Effects on the Bispectral Index during Elective Caesarean Section: A Comparison of Propofol and Isoflurane

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Background: Awareness during general anesthesia has been a particular problem during caesarean section. About 7 percent of patients undergoing elective caesarean section have reported dreaming or recall of voices during the procedure. The bispectral index (BIS), a value derived from the electroencephalogram (EEG), has been shown to be useful in monitoring the depth of anesthesia. Supplementation of propofol or isoflurane for maintenance of anesthesia has been shown to effectively reduce the incidence of awareness. However, the effects of propofol or isoflurane on the BIS index have not been fully investigated. We therefore designed this study to compare the effects of isoflurane or propofol supplementation on the BIS index in 24 healthy parturients undergoing elective caesarean section.

Methods: All patients had induction of anesthesia and orotracheal intubation in rapid sequence made possible by 1 MAC isoflurane with 50% N₂O-50% O₂ as conveyer and atracurium. After delivery, patients were randomly assigned to either of two groups (isoflurane or propofol). Patients in the Isoflurane group (n = 12) received 0.5 MAC isoflurane in 67% N₂O-33% O₂ and fentanyl + droperidol. Patients in the propofol group (n = 12) received propofol (8 mg/kg/h) infusion combined with 67% N₂O-33% O₂ and fentanyl + droperidol.

Results: There was no difference between the two groups in total operation time, maternal blood loss, fetal Apgar scores. No differences between the two groups in heart rate, blood pressure or BIS index values were found throughout the surgery. No patient from either group reported recall of the operative procedure. However, 25% of patients (3 of 12) in the isoflurane group had poor uterine contraction, suggestive of doubtful appropriateness of the use of isoflurane for maintenance of anesthesia in delivery.

Conclusions: We therefore concluded that supplementation of isoflurane or propofol for maintenance of anesthesia can satisfactorily decrease the BIS index and minimize the incidence of awareness in patients undergoing caesarean section under general anesthesia. The BIS index is a reliable monitor of the hypnotic component of anesthesia.

Key words: Caesarean section, Isoflurane, Propofol, Electroencephalography, Awareness.
it is useful in measuring the hypnotic component of the anesthetic state. A good correlation between BIS and patient movement in response to skin incision has also been reported. Titrating propofol in accordance with BIS monitoring during balanced anesthesia has resulted in decreased propofol use and significantly improved recovery. The BIS index has also been shown to be a good method for monitoring awareness during caesarean section.

Propofol infusion coupled with nitrous oxide appears to be a satisfactory technique for caesarean section. Previous research indicated that supplementation with propofol significantly attenuates the incidence of awareness during caesarean section. Isoflurane has been shown to be a good alternative to halothane in anesthesia for caesarean section and can also effectively reduce the incidence of awareness. Abbound et al. demonstrated that propofol is comparable to isoflurane in maintenance of anesthesia for term parturients undergoing caesarean section. However, data regarding the effects of propofol or isoflurane on the BIS index during caesarean section remain lacking. Preliminary data from our institution indicate that supplementation with propofol or isoflurane for maintenance of anesthesia for caesarean section significantly decreases the BIS index. We therefore designed this study to evaluate the effects of propofol infusion or isoflurane supplementation on the BIS index in term parturients undergoing caesarean section under general anesthesia.

Methods and Materials

Patients

The study was approved by the ethics committee at Mackay Memorial Hospital. Informed consent was obtained from 24 parturients (ASA I-II), with age between 22 to 46 years, scheduled for elective caesarean section. The sample size analysis was performed using Sigma Stat (V 2.03) Student’s t-test sample size prediction algorithm with a power of 0.8. Patients were excluded from the study if they had a history of neurologic or psychiatric disorders, or if they were taking anticonvulsant medication. Patients were also excluded if difficult intubation was expected or if intubation was successful after more than one attempt.

Protocols

After arriving at the operation theater, every patient received 500 mL infusion of lactated Ringer’s solution given over 30 min before the operation. Pure oxygen via a face mask was given to each patient for 5 min before induction. After receiving glycopyrrolate (0.005 mg/kg) as premedication, all patients had orotracheal intubation in rapid sequence induction under general anesthesia made possible by pentothal (4 mg/kg) and succinylcholine (1 mg/kg) with cricoid pressure applied by a helper during the act of laryngoscopy and intubation. Following orotracheal intubation, atracurium (0.5 mg/kg) and isoflurane (at an end-tidal concentration of 1.15% ultimately) in 50% N2O-50% O2 were given to each patient before delivery. All patients were then mechanically ventilated (10 mL/kg BW × 10 beats/min ) to maintain an end-tidal CO2 concentration within 30 – 40 mmHg. Body temperature was maintained with a warm blanket and a heating lamp. After delivery of the baby, each patient was given fentanyl (3 μg/kg) and droperidol (5 mg) combined with 67% N2O in O2 for maintenance of anesthesia. An oxytocin infusion was then given to promote uterine contraction. Each patient was then randomly assigned to either the isoflurane or propofol group. Patients in the isoflurane group received isoflurane at an end-tidal concentration of 0.5 throughout the rest of the procedure. Patients in the propofol group received continuous propofol infusion (8 mg/kg/h) instead.

Monitoring

The hypnotic effects of isoflurane or propofol supplementation in each group were detected using BIS index values (Aspect A1000 monitor, BIS version 3.12, Medical Systems Inc., Natick, MA, USA) every minute prior to delivery and every 5 min post delivery by a helper who was blinded to the anesthetic given. If BIS index values reached 75 or more for longer than 5 min during the procedure, the concentration of isoflurane or the propofol infusion rate should be increased. Along with BIS index values, heart rate and blood pressure were recorded. If the mean blood pressure (MAP) was less than 65 mm Hg for more than 3 min, a bolus of 200 mL of lactated Ringer’s solution was given. If the MAP remained less than 65 mm Hg for more than 3 min even after lactated Ringer’s solution bolus, a decrease in isoflurane concentration or propofol infusion rate was then applied accordingly. If poor uterine contraction was diagnosed by the surgeon, an increase in the oxytocin infusion rate and/or direct uterine massage were applied. Pre- and post-op temperature, total maternal blood loss and total operation time in both groups were also recorded. The newborn was evaluated with Apgar score at 1-and 5-min after delivery. We followed up each patient the next day to ask her about recall during anesthesia.

Statistical Analysis

Data are presented as mean ± SEM. Statistical
analysis of the results was accomplished using Student’s t-test (two-tailed) for continuous data and Chi-square test for categorical data. The significance level was set at 0.05. Data were processed using SigmaStat for Windows, Version 2.03 (SPSS Inc., Chicago, IL).

**Results**

**Demographic Data**

There were 12 patients in each group, and there were no statistically significant differences between the groups in age, height, weight, pre-op hematocrits, mean arterial pressure (MAP), heart rate (HR) and pre-induction BIS index (Table 1). No difficult intubation was encountered in all 24 patients. Therefore, there was no exclusion of patients who were initially included in the study.

**BIS index**

Both groups had a similar mean BIS index before induction (97.58 ± 0.29 and 97.33 ± 0.22). In the isoflurane group, induction with pentothal significantly decreased the mean BIS index to 39.19 ± 1.78 within 1 min (Fig. 1). A similar trend was observed in the propofol group (38.00 ± 2.22). Oral tracheal intubation then increased the mean BIS index to 45.25 ± 5.05 (isoflurane group) and 44.58 ± 2.23 (propofol group). Prior to delivery, the mean BIS index was 52.35 ± 2.51 and 52.96 ± 3.58 in the isoflurane and propofol groups under isoflurane (1 MAC) in 50% N₂O-50% O₂ respectively. After delivery, partial replacement of isoflurane by fentanyl.

![Fig. 1](image)

**Table 1. Demographic, Surgical and Fetal Apgar Scores Data**

<table>
<thead>
<tr>
<th></th>
<th>Isoflurane</th>
<th>Propofol</th>
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<tbody>
<tr>
<td>Number of Patients Included</td>
<td>12</td>
<td>12</td>
</tr>
<tr>
<td>Age (yr)</td>
<td>33.46 ± 1.33</td>
<td>33.42 ± 1.79</td>
</tr>
<tr>
<td>Body Weight (kg)</td>
<td>73.88 ± 3.57</td>
<td>70.48 ± 2.62</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>158.58 ± 1.22</td>
<td>159.29 ± 1.90</td>
</tr>
<tr>
<td>Hct (Pre-op) (%)</td>
<td>36.40 ± 1.09</td>
<td>35.95 ± 1.23</td>
</tr>
<tr>
<td>Hct (Post-op) (%)</td>
<td>29.45 ± 1.72</td>
<td>30.77 ± 3.25</td>
</tr>
<tr>
<td>MAP (Pre-op) (mmHg)</td>
<td>93.91 ± 3.03</td>
<td>87.42 ± 3.93</td>
</tr>
<tr>
<td>Heart Rate (Pre-op) (beats/min)</td>
<td>88.40 ± 4.89</td>
<td>83.80 ± 5.54</td>
</tr>
<tr>
<td>Pre-induction BIS Index (Arbitrary Units)</td>
<td>97.58 ± 0.29</td>
<td>97.33 ± 0.22</td>
</tr>
<tr>
<td>BIS Index (5 min post-extubation)</td>
<td>79.23 ± 1.63</td>
<td>80.67 ± 1.45</td>
</tr>
<tr>
<td>BIS Index (10 min post-extubation)</td>
<td>95.75 ± 0.85</td>
<td>96.03 ± 1.08</td>
</tr>
<tr>
<td>Time for Induction (min)</td>
<td>1.79 ± 0.29</td>
<td>2.09 ± 0.29</td>
</tr>
<tr>
<td>Induction to delivery interval (min)</td>
<td>7.32 ± 0.73</td>
<td>7.06 ± 0.60</td>
</tr>
<tr>
<td>Total Operation Time (min)</td>
<td>53.17 ± 4.15</td>
<td>53.92 ± 3.12</td>
</tr>
<tr>
<td>Total Blood Loss (dl)</td>
<td>47.50 ± 6.64</td>
<td>40.91 ± 4.99</td>
</tr>
<tr>
<td>Body Temp (Pre-op, °C)</td>
<td>36.93 ± 0.45</td>
<td>36.53 ± 0.78</td>
</tr>
<tr>
<td>Body Temp (Post-op, °C)</td>
<td>36.17 ± 0.09</td>
<td>36.26 ± 0.09</td>
</tr>
<tr>
<td>Apgar Score (1-min, Arbitrary Units)</td>
<td>8.65 ± 0.27</td>
<td>8.26 ± 0.34</td>
</tr>
<tr>
<td>Apgar Score (5-min, Arbitrary Units)</td>
<td>9.23 ± 0.26</td>
<td>9.50 ± 0.17</td>
</tr>
</tbody>
</table>

Data are shown as mean ± SEM. Isoflurane: isoflurane group. Propofol: propofol group. Hct: hematocrit. BIS Index: bispectral index. No difference was found between these two groups.
and droperidol yielded a mean BIS index of 52.60 ± 0.70 with a range of 32 to 74 in the isoflurane group for the rest of the procedure (Fig. 1). By the same token, total replacement of isoflurane by propofol, in the propofol group yielded a similar mean BIS index of 49.32 ± 0.74 (ranging from 32 to 75). There were 3 out of 12 patients in isoflurane group and 2 out of 12 patients in propofol group found to have the mean BIS index values higher than 75 right before baby delivery. Five and 10 min after extubation the mean BIS index in isoflurane group was 79.23 ± 1.63 and 95.75 ± 0.85 respectively and in the propofol group mean index was 80.67 ± 1.45 and 96.03 ± 1.08 respectively (Table 1). There was no statistical difference in mean BIS index values between the two groups throughout the entire procedure (Fig. 1) except for the cumulative mean BIS index after delivery (52.60 ± 0.70 in the isoflurane group vs. 49.32 ± 0.74 in the propofol group (P = 0.006) (Fig. 2).

Hemodynamic Data

No statistically significant differences were observed in mean arterial pressure (Fig. 3) or heart rate (Fig. 4). Neither were there statistically significant differences in the time required for induction, time until delivery, total operation time, total blood loss, end maternal temperature, nor 1- and 5-min neonatal Apgar scores (Table 1). None of the patients in either group subsequently reported recall of events during the entire course of delivery.

However, 3 out of 12 patients (25%) in the isoflurane group were reported to have poor uterine contraction which required further management including uterine massage and/or intravenous methylergonovine maleate in addition to the routinely used oxytocin infusion. One of these 3 patients required intravenous ephedrine to maintain blood pressure. None of the patients in the propofol group had poor uterine contraction, but one did require intravenous ephedrine to maintain blood pressure. No other adverse effects were noted in any of the patients.

Discussion

This is the first study to report the effects of supplementation with isoflurane or propofol on the BIS index in patients undergoing elective caesarean section under general anesthesia. Our data indicate that supplementation with isoflurane or propofol provides satisfactory hypnosis in these patients. Previous research by Glass PS et al., has indicated that memory function remains intact...
at higher BIS index values of 93 ± 5 (mean ± SD), while recall is absent at lower BIS index values of 70 ± 18 (mean ± SD),7 which was consistent with the results reported by Liu et al.17 Gajraj et al. further indicated that a BIS index value of 55 is the threshold value for a state of unconsciousness, with a specificity of 100%.4 The mean BIS index values in our patients after induction and after delivery were less than 55. Our observation that none of our patients reported recall of events during delivery further confirms that maintaining a mean BIS index value of less than 55 can satisfactorily prevent awareness. This observation also confirms that the BIS index is a good tool for monitoring the hypnotic components of the anesthetic state.

Conflicting data have been noted regarding the effects of propofol vs. thiopental for induction in caesarean section.18,19 However, most researchers agree that thiopental remains a good drug for induction19,20 and propofol is a good agent for maintenance.13,14,21 We therefore designed this study using these two intravenous agents respectively for induction and maintenance of anesthesia afterwards in one of the groups. Celleno et al. indicated that thiopental is a good induction drug for caesarean section.19 Our data confirmed that thiopental offers a hypnotic component of good quality during induction. Propofol has also been demonstrated to provide an anesthesia of good quality.13,14 Our data also indicated that propofol infusion with fentanyl is a satisfactory technique for caesarean section. Our observation that propofol was not associated with poor uterine contraction further indicates that this is a safer regimen.

The use of isoflurane for maintenance has been demonstrated to be a good alternative to halothane.22 Our data also confirm that isoflurane offers a good quality anesthesia. New inhalation agents, such as sevoflurane and desflurane, have been widely used lately due to their low blood/gas solubility. Faster emergence and better recovery have been reported using sevoflurane or desflurane for maintenance of anesthesia.23,24 Previous studies have indicated that these 2 agents also offer satisfactory anesthesia for caesarean section.25,26 However, their effects on BIS index values in caesarean section have not yet reported. Furthermore, our observation that 25% of patients in the isoflurane group had poor uterine contractions suggests that caution should be taken in the use of inhalation agents for caesarean section. Further evaluation is needed to clarify this concern.

We conclude that supplementation with isoflurane or propofol provides a good hypnotic component of anesthesia in parturients undergoing elective caesarean section. Propofol appeared to be a better agent than isoflurane for maintenance due to a high incidence (25%) of poor uterine contraction following the use of isoflurane.

References