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Clinical reports

Two cases of status asthmaticus treated with isoflurane

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Introduction

Status asthmaticus is defined as a severe asthma attack that is unresponsive to usually effective bronchodilators such as adrenergic agents and that may result in death [1]. Inhalational anesthetic agents have been sporadically used to treat this disease for many years [2–4]. Although many of these agents induce serious adverse reactions [5–7], isoflurane produces bronchodilatation through a number of mechanisms without significant adverse effects [8,9].

We report two cases of status asthmaticus that was refractory to conventional therapy but responded dramatically to isoflurane.

Case reports

Case 1

A 45-year-old man with a history of asthma since childhood was admitted to our hospital because of worsening bronchospasm for 1 day following a common cold. He was treated with nebulized β-stimulant, intravenous aminophylline, and hydrocortisone. Despite this therapy, his respiratory status continued to decline and cyanosis appeared. Arterial blood gas values (ABG) were a pH of 7.03, $Paco_2$ of 102 mmHg and Pao_2 of 28 mmHg (FiO_2 of 0.5). He was endotracheally intubated and was transferred to our intensive care unit (ICU). Isoflurane inhalation was initiated, using a ventilator (Siemens Servo 900C Solna, Sweden) with an attached vaporizer. The isoflurane concentration was increased to 2.0%. Therapy with methylprednisolone (1000 mg·day^{-1} for 3 days), antibiotics (cefoperazone 4 g·day^{-1}), and a nebulizing cocktail (tyloxapol, dexamethasone, dibekacin) was also initiated concomitant with isoflurane treatment. Soon after initiation of isoflurane inhalation, marked improvement was observed clinically. The isoflurane concentration was slowly decreased. Isoflurane inhalation was continued for 46 h, after which the patient was successfully weaned from ventilator. He was extubated 60 min after isoflurane treatment was discontinued and consciousness became clear 3 h later. We extubated the patient before emergence to prevent the recurrence of attack due to endotracheal tube. Chest roentgenograms taken before and after isoflurane treatment are shown in Fig. 1(a,b). The remainder of his hospital course was unremarkable. All laboratory values remained within normal limits.

Case 2

A 29-year-old man with a 5-year history of asthma was admitted to our hospital because of severe dyspnea. He arrived in the emergency department unconscious and had gasping respiration, and appeared cyanotic. He was soon intubated endotracheally and transferred to the ICU. On arrival, he was given aminophylline and hydrocortisone intravenously. β-Stimulant inhalation was also initiated. Despite these therapies, his condition deteriorated, and ABG values were a pH of 7.15, $Paco_2$ of 81 mmHg, and Pao_2 of 103 mmHg (FiO_2 of 0.4). Three hours after ICU admission, isoflurane inhalation was initiated via a ventilator and increased to 2.0%. Therapy with methylprednisolone (1000 mg·day^{-1} for 3 days),

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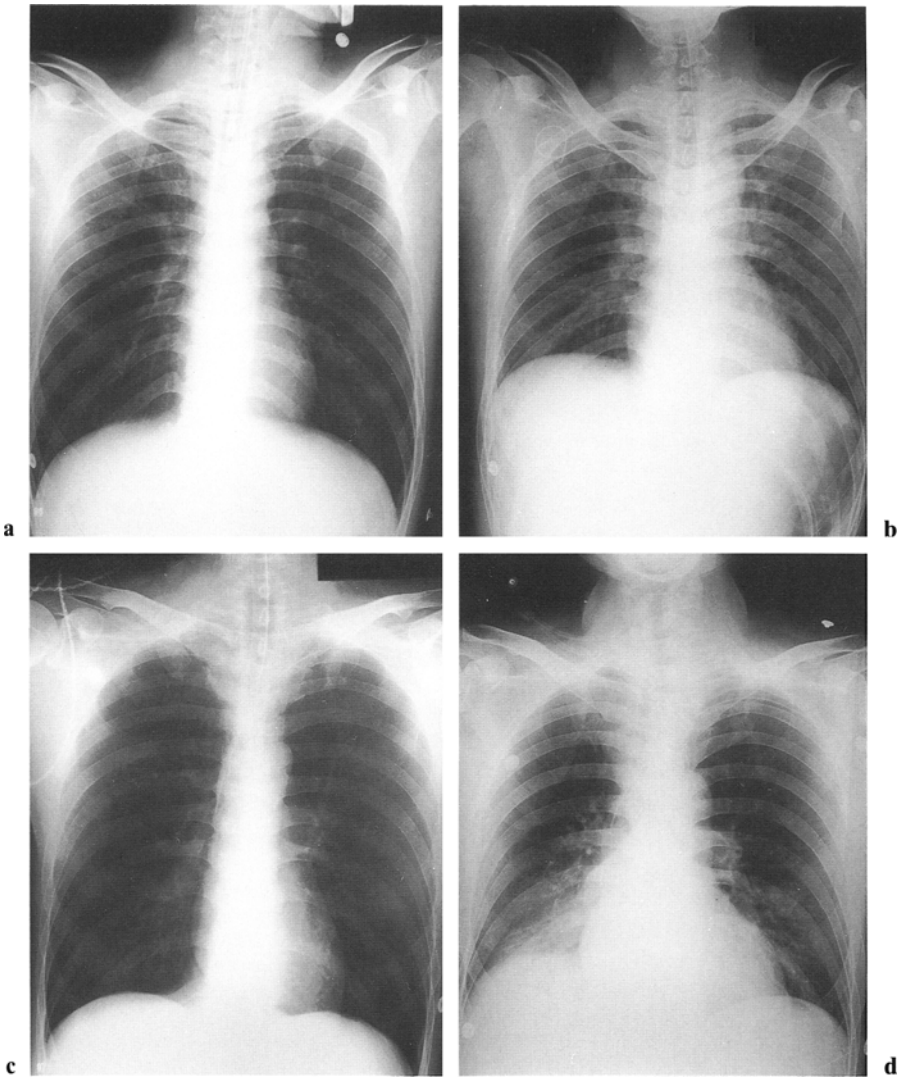

Fig. 1a–d. Chest roentgenograms (**a,b** case 1; **c,d** case 2) taken before isoflurane treatment show diminished vascularity in the central and peripheral zones and pulmonary hyperaeration (**a,c**). Radiographs taken after completion of isoflurane treatment show marked improvement (**b,d**)

antibiotics (ceftazidime 2 g·day^{-1}), nebulizing cocktail (tyloxapol, dexamethasone, dibekacin) was also initiated parallel to isoflurane treatment. After 6 h of therapy, marked clinical improvement was seen and ABG values changed to a pH of 7.33, $Paco_2$ of 44 mmHg and Pao_2 of 194 mmHg (FiO_2 of 0.4) respectively. The isoflurane concentration was decreased gradually and discontinued 40 h after initiation. The patient was weaned from the ventilator and extubated 30 min after isoflurane was discontinued. Awakening occurred 2.5 h later. We extubated the patient before emergence to prevent the recurrence of attack due to endotracheal tube. Chest roentgenograms taken before and after isoflurane therapy are shown in Fig. 1(c,d). The patient had an uneventful hospital course. There was no evidence of hepatic or renal toxicity.

Discussion

Asthma is usually a simple disease to treat and responds to conventional therapy with oxygen, aminophylline, inhaled β-adrenergic agonists, and corticosteroids. Status asthmaticus is a life-threatening illness that fails to respond to these therapies. Additional pharmacological therapy would be desirable in patients with status asthmaticus and the benefits of inhaled anesthetics have been considered.

Inhalational anesthetics produce bronchodilation through direct relaxation of the broncheal smooth muscles, β-adrenergic receptor agonism, antagonism of the action of histamine, and depression of airway relflexes via neuromuscular blockade [9]. However many inhalational anesthetics have serious adverse effects. Diethyl ether and cyclopropane are extremely flammable which precludes their use in the ICU. Halothane has been associated with arrhythmias when

administered in conjunction with epinephrine and aminophylline [5]. The metabolic product of halothane may be responsible for a rare form of hepatic injury [6]. Enflurane causes an increase in the serum fluoride level, which may lead to renal insufficiency [7], while isoflurane is not flammabile and is not associated with arrhythmias. Isoflurane undergoes minimal metabolism (0.2%) [10], and to our knowledge, there are no reports of isoflurane-induced hepatic or renal injury. The blood/gas solubility coefficient of isoflurane is 1.41 [10], and the fat/gas partition coefficient is 94.5. This means isoflurane acts rapidly and the time to recovery of consciousness is not too long. In our two cases, awakening occurred 3 h and 2.5 h, respectively, after the isoflurane treatment was stopped. The total doses of isoflurane were 36 MAC·h and 40 MAC·h, respectively. The emergence from anesthesia is not delayed compared with other reports [11]. For these reasons, isoflurane is useful for the management of life-threatening status asthmaticus.

Isoflurane causes systemic vasodilatation secondary to arterial smooth muscle relaxation [10]. Therefore, hypotension is responsive to plasma volume expansion and vasopressors. Our patients responded to volume expansion and low-dose dopamine ($3–5\ \mu g \cdot kg^{-1} \cdot min^{-1}$).

The effects of long-term anesthetic exposure for ICU staff must also be considered. We installed a simple waste gas scavenging system by connecting the exhaust port of the ventilator to a T-piece that was attached to a reservoir bag. Wall suction was applied to the other end of the T-piece.

The pathophysiology of status asthmaticus constitutes bronchial spasm, edema, and inflammation of the mucous membrane and the formation of mucus plugs [1]. Thus, inhalational anesthetic therapy is insufficient; in such cases, it is necessary to simultaneously reduce the inflammation and eliminate the mucus plugs.

In summary, we describe two patients with life-threatening status asthmaticus refractory to conventional therapy who, when treated with isoflurane, showed rapid bronchodilatation. All patients survived and none experienced significant adverse effects attributable to the drug. Isoflurane may be the drug of choice for additional therapy in status asthmaticus. It is a potent bronchodilator; moreover, its mild adverse effects and lack of toxicity are significant advantages.

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