Case Report

Side Effects of Salbutamol Sulfate Delivered through a Metered-Dose Inhaler in a 14-Year-Old Boy with Bronchial Asthma


Atsutoshi Tsuji,*1 Kaoru Hirasawa,*1 Susumu Manki,*1 Keiko Izumi,*1 Katsumi Kobori,*1 Shiori Aoyama,*1 Gozoh Tsujimoto*2

Abstract

A β-adrenergic agent, salbutamol sulfate, is widely used for the treatment of asthmatic attacks. The use of a metered-dose inhaler (MDI) is a clinically preferred doing technique because it achieves effective bronchodilation within a relatively short period of time with fewer side effects. This article reports the side effects of salbutamol sulfate delivered by MDI in a 14-year-old boy. The patient came to our hospital about 1 hour after inhalation of the agent, with the chief complaint of abnormal feelings in chest. Heart rate was 138 beats/min, and QTc on the electrocardiogram was 0.477 second. The serum potassium level was 2.9 mEq/L, blood glucose 156 mg/dL, peripheral white blood cell count 13,600/μL, and neutrophil percentage 79.5%. Correction of potassium levels by fluid therapy led to improvement of his condition in approximately 24 hours. The patient was using salbutamol sulfate by MDI as the only agent. Based on the intervals and frequency of inhalation, this case seems to represent an adverse event of this agent. Our search of the literature revealed no report of side effects of this agent occurring in children. Thus, this case should serve as a warning to be borne in mind when salbutamol sulfate by MDI is used.

Key words Salbutamol sulfate, Metered-dose inhaler, Side effects

Introduction

The relation between asthmatic death and β-adrenergic agents drew attention in the 1960s, when the leading medication was fenoterol hydrobromide MDI. As a result of various controversies since then, it has been suggested that the risk of asthmatic death associated with the use of β-adrenergic agents by MDI is substantial in children, and that there is also increased risk with salbutamol sulfate MDI. A case in which a variety of side effects of salbutamol sulfate MDI occurred in an asthmatic patient is reported herein.

Case Report

The patient was a 14-year-old boy (weight 50 kg) who was diagnosed as having bronchial asthma at the age of 7 years. His disease was of the intermittent type with strong seasonal dependence. His doctor instructed him on how to use salbutamol sulfate MDI when he was 12 years old, and he had been using the medication since then. The patient usually took one puff of 100 μg at bedtime and morning, which achieved good control of asthma. The night before the present episode, he took one puff later than usual, i.e., after 11 o’clock, and fell asleep. About 7 o’clock the
following morning, he noticed slight respiratory distress, wheezing, and coughing, and took one puff. Because there was no improvement of the symptoms, he took another inhalation, judging by himself that the previous inhalation had been insufficient. Since the symptoms improved, he went to school. At about 8 o’clock in the morning, he began to suffer abnormal feelings in chest and came to the hospital.

Findings on initial physical examination and laboratory tests

The patient had a rather pale complexion and tremor. He exhibited a regular heart rate of 138 beats/min, SpO₂ 96%, QTc 0.477 second on electrocardiogram (normal, 0.425 second or less), peripheral white blood cell count 13.600/μL, neutrophil percentage 79.9%, serum potassium 2.9 mEq/L, and blood glucose 156 mg/dL. The patient’s condition was considered to be a toxic reaction to overdose of the β-adrenergic agent salbutamol sulfate, and therefore potassium correction with fluid therapy (at a dose of potassium of 0.18 mEq/kg/h) was carried out. About 5 hours after the initiation of treatment, his condition improved, showing a heart rate of 98 beats/min, attenuated tremor, and a serum potassium level of 3.7 mEq/L. After that, a potassium dose of 0.02 mEq/kg/h was continued, and the patient’s condition was restored to normal about 22 hours later, with a heart rate of 70 beats/min, eliminated tremor, and a serum potassium level of 4.1 mEq/L.

Discussion

Salbutamol sulfate has hardly any α-adrenergic action and has β₂ selectivity. One puff of 200 μg of this agent by MDI allows a 15% or more increase in forced expiratory volume in one second (EFV₁) to occur as soon as in 5 or 6 minutes and to last for a median 4.2 hours. Because of these properties, this agent is widely used for relieving the acute symptoms of asthmatic attacks in daily living. In children, one puff of 100 μg may be taken four times a day at intervals of at least 3 hours. Therefore, this agent generally is regarded as an important medication for rescue use during asthmatic attacks, but it is also used as prophylactic maintenance therapy. The current patient was instructed to take one puff twice a day, after rising from bed in the morning and at bedtime. On the morning of the day he came to our hospital, he had had an asthmatic attack that was not relieved by a single puff, and he added another puff, using his own judgment.

A variety of findings obtained upon the patient’s physical examination and laboratory tests at the first visit to our hospital suggested side effects of β-adrenergic drug therapy. Tremor, tachycardia, headache, and decreased serum potassium levels as side effects are mentioned in the cautions for use of the product. However, although decreases in serum potassium within the range of reference values have been reported, there has been no report of side effects occurring in children, according to our search of the literature. Our patient also showed a prolonged QT interval, increased peripheral white blood cell count, increased neutrophil percentage, and increased blood glucose.

Reports of asthmatic death in children have been reviewed collectively. Thirteen asthmatic deaths occurred between 1998 and 2001, and two of the 13 cases were attributed to excessive dependence on MDI- or nebulizer-delivered β-stimulant medication. Although it has been pointed out that increased asthmatic deaths due to the use of β-stimulants by MDI are more prominent among children, the causal relationship between side effects and asthmatic death remains a matter of speculation, since the presence/absence of, for example, hypoglycemia and hypokalemia in cases of asthmatic death is not sufficiently clear.

In general, salbutamol sulfate is associated with increasing side effects such as tremor in a dose-dependent manner as the amount of inhalation increases. Cardiac symptoms may lead to a fatal situation in the presence of hypoxemia or hypercapnia, or when other drugs are used concomitantly. In addition, inhalation of salbutamol sulfate during asthmatic attacks causes imbalance of the ventilation-perfusion ratio, resulting in a temporary decrease in arterial oxygen tension, and, therefore, closer attention to the development of side effects is necessary. It has been shown that decreased serum potassium has a negative correlation with the cumulative amount of inhalation of this drug and a positive correlation with increased blood glucose. These side effects usually do not cause clinical problems because the patient gains resistance during prolonged use of the usual dose of the drug.
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patient, however, no resistance to the side effects occurred. Our patient’s development of a variety of side effects seems to have resulted from the following causes: 1) the patient inhaled the drug later than usual on the night before the episode, 2) he took two puffs in the morning during an asthmatic attack, and 3) inhalation by MDI is associated with slower renal excretion than oral dosing. Currently, long-acting β-adrenergic agents are being used more frequently. Since salbutamol sulfate MDI has great value as a medication for rescue use for asthmatic attacks occurring at school, it is important for asthmatics to have a good understanding of the characteristics of this drug and sufficient knowledge of its usage.

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References