A PROSPECTIVE, RANDOMIZED COMPARISON OF THE EFFECTS OF THIOPENTAL AND PROPOFOL ON BISPECTRAL INDEX DURING CAESAREAN SECTION TILL DELIVERY OF NEWBORN

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Abstract

Background: Since in caesarean operations skin incision to delivery time is very short, induction agent could be still effective on BIS level till the time of delivery. Therefore this study was designed to analyze the effect on maintaining adequate bispectral index levels till delivery of neonate of propofol and thiopental as an induction agent for caesarean section.

Methods: Eighty two patients undergoing caesarean section were allocated into two groups. In the group T anesthesia induction was performed with thiopental (5 mg/kg) and in the group P with propofol (2.5 mg/kg). Anesthesia was maintained with sevoflurane. Heart rates, blood pressures and BIS values during significant events of surgery and anesthesia till delivery, durations of surgery, induction to skin incision and to delivery and Apgar scores were recorded. For statistical analysis T-test was used for comparison of means of independent samples.

Results: The groups were comparable with respect to age, weight and gestational age. The patients in the group P had significantly lower levels of bispectral index values during uterus incision; 40.6 vs. 59.5 (p = 0.019) and delivery; 41 vs. 62.9 (p = 0.018).

Conclusion: Anesthesia induction with propofol in a dose of 2.5 mg/kg maintains lower levels of heart rate, blood pressure and BIS till delivery when compared with thiopental in a dose of 5 mg/kg.

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Key words: caesarean; sevoflurane; induction; bispectral index; propofol; thiopental.

Introduction

The bispectral index (BIS) is widely used to monitor the depth of anesthesia and values lower than 60 indicate a low probability of intraoperative awareness1-7. Most researchers focus on the period after the delivery of neonate and they studied the BIS levels as an indicator of adequate depth of anesthesia8,9. For the last decade BIS guided maintenance of anesthesia instead of having a target anesthetic concentration is advocated to prevent anesthesia awareness while allowing decreased anesthetic usage especially in the population having high risk of awareness.
and most importantly decreasing the morbidity and mortality related with surgery\textsuperscript{10-13}. Considering that in caesarean operations skin incision to delivery time is a short period of time, till the time of delivery induction agent could be still effective on BIS level which in turn let one to use lower inhalational anesthetics. Effect on the BIS levels till delivery of the anesthetic induction agent has not yet been studied. Although thiopental is known to be the drug of choice for anesthesia induction of caesarean section operations\textsuperscript{14}, propofol has also been used for the same purpose\textsuperscript{15-17}. Therefore this prospective, randomized study was designed to test the hypothesis that induction agent for caesarean section could be effective on maintaining adequate BIS levels till the delivery of neonate. With this purpose the effect of propofol and thiopental as an induction agent for caesarean section on maintaining adequate BIS levels till the delivery was compared.

\textbf{Materials and Methods}

The prospective, randomized, clinical study was performed between January 2009 and December 2009 at Saad Specialist Hospital, Saudi Arabia. After the Ethics Committee of the hospital had given approval and the patients had given written informed consent, 82 nulliparous parturients were recruited to the study. All the participants were in physical status class I-II according to the American Society of Anesthesiologists guidelines at full term who requested general anesthesia for their elective caesarean section. Following premedication with ranitidine at 50 mg and metoclopramide at 20 mg intravenously in the holding area the patients were assigned randomly to one of the two treatment groups by one of the authors (MK), using a computer-generated randomization table. The treatments were differentiated by the induction agent (thiopental or propofol).

The exclusion criteria were: any previous anesthesia received before the current surgery, parturient with preterm or multiple gestations, fetal distress, and any requirement to administer a drug that was not in the study protocol.

Medications for induction were given via covered syringes by the same anesthetist (MK) who did the randomization. He left the operating theatre right after the induction. All other authors were blinded to the randomization and the induction agents. One of the authors (HE) other than the in charge one who was unaware of any medication given observed the monitor and recorded the precise time of the specific surgical events staying over the surgical side of the screen at all times. The third anesthetist (AM) was in charge of the patient.

Routine monitoring devices (5-lead electrocardiogram, non-invasive blood pressure, and pulse oxymetry-Dräger Infinity Delta XL) were applied. Level of muscle blockade was monitored by using train-of-four stimulation of the ulnar nerve (Dräger, model Infinity Trident). EEG data were acquired continuously and recorded by using BIS monitor (Aspect Medical Systems produced to be used with appropriate Dräger devices, Norwood USA) with its recommended electrode. The BIS electrodes were placed properly according to the manufacturer’s recommendation.

Baseline values of hemodynamic variables and BIS were obtained. Following urinary catheterization and surgical draping of the patient, rapid sequence induction with preoxygenation was performed with 5 mg/kg thiopental and 1-1.5 mg/kg succinylcholine in the group T (n = 42), and 2.5 mg/kg propofol and 1-1.5 mg/kg succinylcholine in the group P (n = 40). The doses were calculated on the basis of prepregnancy weight of the patients. An expiratory concentration of sevoflurane of 1% was maintained with a Zeus Anesthesia workstation (Dräger Medical, Lübeck, Germany) in auto control mode with nitrous oxide 50% in oxygen (\textsubscript{O2}) till delivery. Controlled ventilation was used to maintain the end-tidal pressure of carbon dioxide (ETCO\textsubscript{2}) between 32 and 35 mmHg. The patients were monitored throughout anesthesia with respect to their heart rate, ETCO\textsubscript{2}, percentage of oxygen saturation, inspiratory and expiratory concentrations of the anesthetic agent, and body temperature. Muscle relaxation was obtained with atracurium with an initial bolus of 20 mg and additional boluses as necessary. After delivery 20 IU of oxytocine is given with ongoing intravenous fluid as infusion to avoid any adverse effects. Whenever heart rate or blood pressure higher than 20% of baseline value was detected after delivery of newborn, 1 \textmu g/kg fentanyl was given as an intravenous bolus. Ringer’s Lactated solution at
a constant rate of 999 mL/hour was given through the surgery. In case of intraoperative hypotension, 20% decrease in blood pressure from baseline value; ephedrine in boluses of 5 mg were given. Immediately after skin closure, anesthetic gases were ceased and system was flushed with flush function of the anesthesia machine. Muscle blockade had been reversed if Train of Four ratio was between 0.3 and 0.7 with neostigmin and glycopyrrolate. Controlled ventilation of 100% O₂ at 6 L/min was maintained. Patients were extubated with the return of cough reflex followed by spontaneous regular breathing, facial grimacing and purposeful movements; they were followed in the recovery unit until the modified Aldrete score was 9-10.

Values of BIS, non-invasive blood pressure and heart rate were recorded at the following times: before anesthesia induction, after endotracheal intubation, at skin and uterine incision, at neonatal delivery, and at 5 minutes after delivery. One of the authors (HE) recorded the precise time of the specific surgical events staying over the surgical side of the screen at all times. At the end of operation the same anesthetist (HE) recorded heart rate, blood pressure and BIS values from the computerized recordings printed out from the monitor (Dräger Infinity Delta XL) matching their specific timing. Other values recorded manually included neonatal Apgar scores for 1st and 5th minute, ephedrine requirement, estimated blood loss, time for skin incision and delivery after induction, operation duration.

Power analysis was carried out using the software G*Power 3.0® (Institute of Experimental Psychology, Heinrich-Heine-University, Dusseldorf, Germany), when power (1-β) is 95%, α error probability is 0.05, and the effect size 0.82, the total sample size required was calculated to 66. The statistical analysis was performed using a statistical software package (SPSS 9.01®, SPSS INC. Chicago, IL, USA) and p <0.05 was accepted as statistically significant. All data were recorded as the mean ± standard deviation (SD). T-test was used for comparison of means of independent samples.

Results

The study population comprised 82 parturients who were aged 21-43 years and all were included in the analysis.

The groups were comparable with respect to age, weight and gestational age (Table 1). Induction to skin incision time and to delivery time, duration of surgery, Apgar scores in 1st and 5th minutes, estimated blood loss during the surgery were all comparable in both groups (Table 2). The mean total fentanyl requirement (84 ± 36 µg in group T and 91 ± 33 µg in group P) was similar in both groups. The mean duration of recovery stay in both groups (28 ± 6 minutes in group T and 31 ± 5 minutes in group P) was also statistically comparable.

![Table 1](image1.png)

Demographic data of the patients. (Mean ± SD).

<table>
<thead>
<tr>
<th></th>
<th>Group T (n = 42)</th>
<th>Group P (n = 40)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>30.8 ± 5.1</td>
<td>32.6 ± 4.3</td>
</tr>
<tr>
<td>Weight (kilograms)</td>
<td>79 ± 10.5</td>
<td>83.8 ± 10.8</td>
</tr>
<tr>
<td>Gestation (weeks)</td>
<td>38.6 ± 0.8</td>
<td>37.5 ± 1.4</td>
</tr>
</tbody>
</table>

![Table 2](image2.png)

Surgical data of the patients and mean APGAR scores of the newborns according to the groups (Mean ± SD).

<table>
<thead>
<tr>
<th></th>
<th>Group T (n = 42)</th>
<th>Group P (n = 40)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Induction-to-skin incision time (sec)</td>
<td>78.2 ± 16.3</td>
<td>84.4 ± 14.2</td>
</tr>
<tr>
<td>Induction-to-uterus incision time (min)</td>
<td>2.9 ± 0.9</td>
<td>3.1 ± 1</td>
</tr>
<tr>
<td>Induction-to-delivery time (min)</td>
<td>3.4 ± 1</td>
<td>3.7 ± 0.7</td>
</tr>
<tr>
<td>Duration of surgery (min)</td>
<td>38 ± 6</td>
<td>37.1 ± 5</td>
</tr>
<tr>
<td>Estimated blood loss (mL)</td>
<td>525 ± 100</td>
<td>480 ± 101</td>
</tr>
<tr>
<td>1 min APGAR</td>
<td>8.5 ± 0.5</td>
<td>8.4 ± 0.6</td>
</tr>
<tr>
<td>5 min APGAR</td>
<td>9.5 ± 0.5</td>
<td>9.9 ± 0.1</td>
</tr>
</tbody>
</table>

sec: seconds, min: minutes, mL: millilitres

No intra- or postoperative complications were encountered.

Heart rate, systolic blood pressure and BIS values during the significant events of surgery and anesthesia till delivery of neonate were illustrated in Figs. 1, 2.
and 3 respectively. The mean values of heart rate and systolic blood pressure were significantly lower in the group P than the group T both during uterus incision and delivery. The mean heart rate levels during uterus incision were 102 ± 17 in the group P and 116 ± 18 in the group T; \( p = 0.031 \) and during delivery; 104 ± 12 in the group P and 118 ± 14 in the group T; \( p = 0.038 \). The mean systolic blood pressure values during uterus incision were 126 ± 10 in the group P and 144 ± 11 in the group T; \( p = 0.024 \) and during delivery in the group P and 151 ± 12 in the group T; \( p = 0.022 \). The patients in group P had significantly lower levels of BIS values than the patients in group T during uterine incision; 40.6 ± 20 vs. 59.5 ± 25 (\( p = 0.019 \)) and during delivery; 41 ± 20 vs. 62.9 ± 26 (\( p = 0.018 \)). While 8 patients (19.4%) in the group T had BIS values between 60 and 65, none in the group P did (\( p = 0.024 \)). None of the groups had a patient with a BIS value higher than 65.

No ephedrine required during surgery.

**Discussion**

The results of this study revealed that induction agent for caesarean section could be effective on maintaining adequate BIS levels till the delivery of neonate. Furthermore propofol was more effective to keep BIS levels till delivery of newborn lower than thiopental when it was used as an induction agent.

It has been a common practice to administer 0.5 minimum alveolar concentration of a volatile anesthetic in 50% nitrous oxide and introducing opioid after the delivery of neonate during general anesthesia for caesarean section\textsuperscript{18-19}. However there is evidence suggesting that 0.5 MAC of volatile anesthetics is not enough in providing adequate anesthesia depth\textsuperscript{8}. Chin et al have shown that the use of 1.0% Sevoflurane does not consistently provide adequate BIS values whereas 1.5% Sevoflurane does\textsuperscript{8}. Since sevoflurane was reported to affect uterine tonus in a dose related manner\textsuperscript{20} in this study sevoflurane was used as Chin et al did\textsuperscript{8}. Induction agent might be effective to obtain enough BIS levels till the time of delivery as it is a very short period of time. Many induction agents are being used for caesarean section operations such as thiopental, propofol, ketamine\textsuperscript{14-17} and there has not yet been any study published comparing their effect on BIS values before the delivery of newborn. Ok and co-workers have published that BIS value was raised to range of 69 and 72 during delivery when the induction was performed with thiopental\textsuperscript{9}. They had their induction to delivery time around 3.6 minutes\textsuperscript{9} which is close to the induction to delivery time that was 3.4 minutes encountered in the current study (Table 2). While BIS levels at the time of uterine incision and delivery were 60 or over 60 in the Group T, it was lower than 60 at all times in the Group P (Fig. 3). It is
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known that propofol has a significantly rapid recovery
than thiopental\textsuperscript{21,22}. However, in this study a longer
effect as an induction agent on maintaining adequate
BIS level than thiopental to cover uterine incision and
delivery has been obtained (Fig. 3). This may be related
to the antanalgesic effect of thiopental\textsuperscript{23}. However
there is no blood level measurement of the induction
agents in this study it is difficult to put forward any
mechanism, it is known that barbiturates actually
decrease the pain threshold causing antanalgesic
effect at low blood levels such as with small induction
doses of thiopental or after emergence from thiopental
anesthesia when its blood levels are low\textsuperscript{23}. Clinically,
patients awake from single dose of thiopental 5 to 10
minutes after administration\textsuperscript{23}. During uterus incision
and delivery blood thiopental levels may be low
enough to cause antanalgesic effect. During pregnancy
it is well known that volume of blood and plasma
increases relatively higher than other components\textsuperscript{24}.
It is also known that there are changes related with
the hemodynamic variables; cardiac output, systemic
vascular resistance, heart rate and blood pressure by
advancing pregnancy\textsuperscript{24}. Those changes may affect one
drug’s initial distribution or its redistribution half life
more than the other causing this result.

Anesthesia awareness has been studied previously
and it has been already accepted that BIS values lower
than 60 decreases the incidence of awareness\textsuperscript{4,11,12}.
Since the focus of this study was the effect of induction
agents on BIS values Therefore patients in this study
were not questioned about awareness after surgery.
Furthermore that could initiate different questions
about recall or awareness which might be originating
from different stages of anesthesia other than the
study period. As previously mentioned the focus
was the period till delivery after induction in this
study. According to the results of this study, propofol
for anesthesia induction of caesarean deliveries
appeared to be the better option when the BIS levels
till the delivery of newborn concerned. Studies with
different designs and other available induction agents
for caesarean section procedures may improve the
adequacy of anesthesia till delivery.

As a conclusion; induction agent chosen, propofol
or thiopental, for the anesthesia induction of caesarean
section seem to affect the bispectral index levels
obtained till the time of delivery; anesthesia induction
with propofol in a dose of 2.5 mg/kg maintains lower
levels of bispectral index along with heart rate and
systolic blood pressure till delivery than thiopental in
a dose of 5 mg/kg.

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{fig3.png}
\caption{Mean BIS levels of the patients during significant events of surgery according to the groups.}
\end{figure}

\( ^*p = 0.019, ^\S p = 0.018 \)
References


