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OLGU SUNUMU CASE REPORT

Paradoxical bronchospasm due to fluticasone propionate dry powder inhaler

Flutikazon propiyonat kuru toz inhalere bağlı paradoksal bronkospazm

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ABSTRACT

A 14 years-old girl admitted with the complaints of cough and wheezing during next 20 minutes following the use of fluticasone propionate dry powder inhaler. An open challenge was performed with fluticasone propionate dry powder that resulted with the highest fall in forced expiratory volume in one second (FEV_1) from baseline after 5 minutes (11%) and in peak expiratory flow (PEF) after 2 and 5 minutes (16% and 22%, respectively). During the challenge, cough was occurred and she complained of having chest tightness. A skin prick test with fluticasone propionate dry powder, lactose and fluticasone propionate nebulizer solution were also performed and found negative. Open challenges with fluticasone propionate aerosol and budesonide dry powder (BDP) inhaler were performed every other day and resulted with no changes according to baseline in FEV_1 and PEF, and her treatment was then replaced with budesonide dry powder inhaler, 200 µg, bid. Although a good carrier for dry powder inhaler drugs, lactose may cause bronchospasm in asthmatic patients.

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Key words: Paradoxical, bronchial spasm, lactose

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ÖZET

On dört yaşındaki bir kız hasta flutikazon propiyonat kuru toz inhaler kullanımını takip eden 20 dakika içinde ortaya çıkan öksürük ve hışıltı yakınmaları ile başvurdu. Flutikazon propiyonat kuru toz inhaler ile yapılan açık provokasyonun ardından birinci saniyedeki zorlu ekspiratuar akımda (FEV_1) 5. dakikada %11, zirve ekspiratuar akımda (PEF) ise 2. ve 5. dakikalarda sırasıyla %16 ve %22 azalma oldu. Provokasyon sırasında öksürük oluştu ve hasta göğüste sıkışma olduğundan yakındı. Flutikazon propiyonat kuru toz inhaler, laktoz ve flutikazon propiyonat nebülizer solüsyonu ile prick deri testi yapıldı ve negatif bulundu. Flutikazon propiyonat aerosol ve budesonid kuru toz (BDP) inhaler ile uygulanan provokasyon testlerinde bazal değere göre FEV_1 ve PEF değerlerinde değişiklik tespit edilmedi ve hastanın tedavisi 200 µg/gün BDP ile yeniden düzenlendi. Sonuç olarak; kuru toz inhaler ilaçlar için iyi bir taşıyıcı olan laktozun astımlı hastalarda bronkospazma neden olabileceği gösterildi.

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Anahtar kelimeler: Paradoksal, bronşiyal spazm, laktoz

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INTRODUCTION

Paradoxical bronchospasm, a worsening of symptoms following bronchodilator use has been reported previously for salbutamol, ipratropium bromide and as well as, for inhaled steroids[1,2]. Various mechanisms have been proposed to explain paradoxical bronchospasm, including: reactions to propellants, surfactants or preservatives; hypo- or hyper tonicity of the inhaled solution; deep inspirations used to inhale the drug or examine the effect or a nonspecific reaction to the inhalation of foreign material into the asthmatic airways[2]. We present a case of exacerbation of asthma symptoms by fluticasone propionate dry powder (FPDP) inhaler that includes lactose as carrier.

CASE REPORT

A 14-years-old girl, who had had mild intermittent asthma since seven years of age, was admitted to our paediatric allergy outpatient clinic with the complaints of an increase in her day (every 4-5 days) and night (3-4 nights a month) asthma symptoms and intolerance to exercise during last four months. Her pre- and postbronchodilatory forced vital capacity (FVC), forced expiratory volume at one second (FEV_1) and peak expiratory flow (PEF) were within normal limits with a 15% variability in FEV_1 and 14% in PEF. She had strongly positive skin prick test reactions with 15 mm wheal formation to *Dermatophagoides pteronyssinus* and 14 mm to *Dermatophagoides farinae*. She was diagnosed as having mild persistent asthma and her treatment was started with FPDP inhaler (Flixotide Diskus, GlaxoSmithKline, Turkey) 200 µg, bid[3]. One week later, she admitted with the complaints of cough and wheezing during next 20 minutes following the use of every dose of FPDP. Written informed consent was obtained both from patient and parents and an open challenge was performed with FPDP. Following baseline estimations, FEV_1 and PEF measurements were repeated immediately (0 minutes), and two, five, 10, 15, and 30 minutes after inhalation of drug. All estimations were made in triplicate, with the higher readings being recorded. The highest fall in FEV_1 from baseline was recorded after 5 minutes (11%) and in PEF after 2 and 5 minutes (16% and 22%, respectively) (Table 1).

During the challenge, she developed coughing and complained of having chest tightness. However, her physical examination was normal. A skin prick test with FPDP, lactose (as it was the carrier for active drug) and fluticasone propionate nebulizer solution were also performed and found negative. FPDP and lactose were diluted in 0.9% sodium chloride and used at concentrations of 100 µg/mL and 1 mg/mL, respectively. A positive prick test response was defined as a wheal > 3 mm than the negative

Table 1. Changes in FEV_1 and PEF following the use of FPDP

Time	FEV_1			PEF		
(minute)	Litre	Percent	% change	Litre	Percent	% change
Pre	2.58	104		7.55	137	
Post						
0	2.49	100	-4	6.73	122	-11
2	2.44	99	-5	6.36	115	-16
5	2.28	92	-11	5.87	106	-22
10	2.39	96	-8	6.60	119	-13
15	2.59	105	0	6.52	118	-14
30	2.60	105	1	6.81	123	-10

FPDP: Fluticasone propionate dry powder, FEV_1: Forced expiratory volume in one second, PEF: Peak expiratory flow.

control wheal. Histamine at a concentration of 10 mg/mL and 0.9% sodium chloride were used as positive and negative controls, respectively. Open challenges with fluticasone propionate aerosol and budesonide dry powder (BDP) inhaler (Pulmicort Turbuhaler, AstraZeneca, Turkey) were performed every other day and resulted with no changes according to baseline in FEV_1 and PEF, and her treatment was then replaced with BDP inhaler, 200 µg, bid, that is free of lactose and includes micronised budesonide alone.

Challenges were performed every other day in the pulmonary functions laboratory of our outpatient clinic. Physical examination was done before every challenge and revealed normal. Although the patient was allowed to use salbutamol inhaler if needed during the challenge procedure, she reported no need for it.

DISCUSSION

A positive challenge and symptoms during the procedure with FPDP and a negative challenge with fluticasone propionate aerosol reveal that bronchospasm might be due to lactose in our patient. FPDP inhalers include lactose as a carrier. Although it has been previously reported that lactose caused bronchospasm in an asthmatic adult, Thoren et al. recently investigated the effect of five doses of lactose ranging from 6.25 mg to 100 mg and placebo and found no adverse effect of lactose on airways of stable asthmatic patients[4,5].

To investigate whether an immediate type hypersensitivity reaction was the possible mechanism, we performed a skin prick test with lactose and found negative. Deep inspirations couldn't be the reason of bronchospasm in our patient as the challenge was negative with BDP inhaler. A possible explanation might be a nonspecific reaction to the inhalation of lactose into the asthmatic airways.

Peak flow is effort dependent and PEF measurements alone are not sufficient to make a diagnosis of bronchospasm, and FEV_1 indicates bronchospasm better than PEF. However, we think that this was not the case for our patient and she performed spirometry with a good effort as PEF measurements were not only correlated well with FEV_1 at all measurements, but also with symptoms of the patient.

We think that although lactose may cause bronchospasm in asthmatic patients, this is very rare and does not reduce its reliability as a carrier for inhaler drugs.

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