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Nebulized Saline Solution of Dry Powder Formoterol is Useful for Acute Bronchospasm

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RESUMEN

Dos nuevos beta agonistas de efecto prolongado son actualmente usados clínicamente: salmeterol y formoterol. El primero no ha demostrado efectividad en los casos de asma aguda mientras que el segundo, Formoterol, comparable en su período de latencia al albuterol, no ha sido empleado en el manejo de las crisis de asma. En este estudio utilizamos mediciones de flujo espiratorio pico antes y después de la administración de 12 microgramos de Fumarato de Formoterol (Foradil®) en polvo seco vía nebulización, inmediatamente después de su diluición en solución salina estéril, a treinta pacientes con crisis de asma y grados variables de obstrucción bronquial. Los resultados muestran mejoría significativa a los 5 y 30 minutos después de su administración, sugiriendo estabilidad de este producto así como un novedoso enfoque costo efectivo por su menor dosificación y posible impacto sobre la frecuencia de readmisiones debido a una broncodilatación prolongada.

Palabras Clave: Formoterol, Solución nebulizadora, Manejo de ataque agudo de asma, Agonista Beta 2 de acción larga.

ABSTRACT

Salmeterol and Formoterol, two new long acting Beta agonists, are being clinically employed. Salmeterol lacks efficacy in acute asthma while Formoterol, with a latency period similar to albuterol, has never been used in the acute bronchospastic situation. We measured peak expiratory flows in 30 acute asthma patients with variable degrees of airway obstruction before and after administation of 12 micrograms of Formoterol Fumarate (Foradil®) dry powder, nebulized inmediatly after preparation in sterile saline solution. We found significant improvements at 5 and 30 minutes after administration suggesting stability of this product and a possible new cost effective approach with a need for less dosing and perhaps an impact on the rate of asthma readmisions due to the prolonged bronchodilatador effect.

Key Words: Formoterol, Nebulized solution, Asthma acute management, Long acting Beta 2 agonist.

INTRODUCTION

Frequent use of inhaled (either via MDI or by nebulization) short acting beta agonists is the routine pharmacological treatment for acute asthma exacerbations. Long acting beta agonists have been used in primary care as valuable adjuncts to maintenance inhaled steroids and for symptom control with emphasis on nocturnal and exercise induced asthma(1). Formoterol fumarate* *(* (+ -) -2´- hydroxi-5´-[(RS)-1-hydroxi-2-[(RS)-p-methoxy-alfa-methylphenethyl]-amino]ethyl]-formanilidin dihydrated fumarate)*, a new long acting (dry powder) beta agonist, also has an acute rapid bronchodilating effect comparable to albuterol, suggesting its potential use as an occasional symptom reliever on a pro re nata basis(2). There are patients unable to properly perform inhalatory efforts because of age, breathing difficulties or other factors and in such instances administration of a drug via a nebulized solution can prove helpful. We employed formoterol as a dry powder in saline solution nebulized inmediatly after preparation to patients with acute asthma, in an open uncontrolled study.

METHODOLOGY

Consecutive patients with asthma, as defined by the American Thoracic Society(3), attending the emergency room with acute wheezing exacerbations and able to perform a peak expiratory maneuver were evaluated clinically and with Peak Expiratory Flow (PEF) measurements (Personal Best®, the best of three measurements in the standing position) before, 5 minutes and 30 minutes after nebulization with a single dose of 12 micrograms of Formoterol (Foradil®: 1 capsule diluted in 2 ml of sterile saline solution). The pH of the nebulization solution did not differ from sterile normal saline(4) and was administered inmediately after preparation with a Pari® Jet nebulizer connected to a De Vilbiss® compressor model 5650 D with an output of 0.15 - 0.35 ml/min. Patients with clinical evidence of possible bacterial infection such as high fever, purulent bronchitis and or pneumonitis, as well as those who had received any beta agonists in the previous 4 hours, were excluded. In those patients unable to use the nebulizer mouth piece, a face mask was used as a substitute. The protocol and informed consent document were approved by the Institutional Review Ethical board (Instituto de Clínicas y Urología Tamanaco) and written informed consent was obtained from all patients or parents prior to participation. The student "t" test was employed for the statistical analysis.

RESULTS

Thirty (30) patients (male 11, ages 4 to 62, mean of 25. 6 years), with variable degrees of airway obstruction were studied. A reduction in the mean PEF value of 47.8% of predicted was found before treatment, progressing to 27.9% and 19.9% at 5 minutes and 30 minutes respectively. Mean values for PEF are shown in Table 1.

Table 1.

PEF predicted	**PEF 0 min**	**PEF 5 min**	**PEF 30 min**
433.7 L/min	227.5 L/min *	310.7 L/min*	344.1 L/min*
(150-620 L/min)	(60-400 L/min)	(95-470 L/min)	(110-480 L/min)

** p< 0.0001*

DISCUSSION

Two long acting beta agonists, salmeterol and formoterol have been released, differing substantially in structure, binding to adrenoceptor, B- 2 blockade, onset and mode of action(5).

In stable asthmatics without current symptoms the onset of drug action is less important; however, in the acute bronchospastic situation salmeterol lacks an inmediate effect while formoterol exibits a similar rapid onset of action to albuterol (1 to 3 minutes), achieves maximun bronchodilatation within 2 hours (sustained for up to 12 hours) and has almost no adverse side effects(6). It has been shown to be 100 times more potent than albuterol "in vitro", without clinically reported tachyphilaxis and controversial antiinflamatory properties(6).

Foradil® is ussually prescribed for inhalation in a dry powder form with a friendly user device (Aerolizer®). However, some patients can not perform inhalatory maneuvers for a variety of reasons such as age or difficult breathing and the nebulized administration of an effective Beta 2 agonist, with both an acute and long lasting effect, might give a beneficial therapeutic option in such situations. In this short paper, we have demonstrated that asthmatic patients of different ages with acute wheezing exacerbations of variable severity have a significant improvement of their PEF using formoterol as a dry powder via a nebulized solution. These results suggest the stability of this drug in saline solution when it is administered inmediatly after preparation. Theoretically, a need for less dosing with an impact on the rate of asthma readmisions, because of a prolonged bronchodilatation, might prove cost effective; this will also allow patients to initiate and better keep their maintenance medications program.

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