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Sevoflurane therapy for life-threatening asthma in children

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Editor's key points

- Children with life-threatening asthma are successfully treated with sevoflurane inhalation therapy without serious side-effects.
- Sevoflurane administration corrects high levels of P_{CO_2} and provides clinical improvement within the first hours.
- Prospective research is required to further explore the position of sevoflurane as rescue medication.

Background. Asthma is a common disease in children and often develops early in life. This multicentre retrospective case series describe the use and effectiveness of sevoflurane inhalation therapy in a series of children with severe asthma in the paediatric intensive care unit (PICU).

Methods. Seven children ranging from 4 to 13 yr of age admitted to the PICU of two tertiary care hospitals in the Netherlands were included. They all were admitted with the diagnosis of severe asthma requiring invasive mechanical ventilation and were treated with sevoflurane inhalation therapy.

Results. The median (range) P_{CO_2} level at the start, after 2 h, and at the end of sevoflurane treatment were 14 (5.1–24.8), 9.8 (5.4–17.0), and 6.2 (4.5–11.4) kPa (P=0.05) while the median (range) pH was 7.02 (6.97–7.36), 7.18 (7.04–7.35), and 7.43 (7.15–7.47) kPa (P=0.01), respectively. The median (range) peak pressure values declined from 30 (23–56) to 20.4 (14–33) cm H_2O (P=0.03). No severe adverse effects besides hypotension, with sufficient response to norepinephrine treatment, were seen.

Conclusions. Sevoflurane inhalation corrects high levels of P_{CO_2} and provides clinical improvement in mechanically ventilated children with life-threatening asthma who fail to respond to conventional treatment.

Keywords: anesthetics, inhalation; asthma; pediatrics; sevoflurane

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Asthma is a common disease in children and often develops early in life. It is a chronic inflammation of the airways, with reversible airflow obstruction and enhanced bronchial reactivity.[1] In Western Europe, the prevalence is 9.7% in children from 6 to 7 yr old and 15.8% in children from 13 to 14 yr old.[2] Of these children, respectively, 12.6 and 15.2% have severe asthma; ~9% of the children with asthma visit an emergency department while 2% need hospitalization.[2 3] A severe asthma attack requiring hospitalization is treated with oxygen, corticosteroids, and β_2-agonists, either nebulized or i.v., in combination with anticholinergic agents and magnesium sulphate. Life-threatening asthma requires invasive interventions like mechanical ventilation and can even be fatal.[4 5] There is a positive correlation between asthma prevalence in children and the amount of hospital admissions and mortality rate.[6] It seems, therefore, important to develop more efficient therapies to prevent death in children because of this disease. In 2004, an animal study demonstrated that volatile agents reverse bronchoconstriction in sensitized guinea pigs.[7] For several years, inhalation of volatile anaesthetics, such as halothane and isoflurane, have been used as last resort for the treatment of life-threatening asthma in children.[4 8–10] These agents provide a reversal of bronchospasm in humans as well, but the exact mechanism of its effect is not clear.[11] The proposed mechanisms include lowering of vagal tone, direct relaxation of smooth muscle tissue, inhibition of the release of bronchoconstrictive mediators, and synergy with catecholamines.[4 11] Sevoflurane is a newer volatile anaesthetic agent, and is frequently used in children for the induction and maintenance of anaesthesia. It has a low blood to gas solubility coefficient and for this reason provides a rapid and smooth inhaled induction.[12] An animal study showed the beneficial effect of sevoflurane on asthmatic bronchoconstriction, which was later confirmed in humans.[13–15] We describe a multicentre retrospective case series of the use of sevoflurane therapy in children with asthma on the paediatric intensive care unit (PICU).

Methods

In the PICU database with all patient admission data of two university teaching hospitals, children admitted with asthma over a period of 10 yr (2002–2012) were collected. Children who did not receive mechanical ventilation were excluded. Medical records of the remaining children were analysed. Children who were treated with sevoflurane inhalation therapy with a dedicated anaesthesia system were identified and reviewed. Patient characteristic data, medical history, provocation factor for the current asthma attack, and medication before hospitalization were gathered. To determine the effect of sevoflurane therapy, blood gas and mechanical ventilation parameters, other medication used, and the dose and duration of sevoflurane therapy were collected. Outcomes included clinical improvement of the patient as a subjective measure. Objective measures were improvement of blood gas and mechanical ventilation parameters, and duration of PICU stay. Statistical analysis of the changes in blood gas and mechanical ventilation parameters after administration of sevoflurane was performed with the Mann–Whitney *U*-test and a *P*-value of <0.05 was considered statistically significant.

Results

A total of seven children (age range 4–13 yr) were included. One patient presented with a first exacerbation of asthma and had not been previously diagnosed with this disease. All other patients used daily asthma medication, varying from beclomethason, fluticasone, salmeterol in combination with fluticasone, and montelukast, in combination with salbutamol when necessary. Five patients had no history of hospitalization for asthma exacerbations, and in six children, the asthma attack was triggered because of a viral or bacterial infection. All patients received oxygen and multiple inhalations with salbutamol and ipratropium bromide, followed by i.v. prednisolone, salbutamol, and magnesium sulphate. They showed no improvement of oxygenation and ventilation with the conventional treatment. Because of life-threatening respiratory muscle fatigue or altered mental status, the patients were sedated and intubated with a varying combination of propofol, morphine, rocuronium, esketamine, and midazolam. Sevoflurane treatment was indicated because of respiratory acidosis ($n=5$), hypoxaemia ($n=1$), or a combination ($n=1$). Sevoflurane was administered for a median duration of 24 h, with a range of 0.5–90 h. The peak concentration of sevoflurane ranged from 1 to 8%. Six patients showed an immediate clinical improvement and a progressive correction of blood gas parameters and peak pressures. In Figures 1–3, individual improvement of blood gas parameters is displayed. The first assessment point is 2–3 h after the start of the treatment, except for the patient who only received 0.5 h sevoflurane. The endpoint in the figures varies from 0.5 to 90 h. There was a significant improvement in Pa_{CO_2}, pH, and peak pressure at the end of treatment compared with the start. The median (range) Pa_{CO_2} levels at the start, at the first assessment, and at the end of sevoflurane treatment were 14 (5.1–24.8), 9.8 (5.4–17.0), and 6.2 (4.5–11.4) kPa ($P=0.05$) while the median (range) pH was 7.02 (6.97–7.36), 7.18 (7.04–7.35), and 7.43 (7.15–7.47) kPa ($P=0.01$), respectively. The median (range) peak pressure values normalized from 30 (23–56) to 20.4 (14–33) cm H_2O ($P=0.03$). One patient failed to respond to sevoflurane treatment; afterwards, he was diagnosed with acute respiratory distress syndrome (ARDS). Five patients developed hypotension; of which, four received norepinephrine (0.1–0.6 μg kg h) as vasoactive support, effectively increasing the arterial pressure. One patient had pupils

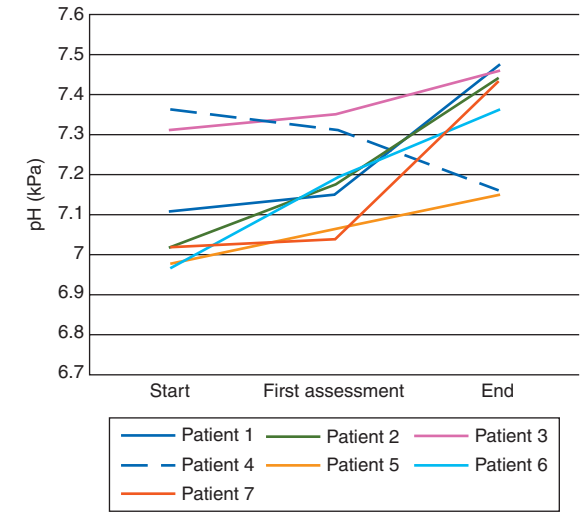

Fig 1 pH values per patient before, after a first assessment, and at the end of treatment with sevoflurane. The dashed line shows the patient who did not respond to sevoflurane therapy.

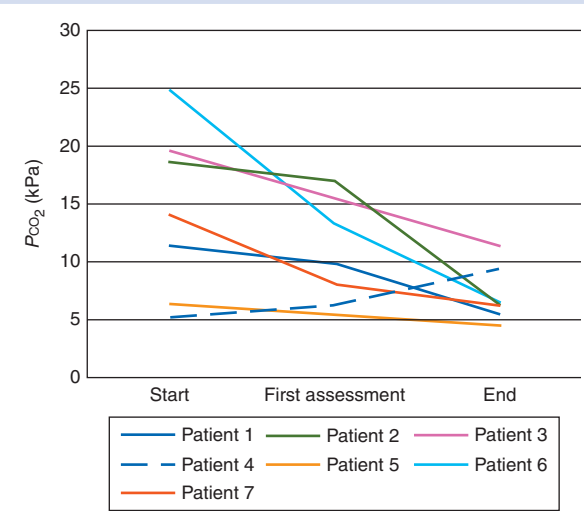

Fig 2 P_{CO_2} values per patient before, after a first assessment, and at the end of treatment with sevoflurane. The dashed line shows the patient who did not respond to sevoflurane therapy.