J Anesth (2014) 28:610–612
DOI 10.1007/s00540-013-1751-0

CLINICAL REPORT

Treatment of life-threatening hypercapnia with isoflurane in an infant with status asthmaticus

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Received: 17 April 2013 / Accepted: 7 November 2013 / Published online: 6 December 2013

Abstract We encountered a 2-year-old child with life-threatening hypercapnia, with a $PaCO_2$ of 238 mm Hg and severe respiratory and metabolic acidosis, due to status asthmaticus that was refractory to steroid and bronchodilator therapy. Suspecting ventilatory failure and excessive ventilation-induced obstructive shock, we started respiratory physiotherapy in synchrony with her respiration, to facilitate exhalation from her over-inflated lungs. Isoflurane inhalation was commenced in preparation for extracorporeal circulation, to reduce the hypercapnia. The combination of respiratory physiotherapy and isoflurane inhalation resulted in a rapid decrease in ventilatory resistance and $PaCO_2$ levels within a few minutes, with recovery of consciousness within 60 min. Isoflurane inhalation was gradually discontinued and steroid and aminophylline therapy were commenced. The patient recovered completely without any recurrence of her bronchospasm and without any residual neurological deficits. In our patient with a severe asthmatic attack, decreased exhalation secondary to asthma and overventilation during artificial ventilation resulted in overinflation of the lungs, which in turn led to cerebral edema and obstructive cardiac failure. The favorable outcome in this case was due to the short duration of hypercapnia. Hence, we conclude that the duration of hypercapnia is an important determinant of the morbidity and mortality of status asthmaticus-induced severe hypercapnia.

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Keywords Status asthmaticus · Hypercapnia · Isoflurane

Introduction

We present a case of status asthmaticus with life-threatening hypercapnia (partial pressure of carbon dioxide being 238 mm Hg) accompanied by circulatory failure that was successfully treated with a favorable neurological outcome because of short duration of severe hypercapnia.

Case

A 2-year-old female child with a history of low birth weight, atrial septal defect (ASD) and anal atresia was admitted at a hospital for refractory cough. She was diagnosed with bronchial asthma at the age of 18 months. Five days prior to her hospitalization, she had received treatment with inhalational steroids as an outpatient.

On admission, the patient was treated with inhalational steroids and β-2 stimulants, and intravenous administration of aminophylline, despite which there was no improvement in her symptoms of prolonged expiration and labored breathing. Subsequently, she developed altered consciousness and hypoxia, for which her trachea was intubated. Two hours after intubation, the attending physicians decided to transfer her to our ICU for further intensive care.

During the transportation to our hospital, which took 2 h, she was ventilated with 100 % oxygen administered via a self-inflating bag by the accompanying physician, without the development of hypoxia on the monitoring of pulse oximeter.

On admission to the ICU of our hospital, the patient was deeply comatose with no response to painful stimuli. Her limbs felt markedly cold. Internal carotid artery pulsations were palpable but weak. Blood pressure and heart rate on admission to the ICU were 138/90 mm Hg and 150 beats/min, respectively, and they decreased to 104/40 mm Hg and 100 beats/min after several minutes. No spontaneous respiration was detectable and ventilation via Jackson-Rees circuit was difficult. Blood gas analysis demonstrated the following: pH 6.71, $PaCO_2$ 238 mm Hg, PaO_2 185 mm Hg, HCO_3^- 13.5 mEq/l, which was suggestive of severe respiratory acidosis caused by ventilatory failure due to bronchospasm and metabolic acidosis caused by excessive ventilation-induced obstructive shock. We immediately performed respiratory physiotherapy by compressing the ribcage using the palms of the hands in synchrony with expiration, to facilitate exhalation of entrapped alveolar gas as previously reported [1]. Simultaneously, inhalation of 1.5 % isoflurane with pure oxygen using an anesthetic device was commenced, as preparation for extracorporeal membrane oxygenation (ECMO). Several minutes after starting serial treatment with physiotherapy and isoflurane inhalation, the airway resistance to manual ventilation was seen to have rapidly decreased. The patient's heart rate also increased to 140 beats/min. At 30 min after starting isoflurane inhalation, blood gas analysis demonstrated a pH of 7.31, $PaCO_2$ of 47 mm Hg, PaO_2 of 250 mm Hg and HCO_3^- of 19.8 mEq/l under manual ventilation. Blood pressure and heart rate at 30 min after starting isoflurane inhalation were also increased to 130/62 mm Hg and 130 beats/min, respectively. Sixty minutes after starting isoflurane inhalation, after observing movement of the patient's extremities, she was weaned from isoflurane inhalation therapy by decreasing the inhalation concentration of isoflurane from 1.5 to 0.5 %. Inhalation of 0.5 % isoflurane under synchronized intermittent mandatory ventilation (respiratory rate; 20 breaths per minute, pressure control; 12 cm H_2O, PEEP; 3 cm H_2O, FiO_2; 0.45) was continued for over 2 h, during which time there was no recurrence of the increased airway resistance. Hence, inhalation of isoflurane was discontinued and instead 125 mg of methylprednisolone and a sustained infusion of aminophylline at the rate of 1 mg/kg/h were administered intravenously. Using several times of bolus injection of 5 μg of fentanyl as sedation, mechanical ventilation was continued, using the continuous positive airway pressure mode (PEEP; 3 cm H_2O, FiO_2; 0.4, respiratory rate; 28 breaths per minute). Twelve hours after ICU admission, results of blood gas analysis were as follows: pH: 7.42, $PaCO_2$: 39 mm Hg, PaO_2: 150 mm Hg, HCO_3^- of 26.5 mEq/l. Blood pressure and heart rate were 122/70 mm Hg and 118 beats/min, respectively. The patient's trachea was extubated 18 h after ICU admission. She responded to verbal command and was almost completely conscious with a blood pressure of 100/50 mm Hg and heart rate of 110 beats/min after extubation. As slight wheezing was heard on auscultation, the sustained infusion of aminophylline was continued and several times of steroid inhalation was started. The wheezing disappeared on the 2nd ICU day. On the 3rd ICU day, the patient was transferred to the pediatric ward for further treatment since there were no further recurrences of asthmatic attacks. The patient was discharged on the 12th day after admission without any neurological complications.

Discussion

Although the mortality rate due to infantile bronchial asthma has decreased over recent years [2], the potential risk of death even during the first attack of childhood bronchial asthma still remains. Rapid and adequate treatment is required to prevent asthma-related deaths. In our patient, despite conventional medical therapy for the asthmatic attack, hypoxemia and altered consciousness developed, which required tracheal intubation and assisted ventilation. Since status asthmaticus is characterized by prolongation of expiration due to bronchospasm, excessive positive pressure ventilation can result in entrapment of alveolar gas and consequent hyperinflation of the lung. This hyperinflation may result in obstructive shock and cardiac arrest in patients with status asthmaticus [3]. During transportation to the ICU, ventilation was performed manually using a self-inflating bag. We consider that the

Table 1 Clinical effects of asthma-induced hypercapnia on neurological outcome

	Our Case	Udy [6]	Adnet [7]	Mezzeo [8]	Rodorigo [9]	Edmunds [10]	Gallucio [11]
Age	2	10	35	8	49	11	56
$PaCo_2$ (max)	238	196	192	293	66	187	119
Duration (h)	3	2	10	10	72	72	250
Complications	None	None	None	None	SAH, brain edema	SAH, brain edema	Brain edema
Outcome	GR	GR	GR	GR	GR	Blindness (left eye)	Brain death

SAH subarachnoid hemorrhage, *GR* good recovery

use of a self-inflating type of bag should be avoided in a patient with severe asthmatic attack because this type of bag can inspire mandatorily, resulting in overinflation of the lung.

Due to the prolonged expiration that is a characteristic of status asthmaticus, it is seldom complicated by hypercapnia. A study using isolated porcine airway smooth muscle cells has demonstrated that decrease in intracellular pH followed by hypercapnia induces relaxation of airway smooth muscle [4]. This phenomenon may be associated with attenuation of bronchial constriction in asthma attack. In a clinical situation, however, hypercapnia has never been recommended and hypercapnia is rather harmful in treatment of severe asthmatic attack.

In one study, a partial pressure of carbon dioxide of up to 100 mm Hg was demonstrated as being relatively safe for brain cells [5]. However, the safe and permissive levels of hypercapnia in humans have not been clearly elucidated. Hypercapnia increases cerebral blood flow by inducing vasodilation, and consequently increases intra-cranial pressure. Moreover, in patients with status asthmaticus, the increase in intra-thoracic pressure caused by prolonged expiration-induced hyperinflation of the lung and subsequent decrease in venous return from the brain, can also possibly increase intra-cranial pressure. It is assumed that both these mechanisms can act together to increase the intra-cranial pressure, which could result in cerebral edema in patients with status asthmaticus. However, in our case consciousness disturbance at ICU admission was thought to be a hypercapnia–induced narcotic action rather than a brain edema-induced effect.

Table 1 shows the comparison between our case and previous reports of asthma-induced hypercapnia, demonstrating the relationship between the level and duration of hypercapnia and neurological outcome. According to some previous case reports, several hours of hypercapnia ranging from 192 to 293 mm Hg in patients with asthmatic attacks resulted in no neurological disorders [6–8]. In other case reports, on the other hand, hypercapnia during an asthmatic attack resulted in brain edema and subarachnoid hemorrhage [9–11]. This shows that the duration of persistent hypercapnia may be more important than the actual partial pressure of carbon dioxide in determining the likelihood of occurrence of neurological complications. In our case, we believe that this favorable outcome was due to the fact that the remarkable hypercapnia was successfully treated within a few hours. Status asthmaticus induced-hypercapnia should be treated as quickly as possible, to prevent the development of cerebral edema and its complications.

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