Increase in serum creatine phosphokinase concentrations after suxamethonium during sevoflurane or isoflurane anaesthesia in children

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Summary

We have studied whether sevoflurane or isoflurane anaesthesia modulates the effect of suxamethonium on serum concentrations of enzyme markers of skeletal muscle function in paediatric patients. Eighty patients undergoing bilateral tonsillectomy, aged 5–12 yr, were allocated randomly to receive anaesthesia with either sevoflurane and nitrous oxide or isoflurane and nitrous oxide. Serum creatine phosphokinase (CK), aspartate aminotransferase (AST), alanine aminotransferase (ALT) and lactate dehydrogenase (LDH) concentrations were measured before, and at 30 min and 20 h after induction of anaesthesia. Mean CK concentrations increased from 97.0 (SD 17.3) to 478 (170) iu litre\(^{-1}\) in the sevoflurane group and from 86.9 (22.4) to 628 (223) iu litre\(^{-1}\) in the isoflurane group, 20 h after induction of anaesthesia. Mean peak serum CK concentration in the sevoflurane group (478 (170) iu litre\(^{-1}\)) was significantly less (\(P<0.05\)) than that in the isoflurane group (628 (223) iu litre\(^{-1}\)). Mean serum AST concentration increased from 17.5 (4.9) to 31.7 (3.5) iu litre\(^{-1}\) in the sevoflurane group and from 17.3 (2.4) to 34.8 (5.7) iu litre\(^{-1}\) in the isoflurane group, 20 h after induction of anaesthesia. Mean peak serum AST concentrations in the sevoflurane group were significantly lower (\(P<0.05\)) than those in the isoflurane group. There were no significant differences in serum ALT or LDH concentrations between the groups either before or after anaesthesia. We conclude that administration of suxamethonium during either sevoflurane or isoflurane anaesthesia caused a marked increase in serum CK concentrations in paediatric patients. The clinical significance of this finding is uncertain. (Br. J. Anaesth. 1997; 78: 372–374).

Key words

Sevoflurane has a low blood-gas partition coefficient (0.63) and the lowest pungency\(^{1,2}\) of commercially available inhalation anaesthetics. Thus a rapid increase in alveolar and tissue anaesthetic partial pressure is achieved easily during induction with sevoflurane, and in children its haemodynamic effects are less than that of halothane.\(^4\) Because of these characteristics, this agent is the most frequently used for induction of anaesthesia in paediatric patients.

Serum creatine phosphokinase (CK) concentrations increase more in children than in adults after i.v. administration of suxamethonium during either halothane or enfurane anaesthesia.\(^5,6\) Peak serum CK concentrations are reported to occur at 9–24 h after administration of suxamethonium. However, data on serum CK concentrations for this period during sevoflurane and isoflurane anaesthesia have not been reported. Thus this study was designed to determine serum concentrations of CK and other enzymes before and after suxamethonium during sevoflurane or isoflurane anaesthesia in paediatric patients.

Patients and methods

The study was approved by the Institutional Ethics Committee and informed consent was obtained from a parent of each patient. We studied 80 ASA I paediatric patients, aged 5–12 yr, undergoing bilateral tonsillectomy.

Patients were allocated randomly to one of two groups to receive either sevoflurane or isoflurane. All patients were premedicated with oral diazepam 0.3 mg kg\(^{-1}\), 60 min before induction of anaesthesia. Anaesthesia was induced in 40 patients with 5.0% sevoflurane in combination with nitrous oxide 2 litre min\(^{-1}\) and oxygen 2 litre min\(^{-1}\). Anaesthesia was maintained with 2.5% sevoflurane and 50% nitrous oxide in oxygen. The remaining 40 patients received 3.0% isoflurane and nitrous oxide 2 litre min\(^{-1}\) and oxygen 2 litre min\(^{-1}\) during induction. Anaesthesia was maintained with 1.5% isoflurane and 50% nitrous oxide in oxygen. I.v. suxamethonium 1 mg kg\(^{-1}\) was given to facilitate tracheal intubation in...
both groups. End-expiratory concentrations of oxygen, carbon dioxide and anaesthetics were monitored using a 5250 RGM analyser (Ohmeda, Madison, WI, USA). Lactated Ringer’s solution was infused at a rate of 4 ml kg⁻¹ h⁻¹ to all patients. The lungs were ventilated mechanically to maintain PEEP, at 4.8–5.6 kPa. Rectal temperature was monitored continuously with an electric thermistor and maintained at 36.5–37.5°C using a warming blanket. Postoperative pain relief was provided by rectal diclofenac sodium 12.5–25 mg every 6 h as needed.

Fasciculations after administration of suxamethonium and postoperative muscle pain the day after surgery were evaluated in all patients. Blood samples were obtained just before, and 30 min and 20 h after induction of anaesthesia. CK was measured using a modification of the Rosalki’s method with a Paramax kit from Baxter (Deerfield, USA). Aspartate aminotransferase (AST) and alanine aminotransferase (ALT) concentrations were measured using a modification of the method of the Scandinavian Society of Clinical Chemistry with a Paramax kit from Baxter (Deerfield, USA). Lactate dehydrogenase (LDH) concentration was measured according to a modification of the method of Gay and colleagues using a Paramax kit. The CK method has a sensitivity of 0.091 mAd min⁻¹ iu⁻¹ litre⁻¹ and a coefficient of variation (cv) of less than 2%. The AST, ALT and LDH assays have a sensitivity of 0.182 mAd min⁻¹ iu⁻¹ litre⁻¹ and a cv of less than 7%. Normal ranges are 38–173 iu litre⁻¹ for CK, 12–45 iu litre⁻¹ for ALT and 180–387 iu litre⁻¹ for LDH.

Data, expressed as mean (sd), were analysed using the Student’s t test for paired and unpaired samples. P<0.05 was considered statistically significant.

Results

There were no significant differences between the two groups in age, weight, duration of surgery and anaesthesia, or rectal temperature (table 1). Laryngospasm, bronchospasm and masseter muscle spasm did not occur in any patient during induction of anaesthesia. Systolic and diastolic arterial pressures and heart rate during anaesthesia were similar in both groups.

Postoperative muscle pain was reported by 33% of patients in the sevoflurane group and by 43% in the isoflurane group. There were no significant differences in serum concentrations of CK or AST between patients with and without muscle pain. Fasciculations were observed in 18% of patients in the sevoflurane and in 15% of patients in the isoflurane group. There were no significant differences in serum concentrations of CK or AST between patients with and without fasciculations. In addition, we did not observe any significant correlation between age and CK concentrations during sevoflurane or isoflurane anaesthesia.

Mean basal serum CK concentrations in the sevoflurane group were 97.3 (sd 37.0) iu litre⁻¹ before anaesthesia, which increased to 478 (170) iu litre⁻¹ (P<0.05) 20 h after injection of suxamethonium. In the isoflurane group, basal serum CK concentrations were 86.9 (22.4) iu litre⁻¹ before anaesthesia and 628 (223) iu litre⁻¹ (P<0.05) 20 h after injection of suxamethonium. Basal AST concentrations in the sevoflurane group were 17.5 (4.9) iu litre⁻¹ before anaesthesia, which increased significantly to 31.7 (3.5) iu litre⁻¹ (P<0.05) 20 h after suxamethonium. In the isoflurane group, basal serum AST concentrations were 17.3 (2.4) iu litre⁻¹ before anaesthesia, increasing significantly to 34.8 (5.7) iu litre⁻¹ (P<0.05) 20 h after administration of suxamethonium. Mean serum CK and AST concentrations in the sevoflurane group were significantly lower (P<0.05) than those in the isoflurane group, 20 h after suxamethonium. Mean serum CK and AST concentrations 30 min after administration of suxamethonium were 113.4 (6.5) and 20.3 (1.7) iu litre⁻¹ in the sevoflurane group and 115.8 (7.0) and 22.1 (2.3) iu litre⁻¹ in the isoflurane group. There were no significant differences in serum ALT and LDH concentrations between groups, 30 min and 20 h after suxamethonium (table 2).

### Table 1 Patient characteristics in the sevoflurane and isoflurane groups (mean (sd or range) or number)

<table>
<thead>
<tr>
<th></th>
<th>Sevoflurane (n=40)</th>
<th>Isoflurane (n=40)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (yr)</td>
<td>7.5 (5.11)</td>
<td>8.0 (5.13)</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>26.9 (9.9)</td>
<td>27.7 (12.1)</td>
</tr>
<tr>
<td>Sex (M/F)</td>
<td>18/22</td>
<td>17/23</td>
</tr>
<tr>
<td>Anaesthesia time (min)</td>
<td>60.6 (17.4)</td>
<td>67.3 (13.5)</td>
</tr>
<tr>
<td>Operative time (min)</td>
<td>48.3 (12.7)</td>
<td>51.7 (14.8)</td>
</tr>
<tr>
<td>Maximum rectal temperature during anaesthesia (°C)</td>
<td>37.3 (0.5)</td>
<td>37.0 (0.6)</td>
</tr>
<tr>
<td>Maximum rectal temperature after anaesthesia (°C)</td>
<td>37.4 (0.7)</td>
<td>37.1 (0.9)</td>
</tr>
</tbody>
</table>

### Discussion

Suxamethonium is known to increase serum CK and myoglobin concentrations when given during halothane or enflurane anaesthesia and to produce larger increases in serum concentrations of these enzymes in paediatric patients. It has been reported that plasma CK and myoglobin concentrations do not correlate with fasciculations after suxamethonium, although children are known not to
fasciculate. Increased CK concentrations in children after suxamethonium could be caused by muscle prematurity, making the muscle prone to release CK or to increase muscle content of CK. 5

Tano and Fujiiwara 10 reported that serum CK concentrations 20 min after administration of suxamethonium during sevoflurane anaesthesia were similar to those during halothane anaesthesia. Noguchi and colleagues 11 found that serum CK and myoglobin concentrations after suxamethonium were lower in patients receiving sevoflurane than in those receiving halothane 60 min after suxamethonium. However, in these studies CK concentrations were measured 20 and 60 min after suxamethonium, well before serum CK concentration reaches its peak, at 9–24 h after administration of suxamethonium. 6

In our study, serum CK concentrations, measured 20 h after suxamethonium, were increased markedly in both groups, in contrast with findings of previous reports. 5 11 12 Moreover, we found that the peak serum concentration of CK was higher in the iso- fluorane than in the sevoflurane group. The increased serum CK originated from skeletal muscle where most of the enzyme is located. Acute muscle necrosis or sudden changes in the permeability of the sarclemma may be responsible for the increase in serum CK concentrations. 13 Serum increases in AST concentrations were also caused by damage to skeletal muscle because postoperative ALT and LDH values were unchanged. Thus differences in serum CK and AST concentrations between both groups may be related to differences in the effects of both anaesthetics on skeletal muscle. The reasons for the higher CK concentrations during isoflurane anaesthesia are unclear. We hypothesize that the immaturity of skeletal muscle in children makes it either prone to release more CK or be richer in CK. In addition, differences in concentrations of CK and AST after suxamethonium between the two anaesthetics may result from differences in intracellular reactions triggered by anaesthetics or from differences in the permeability of the muscle cell membrane to anaesthetics. Using skinned fibres, isoflurane was more potent than sevoflurane, producing Ca(2+)/p59)-induced Ca(2+)/p59)-release (CICR). 14 CICR, which plays an important role in the diagnosis of malignant hyperthermia (MH), may not be directly related to CK release. However, it is interesting that isoflurane, which was more potent than sevoflurane in the test for MH, was also associated with higher concentrations of CK after suxamethonium in our study.

Heart muscle, liver, skeletal muscle and kidney are rich in AST and ALT. LDH is present in high concentration in the kidney, heart muscle and skeletal muscle. AST, ALT and LDH increase in the presence of severe muscle damage. In this study, both CK and AST increased significantly while ALT and LDH did not. The increase in CK during surgery is caused mainly by skeletal muscle injury. However, in our study it was probably a result of an increase in muscle membrane permeability, because minor surgery such as tonsillectomy has little effect on skeletal muscle. Thus the mechanism leading to increased CK in our study is probably different from that after exercise. In our study, serum CK concentrations were increased markedly by suxamethonium 1 mg kg−1 in combination with both anaesthetics. A higher amount of suxamethonium would probably lead to higher serum CK concentrations.

In summary, we have demonstrated that sevoflu- rane preserved skeletal muscle integrity more than isoflurane when suxamethonium was used during induction of anaesthesia. However, because of the marked increase in serum CK concentrations with both anaesthetics, anaesthetists should carefully weigh the risks and benefits of the use of suxa- methonium in children during isoflurane or sevoflurane anaesthesia, in spite of the fact that no clinical signs were observed in this study.

References

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