Clinical reports

Transient renal tubular dysfunction in a patient with severe asthmatic attack treated with sevoflurane

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Introduction

Inhalational anesthetics are effective in treating severe asthmatic attacks resistant to ordinary medical therapies. Since sevoflurane exerts a strong bronchodilating effect and is less irritating to the airway [1], the drug is effective in treating asthmatic attacks [2]. However, the possibility of renal impairment due to long-term sevoflurane administration remains controversial [3]. We report a patient who had a severe asthmatic attack, was treated by inhalation of sevoflurane for 9 days in our intensive care unit (ICU) and developed transient renal tubular dysfunction.

Case report

A 62-year-old man with a 10-year history of asthma had a severe asthmatic attack. The study was approved by the ethical committee of the hospital and informed consent was obtained from the patient and his family on a collection of blood and urine. He resisted ordinary medical treatments and gradually lost consciousness. Oxygen 5 l·min⁻¹ was administered with an oxygen mask to the patient, and arterial blood gas analysis showed the pH, PaO₂, PaCO₂, HCO₃⁻, and Base Excess (BE) to be 7.256, 40.9 mmHg, 64.2 mmHg, 28.5 mmol·l⁻¹, and −0.3 mEq·l⁻¹, respectively, at the time of admission to the ICU. He was intubated and mechanically ventilated. Isoflurane was used for a total of 9 h on the first and second hospital days. However, because isoflurane could not reduce the irritability of his airway, the control of ventilation was difficult with isoflurane. We therefore replaced the drug with sevoflurane. Inhalation anesthetics were passed from a vaporizer and added to a humidifier system attached to a ventilator (Puritan-Bennett 7200ae). Soda lime was not used. Inhaled isoflurane and sevoflurane concentration varied between 0.25% and 6.0% to provide bronchodilation. The end-tidal concentrations of the inhalation anesthetics were continuously measured with an anesthetic analyzer (Capnomac, DATEX, Helsinki). The minimum alveolar concentration (MAC) hours of administered sevoflurane was 298 MAC hours. The age-corrected MAC of sevoflurane in this case was 1.3%. Figure 1 shows the serum and urinary inorganic fluoride concentrations during and after the administration of sevoflurane. The serum inorganic fluoride concentration increased to over 50 μmol·l⁻¹, and its maximum level was 70.5 μmol·l⁻¹. The maximum urinary inorganic fluoride concentration was 2047 μmol·l⁻¹. During sevoflurane administration, the urinary inorganic fluoride concentration did not decrease. Figure 2 plots the urinary concentrations of N-acetyl-β-D-glucosaminidase (NAG) and β-2-microglobulin (BMG). The urinary NAG and BMG concentrations were abnormally elevated, and their maximum levels were 52.3 U·l⁻¹ and 86 000 μg·l⁻¹. These concentrations decreased gradually from the 15th day. The serum BMG concentration was in the normal range (data not shown). Figure 3 shows the data on the urinary volume and daily urinary excretion of NAG and BMG. The daily excretion of NAG and BMG was abnormally elevated, reaching a maximum of 137.5 U·day⁻¹ and 238.7 mg·day⁻¹, respectively. The volume of urine was large (2–6 l daily), but its specific gravity was in the normal range. The values of blood urea nitrogen (BUN), serum creatinine, and creatinine clearance were normal. In the phenolsulphonphthalein (PSP) excretion test, the value at 15 min

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dropped to 17.4% on the 19th hospital day after admission but returned to the normal level on the 23rd hospital day. We administered cefazolin (CEZ), piperacillin (PIPC), fosfomycin (FOM), and gentamicin (GM) to prevent pneumonia in the ICU. The patient was weaned from the ventilator on the 16th hospital day and left the ICU on the 19th hospital day.

**Discussion**

Renal tubular dysfunction is observed when the serum inorganic fluoride concentration exceeds 50μmol·l⁻¹ during methoxyflurane anesthesia [4]. Methoxyflurane is mainly metabolized to inorganic fluoride by cytochrome P450 2E1 in the liver and kidney. Sevoflurane is similarly metabolized to inorganic fluoride by the same enzyme in the liver [5,6]. However, even when the serum inorganic fluoride concentration exceeds 50μmol·l⁻¹ in prolonged sevoflurane anesthesia, no clear renal dysfunction is observed [7,8]. The reason that there is no apparent toxicity in sevoflurane anesthesia irrespective of the compatible peak serum concentration might be the different site of metabolism and the shorter exposure time to an inorganic fluoride level over 50μmol·l⁻¹ compared with methoxyflurane anesthesia. No nephrotoxicity was observed in a patient who was treated with 104 h of inhalation of sevoflurane for an asthmatic attack [2]. However, in that report, the renal function was evaluated by the BUN and serum creatinine values, which mainly indicate renal glomerular function. We evaluated the renal glomerular function using the urine volume and the BUN, serum creatinine, and urinary fluoride concentrations as markers. We assessed renal tubular function on the basis of the urinary concentrations, daily excretion of

**Fig. 1.** Concentrations of serum and urinary inorganic fluoride. *Closed circles and open circles* indicate the serum and urinary inorganic fluoride concentrations, respectively. The serum inorganic fluoride concentration increased to over 50μmol·l⁻¹, and its maximum level was 70.5μmol·l⁻¹. The maximum urinary inorganic fluoride concentration was 2047μmol·l⁻¹

**Fig. 2.** Concentrations of urinary N-acetyl-β-D-glucosaminidase (NAG) and β-2-microglobulin (BMG). The abscissae are logarithmic scales. *Closed circles and open circles* indicate urinary NAG and BMG concentrations, respectively. Urinary NAG concentration increased after the 7th day, and its maximum level was 52.3U·l⁻¹ on the 14th day. Urinary BMG concentration increased after the 2nd day, reaching a maximum of 86000μg·l⁻¹ on the 14th day

**Fig. 3.** Urine volume and daily excretion of urinary NAG and BMG. The urine volume was 2–6 l daily. The daily urinary excretion of NAG increased after the 6th day, peaking at 137.5 U·day⁻¹ on the 16th day. The daily urinary excretion of BMG increased after the 2nd day, peaking at 238.7 mg·day⁻¹ on the 16th day