COMPARISON OF 1.5% ENFLURANE WITH 1.25% ISOFLURANE IN OXYGEN FOR CAESAREAN SECTION: AVOIDANCE OF AWARENESS WITHOUT NITROUS OXIDE

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In clinical practice situations abound in which fetal oxygen supply is compromised. Thus maternal hyperoxygenation may be a reasonable interim measure before Caesarean section and equally reasonable during Caesarean section [1].

A maternal fractional concentration of inspired oxygen \( \left( F_{1_{O_2}} \right) \) of 1.0 results in the greatest concentrations of oxygen in cord blood at delivery by section, during both general and extradural anaesthesia. In the former, umbilical venous oxygen tensions of 4.0, 4.7 and 5.5 kPa, corresponding to maternal \( F_{1_{O_2}} \) values of 0.3, 0.66 and 0.95, have been reported [2]. In the latter, umbilical vein oxygen tension values of 3.7, 4.8, 5.5 and 6.3 kPa, corresponding to maternal \( F_{1_{O_2}} \) values of 0.21, 0.47, 0.74 and 1.0, have been reported [3]. However, no significant improvement in the Apgar scores in the latter series could be related to increased maternal inspired oxygen concentrations. In general anaesthesia it would be useful to establish a reliable technique in which it was possible to administer almost 100% oxygen to the mother from induction to delivery. The technique should fulfil three criteria: no maternal awareness; no undue depression of the fetus; no significant effect on uterine contractility.

Isoflurane and enflurane are satisfactory agents for general anaesthesia in Caesarean section. In combination with 50% nitrous oxide, 0.5% and 1% enflurane [4, 5] and 0.75% isoflurane [5] have been shown to meet the three criteria specified. If nitrous oxide is withdrawn in order to permit higher maternal inspired oxygen concentrations, a proportionate increase in the amount of volatile agent is needed to maintain anaesthesia. Both enflurane and isoflurane are potent analgesic agents and their uptake and excretion is relatively rapid, as both have low blood:gas partition coefficients. Provided they are not administered in excess of 1.5 MAC, there is no important effect on uterine contractility [6]. The intermittent inhalation of 1% enflurane [7], or 0.75% isoflurane [8] for the relief of pain in labour have been shown to be more effective than 50% nitrous oxide. However, both the volatile agents produce more drowsiness than does nitrous oxide.

Preliminary observations were made during Caesarean sections under general anaesthesia, on the effects of withdrawing nitrous oxide and replacing it with an increased inspired concentration of either enflurane or isoflurane. Depth of anaesthesia was monitored using the isolated forearm technique [9]. Either 1.5% enflurane or...
1.25% isoflurane in oxygen only, was found to be acceptable as sole maintenance agent. It was then decided to make a more formal comparison of the use of the two agents in a study approved by the Joint Ethics Committee of the Grampian Health Board and University of Aberdeen.

PATIENTS AND METHODS

A consecutive series of mothers for elective and semi-elective Caesarean section under general anaesthesia were allocated randomly to receive either enflurane or isoflurane. Patients in whom the fetus was at risk because of factors such as prematurity, intra-uterine growth retardation or pre-eclamptic toxaemia were included, as it is the at-risk fetus which is most likely to benefit from maternal hyperoxygenation. According to established custom, all mothers were told that they would be spoken to during anaesthesia. Any explanation required by the mother was given in detail and the purpose of a pneumatic tourniquet on the right arm was stated. Unless there were contraindications, the mother walked from the ward to the operating theatre, accompanied by a nurse. Whenever possible, the mother examined the operating theatre on the evening before the operation.

A standard pre-anaesthetic procedure, including H₂-antagonists, sodium citrate, lateral tilt, pre-oxygenation and cricoid pressure was used. Immediately before induction of anaesthesia, the pneumatic tourniquet was automatically inflated on the restricted right arm. Anaesthesia was induced with thiopentone 250 mg i.v., followed by suxamethonium 100 mg i.v.; the trachea was intubated and the lungs ventilated mechanically with 100% oxygen. Placement of a catheter was performed after the patient was anaesthetized.

Two minutes after the start of the thiopentone injection (which was taken as time zero) the anaesthetic vaporizer was turned to the 3% setting. At the same time the mother was asked to grip and release the anaesthetist’s hand with the hand of her isolated forearm. The request was repeated at 1-min intervals, or as required until delivery. A positive response indicated wakefulness and a mark was entered in the first column on a record form. At the same intervals of time, the amount of spontaneous movement of the hand (0; + = some movement; ++ = sustained movement or posture; +++ = very vigorous movements) was entered in a second column. (These classifications were subsequently scored 0, 1, 2 and 3, respectively.) If the anaesthetist’s hand was gripped without being released on the command to open and shut the hand, it was classified as reflex grip and a mark was entered in a third column.

After 3 min of delivering either enflurane or isoflurane at 3% concentration, the vaporizer was adjusted to deliver 1.5% enflurane or 1.25% isoflurane. The lungs were ventilated using a Blease–Manley ventilator with a fresh gas flow of oxygen 7–8 litre min⁻¹ and the flow was adjusted to maintain an end-tidal carbon dioxide partial pressure of 3.6–4.4 kPa. The last reading observed and recorded before delivery was assumed to apply to the time just before delivery. Neuromuscular blockade was maintained with atracurium 25–30 mg.

Following delivery, oxytocin 10 units was given i.v., 66% nitrous oxide was introduced and the vaporizer setting adjusted down 0.5%. Metoclopramide 10 mg and papaveretum 20 mg were given i.v. Two-millilitre samples of cord arterial and venous blood were taken for analysis.

RESULTS

The records of 113 consecutive patients were analysed. Twenty-five were primiparous. Fifty received enflurane and 63 isoflurane. The age, height, weight and parity distributions were similar in both groups. There were only 24 clinically acceptable “A” patients as defined by Crawford [10], nine of whom received enflurane and 15 isoflurane. Blood loss was unremarkable in all patients and none required fluid replacement. No mother experienced awareness (that is, postoperative recall) and no mother experienced dreams. Wakefulness was observed in 24 patients who received enflurane and in 23 who received isoflurane at the 2-min interval. The overall frequency of wakefulness 2 min after commencing the injection of thiopentone was therefore 42% for the whole series. At the 3-min interval, four patients receiving isoflurane and eight who received enflurane remained wakeful; at 4 min only two patients were wakeful (both receiving enflurane). At the 5-min interval (that is, after the inhalation of volatile agent for 3 min) no mother was wakeful. There was 100% amnesia for episodes of “wakefulness”.

For the 2–5 min intervals inclusive, 14 patients...
in the enflurane group and seven patients in the isoflurane group had total movement scores of 3 or more (fig. 1). For the intervals from 5 min to delivery, 51% of patients in the isoflurane group, but only 6% of patients receiving enflurane, produced no arm movements and were therefore in "surgical anaesthesia" (fig. 2). Because mothers wakeful at 2 min (before the introduction of the volatile agent) might be considered relatively resistant to anaesthesia, their scores after 5 min were considered separately, and are shown in figure 3. None of the patients in this category who had received enflurane became "surgically anaesthetized" before delivery. The mean weight of the mothers who were wakeful in the first few minutes was 76.3 kg, compared with 73.0 kg in those not wakeful ($P > 0.05$).
Induction–incision intervals in both groups were similar. The mean values were 9.2 min for enflurane and 8.7 min for isoflurane. Hand movements on incision were more active in the enflurane group (fig. 4).

Reflex grip, as described earlier, represents the level of anaesthesia just short of wakefulness and was recorded at 2 min in eight patients in the enflurane group and nine patients who received isoflurane and at 3 min in one enflurane patient. In the period from 6 min to delivery, reflex grip occurred in 18 patients in the enflurane group and one who received isoflurane. The mean induction–delivery interval for both groups was 16 min. In the period from 6 min to delivery, wakefulness occurred in only one subject (who received enflurane) at 12 min, the time of delivery.

The distribution of Apgar minus colour (A–C) scores of 8, 7, 6, 5, 4, 3, 2 and 1 at 1 min were, respectively, for isoflurane: 45, 7, 2, 3, 4, 0, 0 and 2 babies, and for enflurane: 36, 6, 4, 0, 3, 0, 1 and 0 babies. At 5 min the scores were, for isoflurane: 58, 3, 1, 0, 0, 0, 1 and 0 babies, and for enflurane: 44, 4, 1, 0, 0, 0, 1 and 0 babies. Two babies with low scores underwent tracheal intubation for elective mechanical ventilation: one at 31 weeks gestation on account of prolonged rupture of the membranes with infection, and one at 32 weeks gestation for intra-uterine growth retardation, increasing Rhesus antibody titre and stillbirth of a previous sibling. Both babies made good progress. There were only two babies with less than perfect Apgar scores at 1 min which could not be accounted for by obstetric pathology, except that in one mother the left lateral tilt may not have relieved aorto-caval compression sufficiently. Both babies had A–C scores of 8 at 5 min; both mothers had received isoflurane.

Because of their relevance to the results of the cord blood samples, the last recorded maternal end-tidal carbon dioxide partial pressure before delivery in each group was compared (table I). Greater mean carbon dioxide tensions and lower pH values were present in umbilical vein blood of
TABLE I. Maternal end-tidal carbon dioxide partial pressure (kPa) shortly before delivery

<table>
<thead>
<tr>
<th></th>
<th>Enflurane (n = 49)</th>
<th>Isoflurane (n = 56)</th>
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<tbody>
<tr>
<td>Mean (SEM)</td>
<td>4.0 (0.05)</td>
<td>3.8 (0.04)</td>
</tr>
<tr>
<td>Range</td>
<td>2.9-4.8</td>
<td>3.3-4.7</td>
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TABLE II. Umbilical vein blood at delivery (mean values (SEM))

<table>
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<tr>
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<th>Enflurane (n = 50)</th>
<th>Isoflurane (n = 63)</th>
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<tbody>
<tr>
<td>pH</td>
<td>7.319 (0.0057)</td>
<td>7.337 (0.0046)</td>
</tr>
<tr>
<td>Pco₂ (kPa)</td>
<td>5.75 (0.073)</td>
<td>5.55 (0.065)</td>
</tr>
<tr>
<td>Po₂ (kPa)</td>
<td>5.15 (0.219)</td>
<td>5.14 (0.220)</td>
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TABLE III. Umbilical artery blood at delivery (mean values (SEM))

<table>
<thead>
<tr>
<th></th>
<th>Enflurane (n = 50)</th>
<th>Isoflurane (n = 63)</th>
</tr>
</thead>
<tbody>
<tr>
<td>pH</td>
<td>7.273 (0.0050)</td>
<td>7.284 (0.0043)</td>
</tr>
<tr>
<td>Pco₂ (kPa)</td>
<td>7.11 (0.088)</td>
<td>6.96 (0.081)</td>
</tr>
<tr>
<td>Po₂ (kPa)</td>
<td>2.47 (0.094)</td>
<td>2.46 (0.103)</td>
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the enflurane group (table II). The blood-gas tensions for the umbilical artery are shown in table III. The three highest cord blood oxygen tensions achieved in umbilical vein were 8.1, 11.1 and 12 kPa, and the highest value achieved in any umbilical artery sample was 4.7 kPa.

DISCUSSION

If it is assumed that the MAC values of isoflurane and enflurane are 1.3 and 1.7 respectively, that the uptake pattern of both agents is the same, and that the ratio of the inspired to the alveolar fraction is approximately 0.6 during the latter half of the induction–delivery interval, it follows that the concentrations of isoflurane and enflurane used were not equipotent. To correspond with a vaporizer concentration of 1.25% isoflurane, we should have used 1.63% enflurane, not 1.5%. However, 1.5% enflurane is easier to select from the calibration markings on the controls of the vaporizer. Furthermore, in preliminary investigations, no episode of wakefulness had developed after the first 5 min in any patient who had received 1.5% enflurane.

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This study suggests that the 3%–1.25% sequence for isoflurane may be used without the isolated forearm technique of monitoring to prevent awareness. In view of the marked isolated forearm activity with 1.5% enflurane, an increased dose with a 3%–1.75% sequence should, perhaps, be used in future. The advantage of using the isolated forearm technique on a regular basis is that, if wakefulness is treated in time, there will be no awareness.

In general, the use of high oxygen concentrations has not been shown to confer any special advantage in obstetric anaesthesia where the baby is not compromised. Therefore, unless one is monitoring for wakefulness, the addition of 50% nitrous oxide to the inhaled gases gives assurance that at least 0.45 MAC of anaesthetic value is being administered.

An anaesthetic technique containing 50% nitrous oxide with 0.5% halothane, 0.75% isoflurane or 1% enflurane does not require monitoring with the isolated forearm technique. It would be exceptional for any mother to suffer awareness with these regimens.

The avoidance of nitrous oxide in general anaesthesia for Caesarean section allows hyperoxygenation. This does not prevent the anaesthetist meeting the three criteria of no awareness, no undue fetal depression, and no significant uterine relaxation. This study shows that it is possible to give a satisfactory general anaesthetic for Caesarean section without nitrous oxide, using one of the two newer volatile agents, isoflurane or enflurane, in oxygen.

Any advantage to the fetus of maternal hyperoxygenation may be lost if perfusion of the intervillous space is not maintained [11]. This depends on avoidance of aorto-caval compression, maintenance of adequate maternal arterial pressure, and avoidance of factors which provoke uterine artery vasoconstriction.

ACKNOWLEDGEMENTS

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REFERENCES

2. Marx GF, Mateo CV. Effects of different oxygen concentrations during general anaesthesia for elective...


