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Comparison of propofol and thiopentone for induction of anaesthesia for elective Caesarean section

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Summary

Propofol 2.5 mg/kg was compared with thiopentone 5 mg/kg as an induction agent for elective Caesarean section. Thirty-two healthy women with cephalopelvic disproportion were included in an open randomised study. The placental transfer of propofol was also studied in 10 other mothers given a single dose of 2.5 mg/kg. The induction characteristics and haemodynamic response to propofol and thiopentone were similar. Side effects were rare with both agents, but propofol caused more discomfort on injection compared to thiopentone. Recovery times were shorter after propofol as evaluated by time to orientation, recovery scoring after anaesthesia and measurements with the Maddox wing. Rapid placental transfer and significant fetal uptake were detected for propofol. There was no significant neonatal depression as assessed by Apgar scores and blood gas analyses. Propofol appears to be a suitable alternative to thiopentone as an induction agent for anaesthesia in elective Caesarean section.

Key words

Anaesthetics, intravenous; propofol, thiopentone.
Anaesthesia, obstetric.

Regurgitation of gastric contents associated with aspiration is a well-known risk at induction of general anaesthesia for Caesarean section because of slow gastric emptying during late pregnancy.[1] Another problem is to minimise drug effects on the fetus, yet avoid the mother's intra-operative awareness. Induction must therefore be smooth and rapid to ensure unconsciousness for the manoeuvres necessary prior to introduction of inhalational agents, but with no residual effect on the neonate at the time of delivery.[2]

Thiopentone has been the routine induction agent of anaesthesia for Caesarean section since the 1930s because of its rapid and predictable action. However, it can also cause marked decreases in arterial blood pressure, and this, together with the rapid placental transfer, may induce some depression of the fetus. Today there are few alternatives to thiopentone. Thus midazolam has been shown to have a great variability of action when used to induce anaesthesia[2,3] while etomidate causes adrenocortical suppression[4,5] which has also been shown to occur in the neonate after elective Caesarean section.[6]

We compared propofol with thiopentone for induction of anaesthesia in elective Caesarean section in the present study. Particular attention was paid to induction characteristics and the neonatal effects of both agents.

Methods

Thirty-two healthy women who had elective Caesarean section because of cephalopelvic disproportion and with no other complications of pregnancy (duration > 38 weeks) were included in an open, randomised study. The study was approved by the Hospital Ethics Committee, and informed consent was obtained from each mother. Their characteristics are given in Table 1.

The mothers fasted overnight and were unpremedicated. They were placed on the operating table in the left lateral tilt position and a cannula was inserted into a vein of the forearm. 500–1000 ml lactated Ringer's solution was infused during the operation. Anaesthesia was induced intravenously after pre-oxygenation, with either propofol 2.5 mg/kg or thiopentone 5.0 mg/kg followed by suxamethonium 1 mg/kg to facilitate tracheal intubation. Sixty percent nitrous oxide in oxygen and isoflurane 0.7% were used from the beginning of anaesthesia to the clamping of the umbilical cord. Anaesthesia was maintained after that with 70% nitrous oxide in oxygen, and isoflurane was discontinued. Vecuronium 0.10–0.12 mg/kg was used for muscle relaxation, and buprenorphine 0.004 mg/kg to provide analgesia during surgery. Droperidol 0.018 mg/kg,

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Table 1. Patient characteristics, mean (SD).

	Propofol ($n=16$)	Thiopentone ($n=16$)
Age, years	27.4 (2.85)	30.5 (5.46)
Weight, kg	79.1 (8.94)	75.9 (8.87)
Height, cm	166.0 (5.98)	166.5 (6.14)
Primiparous, *n*	6	4
Previous Caesarean section, *n*	7	6

as an antiemetic agent, and oxytocin 5 IU were also administered after delivery. Glycopyrronium 0.01 mg/kg and neostigmine 0.05 mg/kg were used to reverse residual neuromuscular block.

The induction agent was injected as a single bolus during 10 seconds, and the induction time, taken as the time from the start of the injection to abolition of eyelash reflex, was recorded. The occurrence of any side effects at induction or during maintenance of anaesthesia was noted. The anaesthetists (J.K. and M.V.) assessed the quality of induction and maintenance of anaesthesia as good, adequate or poor.

Systolic and diastolic arterial pressures and heart rate were measured indirectly (Cardiocap, Datex Co.), before and after insertion of the cannula, immediately after injection of the induction agent, after tracheal intubation, after the beginning of surgery and thereafter at 5-minute intervals throughout the procedure. The end-tidal carbon dioxide ($P_{E}CO_2$) was monitored continuously (Cardiocap) and the ventilation variables were adjusted to maintain the $P_{E}CO_2$ at 4.5–5.5 kPa. The ECG was displayed continuously and neuromuscular block was monitored using a Datex Relaxograph.

Neonatal assessments included Apgar scores at 1, 5 and 15 minutes and neonatal weights; blood gas tensions and pH were measured from the umbilical vein and artery (178 pH-blood gas analyser, Corning). Samples were taken immediately after birth from a double-clamped section of the cord and analysed within 5 minutes. The time from induction of anaesthesia to uterine incision, from uterine incision to clamping of umbilical cord and from induction to blood sampling were recorded. The duration of the whole operation was also noted.

The completeness of recovery was assessed by using the critical flicker fusion frequency (CFF),[7] a Maddox wing apparatus[8] and the visual analogue scale (VAS) (subjective sedation).[9] These measurements were made before the induction of anaesthesia and at 15, 30, 45, 60, 90 and 120 minutes after orientation, which was taken as the time when the patients could recall their date of birth. In addition a scoring system to assess the patient's awakeness (2, fully awake; 1, rousable; 0, not responding), ventilation (2, is able to cough; 1, breathing easily; 0, airway requires attention) and movement (2, moving purposefully; 1, moving involuntarily; 0, not moving) was used at 3, 15, 30 and 180 minutes after orientation. A fully recovered patient therefore had a score of six.

The placental transfer of propofol was studied with 10 other patients [age 22–38 years (mean 28.5); weight 62–103 kg (mean 77.0); five primiparous and five multiparous]. Anaesthesia was induced with propofol 2.5 mg/kg injected over 10 seconds, and maintained as above. The propofol concentration in maternal venous blood (MV), in umbilical venous (UV) and arterial (UA) blood was determined by a high-performance liquid chromatographic method.[10] This method has a lower limit of sensitivity of approximately 2 ng/ml, and intra-assay coefficient of variation was about 5%.

Table 2. Induction time, time from induction to uterine incision (I–I time) and time from uterine incision to cord clamping (I–C time) in both groups, mean (SD).

	Propofol ($n=16$)	Thiopentone ($n=16$)
Induction time, seconds	27.3 (4.3)	32.4 (10.4)
I–I time, minutes	4.4 (0.8)	4.4 (1.1)
I–C time, seconds	46.1 (14.0)	49.6 (25.4)

Data are presented as mean (SD). Mean arterial pressure (MAP) was calculated as $\frac{1}{3} \times$ (systolic + 2 × diastolic pressures). The statistical analysis was performed using two-way ANOVA (repeated measures on two factors) followed by the Newman–Keuls test.[11] Differences between groups were analysed with Student's *t*-test for parametric data and Fisher's exact test for nonparametric data. Scored data were analysed with the Mann–Whitney *U* test. A level of 0.05 was considered statistically significant.

Results

The groups were comparable for age, weight, height and pregnancy characteristics (Table 1). The induction characteristics for propofol and thiopentone were similar, and the onset of anaesthesia was rapid with both agents [propofol 27.3 seconds (4.3); thiopentone 32.4 seconds (10.4)] (Table 2). The quality of induction did not differ between the groups, and side effects were rare (Table 3). However, propofol caused significantly more discomfort on injection compared to thiopentone (6 versus 1, $p = 0.042$).

There were no significant differences in haemodynamic response between the groups during the induction and maintenance of anaesthesia (Fig. 1). Compared with the baseline values, the mean arterial pressure was stable after induction and increased 18–29% ($p < 0.01$) after tracheal intubation. The heart rate increased from the baseline values by 18–21% after induction and by 26–30% after intubation ($p < 0.01$), Figure 1. The duration of the procedure did not differ between the propofol and thiopentone groups [45.0 minutes (11.1) for propofol and 46.9 minutes

Table 3. Assessment of the quality of induction and numbers of patients with side effects during induction and recovery.

	Propofol ($n=16$)	Thiopentone ($n=16$)
Assessment by anaesthetists (*n*)		
Good	11	8
Adequate	5	8
Poor	0	0
Side effects (*n*)		
Induction:		
excitation	4	6
discomfort on injection	6	1*
Recovery:		
respiratory upset	2	3
vomiting	0	2
flush	0	1
restlessness	2	0
headache	1	0

*$p = 0.042$ (Fisher's exact test).

Table 4. Duration of anaesthesia and recovery time from the end of anaesthesia to opening eyes on command and time from opening eyes to orientation in both groups, mean (SD).

	Propofol ($n=16$)	Thiopentone ($n=16$)
Duration of anaesthesia, minutes	45.0 (11.1)	46.9 (17.6)
Time to opening of the eyes, minutes	3.2 (2.9)	5.0 (7.5)
Time to orientation, minutes	1.0 (0.9)	2.3 (1.0)*

*p=0.0011 (Student's *t*-test).

(17.6) for thiopentone]. The recovery times from the end of the procedure to opening eyes on command did not differ statistically between the groups, but the time to orientation was significantly shorter after propofol (p = 0.0011; Table 4).

The recovery scoring after anaesthesia also showed a significant difference between the groups at 3, 15 and 30 minutes (Table 5). The recovery results measured with VAS and CFF did not reach statistical difference, but measurements with the Maddox wing apparatus indicated shorter recovery times after propofol than after thiopentone at 30, 45 and 60 minutes after orientation (Fig. 2).

The incidence of side effects during recovery did not differ between the groups (Table 3). None of the patients reported any awareness during anaesthesia and all found the course of anaesthesia acceptable.

The Apgar scores of the neonates did not differ significantly (Table 6). The weights (Table 6) and the blood gas analyses (Table 7) of the neonates were also comparable and within the normal range.

The propofol concentrations in maternal venous blood

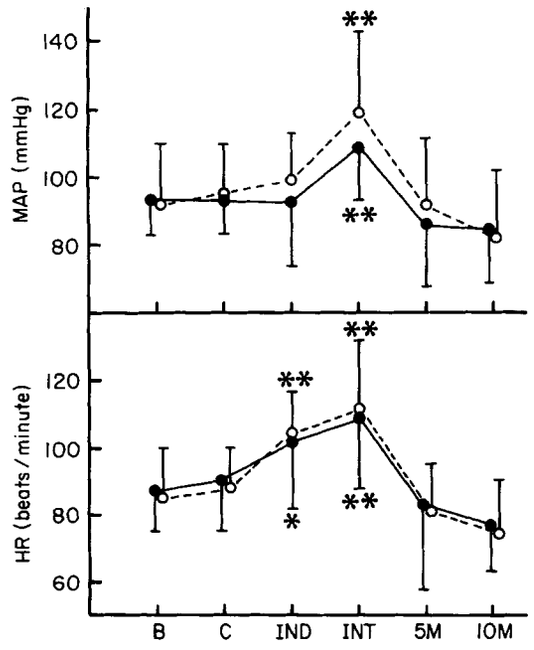

Fig. 1. Mean arterial pressure (MAP) and heart rate (HR) before induction of anaesthesia (B), after insertion of the cannula (C), immediately after injection of the induction agent (IND), immediately after intubation (INT) and 5 minutes (5M) and 10 minutes (10M) after the induction of anaesthesia in propofol (●) and thiopentone (○) groups. Mean SD, repeated measures ANOVA followed by Newman-Keuls test. * = $p < 0.05$ and ** = $p < 0.01$ compared to the baseline value (B).

Table 5. Recovery scores concerning the patients' awakeness, ventilation and movements (maximum total score 6) at 3, 15, 30 and 180 minutes after the orientation of patients in both groups, mean (SD).

	Propofol ($n=16$)	Thiopentone ($n=16$)
Recovery scores (0–6)		
3 minutes after orientation	3.88 (1.15)	3.00 (0.73)*
15 minutes after orientation	5.38 (0.89)	4.12 (1.15)**
30 minutes after orientation	5.81 (0.41)	4.87 (0.88)***
180 minutes after orientation	6.00 (0.00)	5.75 (0.45)ns

* p=0.035
** p=0.0039
*** p=0.0026
ns, not significant (Mann-Whitney *U* test).

and in umbilical venous and arterial blood are presented in Table 8. The concentration in MV was slightly higher than in UV [2.70 μg/ml (0.43) versus 2.26 μg/ml (0.52)] and significantly higher than in UA [1.80 μg/ml (0.36) p = 0.0001]. The concentration in UV was also significantly higher than in UA (p = 0.030).

Discussion

Elective Caesarean section is usually performed with epidural or general anaesthesia. It is clinically important, when the latter is used, that the anaesthetic agent provides stable conditions while limiting intra-operative recall. The

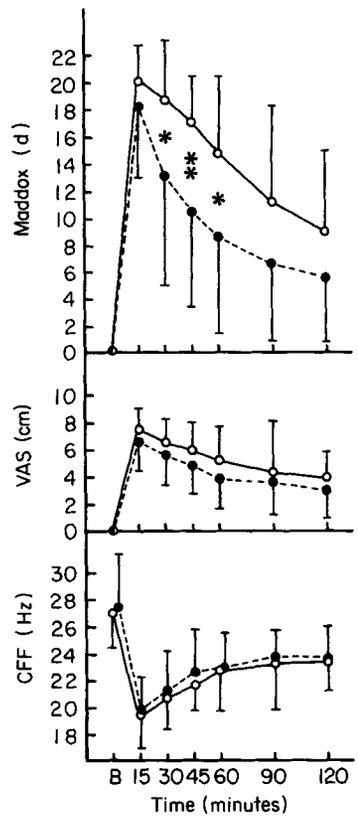

Fig. 2. Completeness of recovery assessed by Maddox wing (Maddox), visual analogue scale (VAS) and critical flicker fusion (CFF) as a function of time in propofol (●) and thiopentone (○) groups. Mean SD, repeated measures ANOVA followed by Newman-Keuls test. * = $p < 0.05$ and ** = $p < 0.01$ compared between the groups.

Table 6. Neonatal weights, mean (SD) and Apgar scores (median and range) at 1, 5 and 15 minutes after delivery.

	Propofol ($n=16$)	Thiopentone ($n=16$)
Neonatal weights g	3224.4 (539.1)	3510.6 (664.0)
Apgar scores (0–10):		
at 1 minute	9 (6–10)	9 (7–10)
at 5 minutes	9 (8–10)	9 (8–10)
at 15 minutes	9 (8–10)	9 (8–10)

number of patients in the present study was small, but none reported awareness during the procedure. Nor was any significant cardiovascular depression found after induction of anaesthesia with propofol or thiopentone. The induction characteristics were good with both agents, but discomfort on injection was a frequent finding (37.5%) in the propofol group. However, this fact did not affect the patients' acceptance of propofol as an induction agent. It has been shown that injection into a large vein or the mixing of lignocaine with propofol decreases the incidence of this discomfort.[12–15] Some excitation was also found during induction with both agents.

The measurements carried out with Maddox wing and the recovery scores indicated shorter recovery times after propofol than thiopentone. In addition, the time from opening eyes after anaesthesia to patients' orientation showed a statistically significant difference in favour of propofol. This offers a significant advantage when recovery room capacity is limited, and patients often subjectively report rapid recovery. The CFF and VAS were both less sensitive in the detection of the differences between the two drug effects as compared to Maddox wing. This finding also agrees with some previous studies.[8,16,17]

A rapid and reliable intravenous anaesthetic agent should rapidly cross the blood/brain barrier, and this feature is usually followed by rapid placental transfer.[18,19] Propofol is a very lipophilic undissociated agent with a low molecular weight, and the placental transfer of propofol apparently depends on placental blood flow and the concentration gradient between the mother and fetus. Thus, the induction dose of propofol and the time from induction of anaesthesia to clamping of umbilical cord probably have important effects on the concentration of propofol in the fetus.

Table 7. Blood gas tensions and pH samples of umbilical vein and artery (178 pH-blood gas analyser, Corning) and time from the beginning of anaesthesia to obtaining the blood samples, mean (SD).

	Propofol ($n=16$)	Thiopentone ($n=16$)
Umbilical vein		
pH	7.37 (0.044)	7.35 (0.037)
P_{CO_2} (kPa)	5.44 (1.21)	5.47 (0.82)
P_{O_2} (kPa)	5.10 (1.62)	4.39 (1.14)
Standard bicarbonate (mmol/litre)	22.4 (2.5)	21.4 (2.0)
Base excess (mmol/litre)	−2.0 (1.2)	−2.6 (1.9)
Umbilical artery		
pH	7.32 (0.038)	7.31 (0.041)
P_{CO_2} (kPa)	6.46 (0.89)	6.79 (1.30)
P_{O_2} (kPa)	3.14 (1.23)	2.90 (0.88)
Standard bicarbonate (mmol/litre)	21.9 (1.2)	20.8 (1.7)
Base excess (mmol/litre)	−1.7 (1.0)	−2.6 (2.1)
Time of blood samples, minutes	5.1 (0.9)	5.5 (1.6)

Table 8. The concentrations of propofol in maternal venous blood (MV), in umbilical venous (UV) and arterial (UA) blood after an induction dose of 2.5 mg/kg.

Patient	Time (minutes)	MV (μg/ml)	UV (μg/ml)	UV/MV ratio	UA (μg/ml)	UA/MV ratio
1	4.03	2.66	2.75	1.03	1.73	0.65
2	4.58	3.09	3.14	1.02	2.51	0.81
3	4.75	3.21	2.15	0.67	2.20	0.69
4	5.67	3.12	2.59	0.83	1.42	0.46
5	5.92	3.01	2.14	0.71	1.75	0.58
6	6.00	2.01	2.20	1.09	1.85	0.92
7	6.25	2.63	2.53	0.96	1.77	0.67
8	6.42	2.76	1.65	0.60	1.84	0.67
9	6.43	2.36	2.14	0.91	1.63	0.69
10	7.42	2.10	1.36	0.65	1.25	0.60
Mean	5.75	2.70	2.26	0.85	1.79	0.67
SD	1.02	0.43	0.52	0.18	0.36	0.12

* $p=0.058$
** $p=0.030$
*** $p=0.0001$ (Student's *t*-test).

The concentration of propofol returning to the placenta in umbilical arterial blood is determined by the drug concentration in umbilical venous blood and fetal drug uptake, although some nonplacental drug transfer is also possible.[19] Our results indicate a significant fetal propofol uptake. Rapid placental transfer has also been reported with thiopentone.[20] Thus these facts could cause some unwanted residual effects on neonates. However, no clinically significant depression of the neonates was indicated by the Apgar scores or the blood gas analyses in either the propofol or the thiopentone group.

In conclusion, propofol was found to be similar to thiopentone in induction characteristics and in the effects on the neonates. Recovery times after anaesthesia were shorter with propofol, and this fact may be advantageous in some situations. Propofol appears to be a suitable alternative to thiopentone as an induction agent for anaesthesia in elective Caesarean section.

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