseness had gradually improved and he had not experienced any subsequent hoarseness. He was instructed to continue this regimen. He has since been seen on one subsequent visit and was having no problem with coughing or hoarseness.

Discussion

From the patient's perspective, the most distinctive clinical feature of asthma is the presence of symptoms which can markedly

interfere with their ability to perform everyday activities. Short-term clinical studies in symptomatic asthma patients have shown that HFA-BDP is at least as effective as CFC-BDP and budesonide at half the daily dose and fluticasone at the same daily dose in terms of improving lung function[2,9-15]. This equivalent efficacy is presumably a consequence of the increased lung deposition seen with HFA-BDP compared with CFC-BDP, budesonide and fluticasone.

As can be seen from the patients described in these case reports, there are considerable differences between HFA-BDP extrafine aerosol and other ICS preparations with regard to symptom control and oropharyngeal side effects. The patients described in Cases 2 and 3 were poorly controlled on conventional ICS preparations, experiencing significant exacerbations of their asthma and increasing asthma symptoms. However, since switching to HFA-BDP extrafine aerosol at an equivalent dose, their asthma symptoms have improved and they have been able to perform normal daily activities.

Results from two long-term clinical studies have also indicated that there are differences between HFA-BDP and other ICS preparations with regard to symptom control[16,17]. In the first of these studies, well-controlled patients were switched from a stable dose of CFC-BDP (400–1600 µg/day), or an equivalent ICS, to 12 months' treatment with HFA-BDP at approximately half the daily dose, without loss of lung function[16]. However, fewer patients who were switched to HFA-BDP extrafine aerosol than those who remained on CFC-BDP experienced an acute asthma episode or increased asthma symptoms. Similar results were reported in a 6-month study comparing CFC-BDP 1500 µg/day with HFA-BDP 800 µg/day in patients with stable asthma[17].

The improvement in symptom control following a switch to HFA-BDP extrafine aerosol might reflect the increased delivery of active drug to the peripheral airways[4,8]. The small airways are a major site of inflammation in asthma[18], and are poorly penetrated by conventional ICS preparations. It is possible that the resulting anti-inflammatory effects in the peripheral airways may be apparent to the patient, manifesting as improved symptom control and reduced side effects.

The reduced oropharyngeal deposition of HFA-BDP extrafine aerosol would be expected to result in a lower incidence of oropharyngeal adverse effects such as dysphonia or candidiasis compared with other ICS preparations. The presence of such symptoms can significantly affect the patient's quality of life, their compliance with medication and ultimately the outcome of treatment. For example, in Case 1 the patient experienced persistent hoarseness during treatment with fluticasone and so refused to comply with the treatment regime despite poor asthma control. On switching to treatment with HFA-BDP, the patient experienced control of her asthma symptoms without oropharyngeal adverse effects. Similar experiences were recorded for the patients described in Cases 2, 3 and 4.

In conclusion, these case reports illustrate the clinical benefits that patients with asthma may experience following a switch from conventional ICS preparations to the new HFA-BDP extrafine aerosol, in terms of both improved symptom control and reduced oropharyngeal adverse effects.

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