Uptake of halothane and isoflurane by mother and baby during Caesarean section†

R. Dwyer, J. P. H. Fee and J. Moore

Summary

Twenty-three patients undergoing Caesarean section received either 0.5% halothane or 0.8% isoflurane to supplement nitrous oxide-oxygen anaesthesia. We studied the rate of uptake of the agents by the mother and fetus by measuring partial pressures in maternal arterial (Pa) and fetal umbilical venous (Puv) blood. Mean induction-delivery interval did not differ between the halothane (10.8 min) and isoflurane (11.7 min) groups. There were no differences in maternal heart rate, arterial pressure, pH and blood-gas tensions and fetal pH, blood-gas tensions or Apgar scores between the two groups. Isoflurane uptake by the mother was more rapid than halothane; at delivery, mean Pa of isoflurane as a fraction of the inspired partial pressure (Pi) was 0.44 compared with 0.35 for halothane (P < 0.05). Mean Puv as a fraction of maternal Pa at delivery was 0.71 for both agents; thus placental transfer was the same for both agents. Consequently mean Puv/Pi was greater for isoflurane (0.32) than halothane (0.26) (P < 0.05).

We conclude that both halothane and isoflurane are suitable agents for general anaesthesia for Caesarean section. The rate of uptake of isoflurane by the mother during Caesarean section was more rapid than halothane. The rate of uptake from the mother was the same for halothane and isoflurane, so that fetal partial pressure as a fraction of the inspired partial pressure was greater for isoflurane than halothane. (Br. J. Anaesth. 1995; 74: 379-383)

Key words


General anaesthesia for Caesarean section should prevent awareness in the mother but have minimal depressant effects on the fetus. The standard agents used to maintain anaesthesia, after i.v. induction and tracheal intubation, are nitrous oxide in oxygen, supplemented by halothane or isoflurane. Isoflurane has theoretical advantages over halothane; because of its lower blood-gas partition coefficient, uptake of isoflurane by the mother and elimination from the fetus should be more rapid, preventing maternal awareness and reducing neonatal depression. Isoflurane has been shown to be an acceptable alternative to halothane for Caesarean section during general anaesthesia [1–3].
A 22-gauge cannula was inserted into the radial artery after induction of anaesthesia for arterial blood sampling. Samples of maternal arterial blood were obtained 5 and 10 min after introduction of the volatile agent and at the time of delivery (defined as the time of clamping the umbilical cord) for measurement of the partial pressure of isoflurane or halothane. Before division of the umbilical cord, a section was isolated by clamps. Samples were obtained within 1 min of clamping from the umbilical vein and artery for measurement of the partial pressure of isoflurane or halothane. A sample of the inspired gas was obtained from the inspiratory limb of the ventilator breathing system at delivery for measurement of the inspired partial pressure of isoflurane or halothane. Maternal arterial and fetal umbilical venous samples were obtained at delivery for measurement of blood-gas tensions and pH.

Samples for measurement of volatile agent partial pressure were obtained in heparinized glass, gastight syringes (Hamilton 1010 TLL). Syringes were sealed with a Teflon stopcock until analysis. Blood samples consisted of 5.5 ml of blood (approximately) except in the case of the umbilical artery where samples were smaller because of difficulty in obtaining this volume of blood. Analysis of samples for volatile agent partial pressure began within 1 h of obtaining the samples. Partial pressures of volatile agent in blood and gas were measured by gas chromatograph with a flame ionization detector, calibrated using volumetrically prepared standards. Gas samples were injected directly into the gas chromatograph. Blood partial pressures of volatile agent were measured using the headspace method described by Fink and Morikawa [4]. This has been described previously by us in detail [5].

In brief, blood was ejected from the syringe until 5 ml remained and 5 ml of humidified air was drawn in. After 30 min of equilibration of volatile agent partial pressure between the blood and gas phases, the partial pressure of volatile agent in the headspace gas (P1) was measured by injecting the gas into the chromatograph. All gas was expelled from the syringe and another 5 ml of air drawn in. After further equilibration between gas and blood phases, the volatile agent partial pressure in the gas was again measured (P2). The partial pressure of volatile agent in the original blood sample (P0) was calculated as the product of P1 and the ratio of P1 to P2 (P1/P2). As equilibration was carried out at room temperature, blood partial pressures were corrected to partial pressures at body temperature, using the ratio of the saturated vapour pressure (SVP) at body temperature to the SVP at room temperature, according to the theory of Fink and Morikawa [4]. SVP at each temperature was calculated using the Antoine equation, as described for isoflurane [6] and halothane [7]. The coefficient of variation for measurement of volatile agent tensions in gas samples was 1.5% for isoflurane and less than 1% for halothane. The coefficient of variation for measurement of blood tensions was calculated on 10 samples obtained from a subject at a stable end-tidal concentration of each agent, and found to be 2.4% for isoflurane and 5.6% for halothane.

Data were analysed statistically by analysis of variance and unpaired t tests as appropriate. P < 0.05 was considered statistically significant.

Results

One infant in the halothane group weighed less than 2500 g; this was thought to be caused by placental insufficiency and the patient was excluded from analysis. Thus there were data from 11 patients in the halothane group and 12 in the isoflurane group. Age, weight, parity, gestation and haemoglobin concentration were comparable in the two groups (table 1). Mean volume of Ringer’s lactate administered before delivery did not differ between the groups. Mean times from induction of anaesthesia until delivery of the baby did not differ significantly between the groups (halothane 10.8 (sd 2.3) min, isoflurane 11.7 (2.0) min). The duration of administration of volatile agent before delivery did not differ significantly between groups (halothane 9.7 (2.2) min, isoflurane 10.6 (1.9) min).

Heart rate and arterial pressure before delivery (table 2) and maternal arterial blood-gas tensions and pH at delivery did not differ significantly between the halothane and isoflurane groups. No subjects were aware during surgery.

Mean fetal weight was comparable in both groups (range 2500–4020 g) (table 1). Fetal condition, as judged by fetal pH and PO2 at the time of delivery and Apgar scores 1 and 5 min after delivery, did not differ between the groups (table 3). Maternal PO2 correlated positively with fetal PO2 (% atm). Arterial partial pressures (Pa) as a fraction of the inspired partial pressure (Pi) were significantly greater for isoflurane than halothane, 5 min after delivery.

Table 1 Maternal characteristics, haemoglobin (Hb) concentration and fetal weight in the groups receiving halothane and isoflurane (mean (range or sd))

<table>
<thead>
<tr>
<th></th>
<th>Halothane group</th>
<th>Isoflurane group</th>
</tr>
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<tbody>
<tr>
<td>n</td>
<td>11</td>
<td>12</td>
</tr>
<tr>
<td>Age (yr)</td>
<td>29 (21–38)</td>
<td>31 (18–41)</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>69 (8)</td>
<td>73 (15)</td>
</tr>
<tr>
<td>Gestation (weeks)</td>
<td>38 (1)</td>
<td>39 (1)</td>
</tr>
<tr>
<td>Parity</td>
<td>2.1 (1.6)</td>
<td>1.9 (2.5)</td>
</tr>
<tr>
<td>Hb (g dl–1)</td>
<td>12 (0.5)</td>
<td>11.5 (1.0)</td>
</tr>
<tr>
<td>Fetal weight (kg)</td>
<td>3.30 (0.3)</td>
<td>3.28 (0.4)</td>
</tr>
</tbody>
</table>

Table 2 Mean (sd) heart rate and systolic arterial pressure in the halothane and isoflurane groups

<table>
<thead>
<tr>
<th></th>
<th>Heart rate (beat min–1)</th>
<th>Arterial pressure (mm Hg)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Halothane</td>
<td>Isoflurane</td>
</tr>
<tr>
<td>Preop.</td>
<td>94 (15)</td>
<td>92 (12)</td>
</tr>
<tr>
<td>+ 2 min</td>
<td>110 (14)</td>
<td>119 (15)</td>
</tr>
<tr>
<td>+ 5 min</td>
<td>101 (19)</td>
<td>116 (17)</td>
</tr>
<tr>
<td>+ 10 min</td>
<td>91 (18)</td>
<td>102 (28)</td>
</tr>
</tbody>
</table>
Uptake of halothane and isoflurane during Caesarean section

Table 3 Percentage of fetal Apgar scores above 7 at 1 and 5 min after delivery in the halothane and isoflurane groups

<table>
<thead>
<tr>
<th></th>
<th>Halothane group</th>
<th>Isoflurane group</th>
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<tbody>
<tr>
<td>Apgar &gt; 7 at 1 min</td>
<td>82%</td>
<td>92%</td>
</tr>
<tr>
<td>Apgar &gt; 7 at 5 min</td>
<td>100%</td>
<td>100%</td>
</tr>
</tbody>
</table>

Figure 1 Mean (sd) arterial partial pressures of halothane (●) and isoflurane (□) in the mother (Pa) as a fraction of inspired partial pressure (Pi). *P < 0.05.

Figure 2 blood partial pressures (Pa) of halothane (●) and isoflurane (□) as a fraction of inspired partial pressure (Pi) at delivery.

Figure 3 Arterial partial pressure of isoflurane (Pa) as a fraction of inspired partial pressure (Pi) in pregnant (□) and non-pregnant (●) subjects (mean, sd).

introduction of the agents (fig. 1) and at delivery (fig. 2). Differences between the agents 10 min after introduction were not statistically significant (by this

time four infants in the halothane group and two in the isoflurane group had been delivered, leaving seven and 10 patients, respectively, in each group). At delivery, Pa/Pi was 0.44 (0.08) for isoflurane and 0.35 (0.06) for halothane (P < 0.05) (fig. 2). Thus uptake of isoflurane by the mother was significantly faster than uptake of halothane.

The rate of uptake of halothane and isoflurane was compared between pregnant and non-pregnant young adults using data from a previous study (in which the anaesthetic technique was different) [5]. There was no significant difference in Pa/Pi between pregnant and non-pregnant subjects 5 or 10 min after introduction of halothane or isoflurane (figs 3, 4).

Table 4 Umbilical vein partial pressure (Puv) as a fraction of maternal arterial partial pressure (Pa) and inspired partial pressure (Pi), and umbilical artery partial pressure (Pua) as a fraction of Puv at delivery (mean, sd).

<table>
<thead>
<tr>
<th></th>
<th>Halothane group</th>
<th>Isoflurane group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Puv/Pa</td>
<td>0.71 (0.16)</td>
<td>0.71 (0.08)</td>
</tr>
<tr>
<td>Puv/Pi</td>
<td>0.26 (0.08)</td>
<td>0.32 (0.06)*</td>
</tr>
<tr>
<td>Pua/Puv</td>
<td>0.38 (0.12)</td>
<td>0.39 (0.11)</td>
</tr>
</tbody>
</table>

Figure 4 Arterial partial pressure of halothane (Pa) as a fraction of inspired partial pressure (Pi) in pregnant (□) and non-pregnant (●) subjects (mean, sd).

Figure 5 Partial pressures of halothane and isoflurane as a fraction of inspired partial pressure (Pi) in maternal (Pa), umbilical venous (Puv) and umbilical arterial (Pua) blood at delivery (mean, sd).
(Puv/Pa) were identical for halothane (0.71 (0.15)) and isoflurane (0.71 (0.08)). Umbilical arterial partial pressures as a fraction of umbilical venous partial pressures (Pua/Puv) did not differ significantly between halothane and isoflurane (table 4). Both Puv/Pa and Pua/Puv correlated with duration of volatile agent administration before delivery for halothane (P < 0.05) but not for isoflurane.

Figure 5 shows the gradient in volatile agent partial pressures, at the time of delivery, from inspired gas to maternal blood to fetal umbilical venous blood (i.e. fetal arterial) to fetal umbilical arterial blood (i.e. fetal mixed venous blood). At delivery, Puv/Pi was 0.26 for halothane and 0.32 for isoflurane (P < 0.05).

Discussion

Isoflurane and halothane are suitable supplements to nitrous oxide–oxygen anaesthesia for Caesarean section. We found no significant difference in the condition of the mother or baby with the use of these agents. This is consistent with results from previous studies [1–3].

Uptake of isoflurane is more rapid than halothane because of its lower blood–gas partition coefficient [5]. Blood partial pressures of both agents increased rapidly. The smallest arterial partial pressure of isoflurane in any patient after administration of 0.8 % isoflurane for 5 min was 0.23 %. Taking into account the reduction in anaesthetic requirements in pregnancy [8], this partial pressure of isoflurane is equipotent to that found by Chorvatoff, Bennett and Eger to prevent recall in volunteers when combined with 40 % nitrous oxide [9]. It is not surprising therefore that this technique is adequate to prevent awareness during Caesarean section.

We found no difference between the rate of uptake of halothane and isoflurane in this study and the rate of uptake in non-pregnant young adults in a previous study [5]. However, there were important differences between the anaesthetic techniques used in the two studies: (i) the non-pregnant patients received diazepam 0.15 mg kg⁻¹ as premedication, and alfentanil 15 μg kg⁻¹ and pancuronium 0.1 mg kg⁻¹ before intubation and introduction of the volatile agent; and (ii) the pregnant patients received 50 % nitrous oxide in oxygen while the non-pregnant patients received 100 % oxygen. These differences in anaesthetic technique may alter the rate of uptake by effects on the cardiovascular system or by the second gas effect. We cannot comment on how the rates of uptake compare between pregnant and non-pregnant patients if identical anaesthetic techniques are used.

Other studies have measured rate of uptake of isoflurane and halothane during Caesarean section. McCrirrick, Evans and Thomas measured arterial isoflurane concentrations which, if converted to partial pressures (using blood–gas partition coefficients measured by Gibbs, Munson and Tham [10], correspond to Pa/Pt values of 0.62 and 0.64 after 5 and 10 min of isoflurane administration, respectively [11]. Tunstall and Hawksworth measured blood halothane concentrations which, if corrected to blood partial pressures [10], correspond to Pa/Pt ratios of 0.41 and 0.49 after 5 and 10 min of halothane administration, respectively [12]. We found values for Pa/Pt which were considerably less than these; the reason for this is not clear.

We found that uptake of isoflurane and halothane by the fetus from maternal blood occurred at the same rate; Puv/Pa ratios for the two agents at delivery were identical. Volatile agents are highly lipid soluble and cross the placenta freely so that Puv approached Pa. As Pa/Pt was significantly greater for isoflurane than halothane at delivery, Puv/Pt was also significantly greater for isoflurane than halothane.

The Puv/Pa ratios we noted are comparable with those reported for nitrous oxide by Marx, Joshi and Orkin (0.79) and Hay (0.71) [13, 14]. Stenger, Blechner and Prystowsky found a Puv/Pa ratio of 0.91 for nitrous oxide after prolonged anaesthesia (mean duration 35 min) [15]. Latto and Waldren measured maternal and fetal blood concentrations of halothane at delivery after administration of 0.65 % halothane [16]. When these concentrations were converted to partial pressures using the blood–gas partition coefficients measured by Gibbs, Munson and Tham [10], the Puv/Pa ratio was 0.49. Tunstall and Hawksworth found a mean Puv/Pa ratio of halothane at delivery of 0.75 [12]. Stenger, Blechner and Prystowsky found that Puv/Pa ratios correlated with the duration of administration of nitrous oxide [15]; we found a positive correlation between Puv/Pa and duration of administration of halothane (P < 0.05) but not isoflurane.

Blood-gas partition coefficients are significantly less in the newborn infant than in adults [10] so that elimination of volatile agents should be rapid when respiration has been established. Fetal washout was not measured but Apgar scores were satisfactory in all infants at 5 min after delivery, suggesting that volatile agents are rapidly eliminated by the fetus. Elimination of enfurane by the neonate occurs rapidly [17] and as isoflurane has a lower blood solubility, it should be eliminated even more rapidly.

Acknowledgements

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References

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