# A Case of Accidental Ingestion of A Salbutamol Sulfate Inhalant, Venetlin®

Shin-ichi MATSUDA, Masahiro SHIKADA, Tadakazu SAKAI, Takako NAKANO and Yasumasa OH

*Department of Pediatrics, Tokai University School of Medicine*

(Received October 29, 2007; Accepted June 19, 2009)

**Pediatricians examine increasing numbers of children with bronchial asthma every year. In Japan, medical institutions can provide standardized therapies according to the Japanese Pediatric Guideline for the Treatment and Management of Asthma 2005. Inhalation therapy is highly beneficial, and a substantial proportion of patients choose to purchase inhalators and practice inhalation therapy at home. Recently, we experienced a case of accidental ingestion of a salbutamol sulfate inhalant by a non-asthmatic child, which reminded us anew of the importance of managing the medicines for asthma. We also recognized the need to educate patients and their families on the knowledge of these medicines. In this report, we analyze the case and discuss measures that pediatricians can implement to avoid accidental inhalant ingestion by children.**

**Key words: Salbutamol sulfate inhalant, β2-agonist, accidental ingestion.**

## INTRODUCTION

Childhood asthma has been on the rise in Japan as well as overseas with some variations for regions, and its prevalence in Japan ranks approximately average in the world [1–3]. The 2005 Guideline recommends the use of β2-agonist inhalation at home for asthmatic attacks [4]. As the β2-agonist inhalation therapy becomes widely exercised at home, the therapy drugs become accessible to children, increasing the risk of children accidentally ingesting β2-agonist inhalants.

Herein we report a case of a child accidentally ingesting a salbutamol sulfate inhalant that we have encountered, analyze the factors behind the accident and discuss measures that pediatricians can apply to the prevention of such accidents.

## CASE DESCRIPTION

*Patient*: A 2-year-old boy.

*Major complaint*: Accidental ingestion.

*History of the present disease*: The patient had been well since birth. On July 8, 2001, the patient accidentally ingested salbutamol sulfate inhalant (Venetlin® inhalant; 0.5%, 30 ml/bottle) prescribed for the patient's elder brother. The inhalant was stored in a refrigerator. Mother happened to witness the accident and immediately brought the patient to a nearby physician. Since the inhalant had been little used by the asthmatic brother and one half of the content was remaining, the ingested volume of the inhalant was estimated to be 15 ml. The patient underwent gastrolavage and received activated charcoal 30 minutes after the accidental ingestion. Because tachycardia and tremor persisted, the patient was admitted to our department for systemic management.

*Previous history*: None remarkable.

*Family history*: The patient's 5-year-old elder brother was diagnosed with bronchial asthma and had been on regular inhalation therapy with disodium cromoglicate (Intal®; hereinafter abbreviated as DSCG) and salbutamol sulfate.

*Conditions at admission*: Height 90.0 cm, weight 12.5 kg, body temperature 36.9 ˚C, blood pressure 156/80 mmHg, pulse rate 190/min, and respiration rate 44/min. Consciousness clear, facial color good, no anemia, no jaundice, lung fields clear, heart sounds dull, abdomen soft, no hepatomegaly, no deep tendon hyperreflexia, and tremor in all four limbs.

*Laboratory findings at admission* (Table 1): Peripheral blood showed a slight increase in white blood cell count, with no anemia or decrease in platelet count. Blood biochemistry revealed increased blood glucose and decreased serum potassium. Urinalysis showed that the patient was strongly positive for urinary glucose at 3+, with no occult blood or proteinuria. Electrocardiography showed no notable abnormalities other than supraventricular tachycardia. Plane chest radiographic findings were normal.

*Course after the admission*: Because tachycardia, hypokalemia and other conditions were recognized, we continued fluid infusion and management, including correction of electrolyte levels, and conducted diuresis while the patient was on a cardiorespiratory monitor. Tremor subsided by 8 hours after the onset of the disease, and blood glucose and serum potassium levels were normalized by 12 hours after the onset. Pulse rate and blood pressure became normal 24 hours after the onset. In order to examine for the presence or absence of sequela, various tests were performed including cranial CT, electroencephalography, electrocardiography, and echocardiography, revealing no apparent abnormal findings. We lectured the family the effects, method of use, adverse effects and management of the medicines for bronchial asthma. After gaining

Yasumasa OH, **Department of Pediatrics Tokai University School of Medicine Tel: +81-463-93-1121 Fax: +81-463-94-3426 E-mail: yasumasaoh@yahoo.co.jp**

**Table 1** Laboratory findings at admission

| Hematology | | Urinalysis | |
|---|---|---|---|
| WBC | 12800/μl | glucose | 3+ |
| Hb | 11.3 g/dl | occult blood | – |
| Platelet | 24.9×10⁴/μl | protein | – |

| Blood Biochemistry | | Electrocardiography |
|---|---|---|
| glucose | 172 mg/dl | supraventricular tachycardia |
| Na | 145 mEq/l | |
| K | 2.9 mEq/l | Plain chest radiography |
| Cl | 112 mEq/l | no notable abnormalities |
| GOT | 27 IU/l | |
| GPT | 13 IU/l | Cranial CT |
| CRP | <0.3 mg/dl | no notable abnormalities |

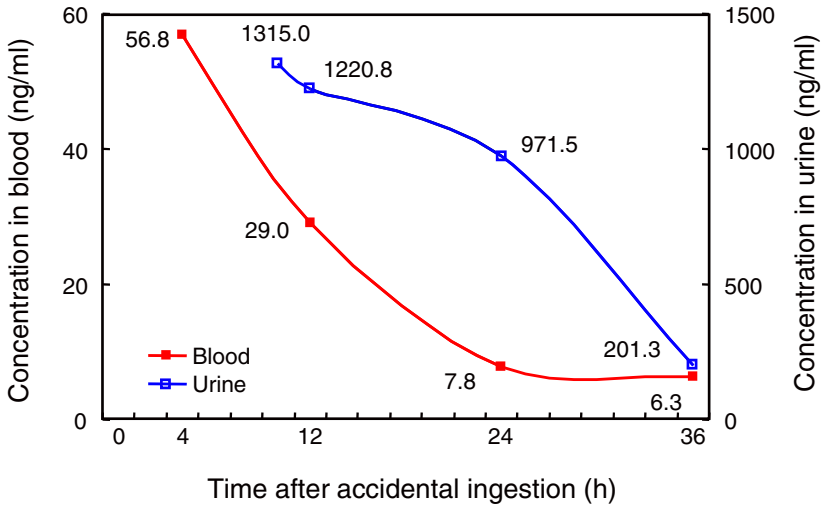


**Fig. 1** Changes in salbutamol sulfate concentrations in blood and urine
Concentration of salbutamol sulfate was determined in blood and urine through the courtesy of GlaxoSmithKline Ltd. from the time of admission until 36 hours after the accidental ingestion.

thorough understanding from the family, we set the discharge date on the 6th hospital day.

Concentration of salbutamol sulfate was monitored in blood and urine from the time of admission until 36 hours after the accidental ingestion (Fig. 1).

## DISCUSSION

Previous cases of accidental ingestion of β2-agonists in excessive quantities mostly involved oral medicines. Our literature search found only one report of accidental β2-agonist inhalant ingestion presented at the 16th Meeting of the Japanese Society of Emergency Pediatrics in 2002 [5]. This case report describes a 2-year-old boy who presented with mild wheezing and was prescribed Venetlin® for inhalation at home. After returning home, his mother saw the boy drinking the drug at around 12:45 and brought him back to the hospital at 13:00. He ingested 10 ml of the drug. While in the waiting room, he became agitated, showed facial pallor and vomited. His heart rate was about 200/min. Gastrolavage was performed and fluid infusion initiated immediately. At 14:00, he had sinus tachycardia with a heart rate of 210/min, and blood pressure was 118/50 mmHg; gastrolavage was again performed, and activated charcoal and magnesium sulfate were administered. At 17:00, his heart rate began to decrease and was 150/min at 19:00. Laboratory findings revealed hyperglycemia and hypokalemia during treatment.

Our patient showed the course of disease and laboratory findings similar to those of the above report [5]. In either case, the patient showed typical symptoms of β2-agonist overdose, including tachycardia, hyperglycemia and hypokalemia, although muscle cramps were absent. Treatment consisted of gastrolavage and activated charcoal in conjunction with diuretics or laxatives, as well as symptomatic treatments, including fluid infusion. Table 2 summarizes the characteristics of salbutamol sulfate. Upon oral administration of 10 mg of salbutamol sulfate, the time until the peak blood concentration is 1 to 2 hours, the half-life in blood is 1.5 to 2 hours, and urinary excretion within 24 hours is 90%. The blood and urinary concentrations of salbutamol sulfate monitored in our patient (Fig. 1) agree well with these values and explain the patient's course after treatment. The patient of the

**Table 2** Characteristics of salbutamol sulfate

| | |
|---|---|
| Selective agonist of β2 receptor | |
| | a selective agonist of β2 receptor with superior bronchodilator activity |
| Side effects | |
| | a large decline of serum potassium level, palpitation, headache, loss of appetite |
| Time until the peak blood concentration | |
| | 1 to 2 hours with oral 10 mg administration |
| Half-life in blood | |
| | 1.5 to 2 hours |
| Excretion | |
| | 90% excreted in urine within 24 hours |
| LD50 of toxicity | |
| | mice: oral 4620 mg/kg |
| | rats: oral >2500 mg/kg |

above cited accidental Venetlin® ingestion [5] recovered sooner than our patient, probably because the ingested quantity was 2/3 of that of our patient.

While salbutamol sulfate is well tolerated, there exists the potential for adverse reactions, especially when given in high doses, or when taken orally or intravenously. A maximum dose for oral inhalation is 0.8 and 1.6 mg per day for children and adults, respectively. Since Venetlin® contains 0.5% salbutamol sulfate, the ingested amount of salbutamol sulfate was 75 mg in our patient and 50 mg in the previous report [5], both of which are apparently an overdose. Overdose of salbutamol sulfate and other β2-selective bronchodilators involves unwanted β sympathomimetic effects, including cardio-selective β1 receptor activation, peripheral vasodilatation, muscle cramps, hyperglycemia and hypokalemia. Sinus tachycardia develops due in part to a decrease in peripheral resistance associated with a reflex increase in cardiac output. Readily absorbed from the gastrointestinal tract, salbutanol sulfate can cause potentially serious hypokalemia upon parenteral and nebulised administration. Treatment is primarily aimed at eliminating the ingested β2-agonist by means of gastrolavage, diuresis and induction of laxation and, if necessary, a cardio-selective β blocker such as metroprolol may be given by injection. Non-selective β blockers are contraindicated for asthma. It is recommended to monitor the serum potassium and glucose levels for possible hypokalemia and hyperglycemia, and to secure fluid infusion route. The patient should not be made to throw up, because it would result in loss of fluid and electrolytes and aggravate the condition. Therefore, it is best for family members to bring the patient to a physician's care immediately.

More important than the consequence and treatment of accidental β2-agonist inhalant ingestion is the means of its prevention. Certainly the most practical and effective preventive measure is to keep drugs out of the reach of children, as is stated on drug packages and containers. The mother of our patient received such instructions and was well aware of the danger of inhalant ingestion. However, the fact that the patient took out the inhalant from the refrigerator is a telling testimony that "to keep the inhalant out of the reach of children" is too abstract and ineffective. In this regard, both the previous [5] and present cases of accidental β2-agonist inhalant ingestion display revealing factors behind childhood accidental ingestion: the patient's age and the circumstance of the accident. In both cases, the patient was 2-year old and ingested the drug in the presence of adult witnesses.

According to the 2006 report of "Survey for Household Supplies-Related Accidents Monitored at Hospitals" from the Ministry of Health Welfare and Labor [6], medical and quasi drugs are among the top 10 causes of childhood accidental ingestion, second only to cigarettes and followed by toys, plastic products, coins, food stuff, detergents and washes, cell batteries and stationeries. Cigarettes and medical and quasi drugs accounted for 35.8 and 16.4%, respectively, of 646 cases reported to the pediatric departments of 8 hospitals participating the survey and have been the top two for twenty-eight years since the survey was initiated in 1979. Cigarette ingestion was most frequent in 6 to 11-month old infants, accounting for 53.7% of all cigarette ingestion cases, and 82.7% of the cases were caused by 6 to 17-month-old infants. In contrast, a majority (68.9%) of drug ingestion cases involved 1 to 2-year-old infants. Infants learn to crawl on all fours around 6 to 11 months of age and, by 1 year of age, can move around actively, gaining access to any objects in sight, for example, cigarette butts on an ash tray. At the age of 1 to 2 years, children are able to open packages and containers, allowing them to imitate adults and drink or swallow the contained materials, such as drugs. This age distribution of accidental ingestion should be taken in consideration when instructing asthma patients and their families on the management of the inhalant.

The form of drug container also needs to be considered. Of the commonly used β2-agonist inhalants, Venetlin® is still provided in a 30-ml bottle form, from which a one-dose quantity is transferred to inhaler or nebulizer; this feature of Venetlin® inhalant is among the underlying causes of the present case because the leftover was ingested by the patient. A more recently commercialized procaterol hydrochloride inhalant (Meptin®) is available in an ampoule form and, similar to Intal® ampoules, is for single use. Ampoules, however, can be brake opened easily by infants and chil-

dren, therefore, would not be sufficiently safe against mischief of youngsters. Thus, strictly speaking, none of the currently available β2-agonist inhalants guarantee safety against childhood accidental ingestion.

We recommend that families with infants and pre-school age children keep the inhalant essentially inaccessible to children by storing the drug in a tightly capped container, on a high place or even in a locker, because children of this age group are too young to understand the danger of the inhalant. In addition, pediatricians should discuss with parents as long as time allows the specifics of where in the house the inhalant can be stored. Such a practice may cause inconvenience to asthmatic children who need adults' assistance in taking out the inhalant from where it is stored. However, this practice ensures that only asthmatic children gain access to the inhalant and may be helpful to minimize the use of the inhalant.

In conclusion, this case report described a 2-year-old boy accidentally ingesting a salbutamol sulfate inhalant and discussed possible means of its prevention. Childhood accidental ingestion of drugs is far more prevalent than we realize. Thus, when prescribing potentially dangerous drugs, pediatricians need to spend a little more time with parents and instruct them specifically where and how drugs can be stored at home.

## ACKNOWLEDGMENTS

This study was presented in abstract form at the 34th Meeting of the Japanese Society of Pediatric Pulmonary Disease at Fukushima, October, 2001.

## REFERENCES

1) Nishima, S. and Odajima, H. 2002. Morbidity of childhood allergic diseases in the phase I trial by the International Study of Asthma and Allergies in Childhood. Jpn. J. Pediatr. Allergy Clin. Immunol. 16: 297–20.
2) Furusho, M. 1995. Epidemiology of bronchial asthma. Asthma 18: 13–16.
3) Worldwide variation in prevalence of symptoms of asthma, allergic rhinoconjunctivitis, and atopic eczema. The International Study of Asthma and Allergies in Childhood (ISAAC) Steering Committee. Lancet 351: 1225–1232. 1998
4) Morikawa, A. and Nishima, S. The Japanese Pediatric Guideline for the Treatment and Management of Asthma 2005. The Japanese Society of Pediatric Allergy and Clinical Immunology. Kyowa Kikaku, Tokyo, 2005.
5) Yano, I. A case of a 2-year-old boy accidentally ingesting 10 ml of Venetlin inhalant. J. Jpn. Soc. Emergency Pediatr. 1: 73. 2002
6) The Ministry of Health Welfare and Labor. 2006 Report of "Survey for Household Supplies-Related Accidents Monitored at Hospitals".
7) Kurihara, K. Asthma practice at outpatient clinics. How to decrease medicines for asthma. Journal of Pediatric Practice 70: 1273–1277. 2007