Propofol infusion anaesthesia for Caesarean section

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Two propofol infusion regimens and a standard general anaesthetic were compared in thirty Chinese women undergoing elective Caesarean section. After induction of anaesthesia with propofol $2 \text{ mg} \cdot \text{kg}^{-1}$, ten patients received propofol $6 \text{ mg} \cdot \text{kg}^{-1} \cdot \text{hr}^{-1}$ and nitrous oxide 50 per cent in oxygen while ten were given propofol $9 \text{ mg} \cdot \text{kg}^{-1} \cdot \text{hr}^{-1}$ with 100 per cent oxygen. The other ten patients received thiopentone $4 \text{ mg} \cdot \text{kg}^{-1}$ and nitrous oxide 50 per cent in oxygen with enflurane one per cent. Maternal recovery times and psychomotor performance were recorded. Neonates were assessed by Apgar scores, neurologic and adaptive capacity scores (NACS) and umbilical cord blood gas analysis. Haemodynamic changes were similar immediately following induction but the low propofol infusion group had the best haemodynamic stability subsequently. Recovery times were fastest in the low-infusion group but there were no differences in later postbox testing. Neonatal Apgar scores and umbilical blood gas analysis were similar but NACS at two hours were poorer in the high infusion group. A propofol infusion coupled with nitrous oxide appears to be a satisfactory technique for Caesarean section.

Lors de leur césarienne élektive, trente chinoises nous ont permis de comparer deux modes de perfusion de propofol et un autre mode d'anesthésie générale. Après une induction anesthésique avec $2 \text{ mg} \cdot \text{kg}^{-1}$ de propofol, nous avons donné à dix d'entre elles $6 \text{ mg} \cdot \text{kg}^{-1} \cdot \text{h}^{-1}$ de propofol et 50 pour cent de N_2O avec O_2 tandis que dix autres recevaient $9 \text{ mg} \cdot \text{kg}^{-1} \cdot \text{h}^{-1}$ de

propofol et 100 pour cent d' O_2 . Enfin, nous donnions aux dix dernières, $4 \text{ mg} \cdot \text{kg}^{-1}$ de pentothal, 50 pour cent de N_2O avec O_2 et un pour cent d'enflurane. Nous avons évalué le réveil des mères, leurs performances psychomotrices, les scores d'Apgar, les "Neurologic and Adaptive Capacity Scores" (NACS) des nouveaux-nés et les gaz sanguins du cordon ombilical. Après l'induction, les valeurs hémodynamiques variaient de la même façon mais par la suite, la perfusion de propofol à faible dose assurait une meilleure stabilité. Elle permettait aussi un éveil plus rapide quoique à moyen terme, la récupération était la même pour toutes. Quant aux nouveaux-nés, les gaz sanguins et les scores d'Apgar étaient comparables mais le NACS était moins bon, deux heures après la naissance, dans le groupe à haute dose de propofol. Une perfusion de propofol couplée à du protoxyde d'azote constitue une technique appropriée à une césarienne.

Key words

ANAESTHESIA: obstetrical, neonatal assessment;
 ANAESTHETICS, INTRAVENOUS: propofol;
 ANAESTHETIC TECHNIQUES: intravenous;
 RECOVERY: assessment.

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Propofol infusions for the maintenance of anaesthesia during Caesarean section may offer some advantages. Recovery from propofol infusion is rapid¹⁻⁵ and this would be desirable for mothers who are still at risk from acid aspiration in the postoperative period. The rapid recovery characteristics of propofol may also be beneficial for the neonate after delivery. However, placental transfer of propofol is rapid⁶ and infusions present the fetus with a large dose of drug which may cause neonatal depression after delivery. Decreases in blood pressure after propofol have been reported,⁷ and often to a greater degree than with thiopentone.^{8,9} This could be detrimental to placental perfusion and neonatal outcome. Nevertheless, studies during maintenance of anaesthesia show similar haemodynamic profiles in patients given propofol infusions compared with inhalational agents.^{1,2,4}

High inspired maternal oxygen concentrations may be beneficial for the fetus at risk of intrauterine asphyxia.¹⁰ A propofol infusion may permit the use of 100 per cent oxygen without risk of maternal awareness or the need for higher concentrations of volatile agent.

This study evaluated propofol infusions for Caesarean section. Two different infusion regimens and a standard thiopentone, enflurane and nitrous oxide general anaesthetic were compared. One infusion regimen substituted

TABLE I Anaesthetic techniques

	<i>Thiopentone</i> <i>n</i> = 10	<i>High infusion</i> <i>n</i> = 10	<i>Low infusion</i> <i>n</i> = 10
Induction	Thiopentone 4 mg · kg ⁻¹	Propofol 2 mg · kg ⁻¹	Propofol 2 mg · kg ⁻¹
Maintenance	Enflurane 1% N ₂ O 50% in O ₂	Propofol 9 mg · kg ⁻¹ · hr ⁻¹ O ₂ 100%	Propofol 6 mg · kg ⁻¹ · hr ⁻¹ N ₂ O 50% in O ₂
Post-delivery	Enflurane 0.5% N ₂ O 70% in O ₂	Propofol 9 mg · kg ⁻¹ · hr ⁻¹ O ₂ 100%	Propofol 6 mg · kg ⁻¹ · hr ⁻¹ N ₂ O 70% in O ₂

propofol for thiopentone and enflurane and the other used a higher infusion rate of propofol with 100 per cent oxygen.

Method

Approval for the study was obtained from the Chinese University Ethics Committee and informed consent was obtained from each woman entered into the trial. Thirty Chinese women of ASA physical status I undergoing elective Caesarean section for a normal, singleton, term pregnancy were studied. Patients were excluded if there was evidence of pre-eclampsia, overt supine hypotension, diabetes, intrauterine growth retardation or fetal abnormality. All mothers had normal full blood count, electrolytes, renal and liver function tests.

The patients were randomly assigned to one of three groups as shown in Table I. Ranitidine, 150 mg, was given orally the night before, and again two hours before surgery. The patients were transported to the operating room in the lateral position and a 15° left lateral tilt was maintained on the operating table. Sodium citrate 0.3 M 30 ml was administered 15 min before induction of anaesthesia. Electrocardiographic monitoring was started prior to induction and the blood pressure was monitored non-invasively (Dinamap 1846SXP, Critikon Inc) using the appropriately sized cuff. Each patient was preoxygenated for three minutes. After a baseline blood pressure was recorded, anaesthesia was induced with either thiopentone 4 mg · kg⁻¹ or propofol 2 mg · kg⁻¹ over 20 sec followed by succinylcholine 1.5 mg · kg⁻¹. Laryngoscopy followed the next Dinamap recording at one minute, and tracheal intubation was accomplished before the second minute recordings. Cricoid pressure was applied from the beginning of the induction sequence until the trachea was intubated and the cuff tested for leaks. Pain on injection and movement, coughing or lacrimation during laryngoscopy and intubation were noted. The methods for maintenance of anaesthesia are summarised in Table I. In the propofol groups, the infusions were started at the same time as the initial bolus induction dose. Neuromuscular blockade was maintained with atracurium 0.5 mg · kg⁻¹, with subsequent doses of 0.1 mg · kg⁻¹ as required, and

ventilation was controlled to maintain end-tidal carbon dioxide levels of 4.0–4.5 per cent (Normocap, Datex Ltd). A 500 ml infusion of Hartmann's solution was given over the first ten minutes. Systolic (SAP), mean (MAP) and diastolic (DAP) arterial pressures and heart rate (HR) were recorded every minute for the first 20 minutes of the procedure. All anaesthetic agents were discontinued at the last skin suture and residual paralysis was reversed with neostigmine 2.5 mg and atropine 1.2 mg. A stopwatch for assessment of maternal recovery was started at this point.

Following delivery of the infant an infusion of oxytocin (20 units in 500 ml 5 per cent glucose) was started and morphine 0.2 mg · kg⁻¹ was given IV.

The time that each patient took to open her eyes to command and the time to give her correct date of birth were recorded. Psychomotor recovery was also assessed by recording the patient's ability to perform a modified "postbox" test¹¹ at 25 and 60 min postoperatively compared with her preoperative score. The postbox had a series of holes through which the patient had to pass matching shapes. The number of shapes that the patient could complete in one minute was recorded and the best of three attempts was accepted. All women were interviewed the next day about dreaming or awareness during the operation.

Umbilical venous and arterial blood gas analysis were performed at delivery. All neonates were assessed by one paediatrician who was unaware of the anaesthetic technique. Apgar scores at one and five minutes, and Neurologic and Adaptive Capacity Scores (NACS)¹² at 15 min, 2 and 24 hr were recorded.

Demographic data and umbilical blood gas analysis were compared using one-way analysis of variance and haemodynamic data by repeated measures analysis of variance. The protected least-significant difference test was used for inter-group comparisons. Maternal recovery, Apgar scores and NACS scores were compared using Kruskal Wallis analysis of variance. If a significant difference was detected among the three groups, inter-group comparisons were made using the Mann Whitney U test with Bonferroni correction. Kendall Rank correlation was used to compare recovery times to anaesthetic

TABLE II Mean systolic blood pressure (SAP) changes (mmHg) before and up to five minutes after induction of anaesthesia

	<i>Thiopentone</i>		<i>High infusion</i>		<i>Low infusion</i>	
	<i>mean</i>	<i>SD</i>	<i>mean</i>	<i>SD</i>	<i>mean</i>	<i>SD</i>
Awake	117.6	14.0	121.1	13.8	115.5	12.7
1 min (post-induction)	118.8	15.9	117.3	21.0	119.8	18.7
2 min (post-intubation)	*148.0	23.4	*147.3	24.3	*139.0	10.1
3 min	*140.3	23.4	*142.7	16.5	*127.4	14.6
4 min	*134.8	17.6	*133.9	15.0	†110.3	12.07
5 min	127.9	19.3	*137.6	15.5	†108.0	7.36

* = $P < 0.01$ compared to awake SAP.

† = $P < 0.01$ compared to other groups.

duration and total propofol dose. Statistical significance was accepted when $P \leq 0.05$.

Results

There were no significant demographic differences among the groups with the overall mean $\pm$ SD age being 28.4 ± 4.6 yr, weight 62.6 ± 8.7 kg and height 153 ± 6.3 cm. Due to the nature of rapid-sequence induction, the quality of induction was difficult to assess. No patients complained of pain on injection and intubation conditions were satisfactory in all cases.

Haemodynamic effects

The normal size adult blood pressure cuff was appropriate for all patients. Changes in SAP are shown in Table II. Compared with awake values, there were no significant changes in SAP immediately after induction of anaesthesia in any group. The SAP increased after intubation in all groups ($P < 0.01$) and returned to baseline levels by four minutes in the low propofol group, five minutes in the thiopentone group and 12 minutes in the high propofol group.

Changes in MAP are shown in Figure 1. These mirror the changes in SAP. Within each group, MAP increased above awake values after laryngoscopy ($P < 0.01$) and returned to baseline levels by three minutes in the low propofol group, five minutes in the thiopentone group and eight minutes in the high propofol group. Consequently, the low propofol group MAP was lower ($P < 0.05$) than the other groups between three and five minutes. The trend over the next 20 min showed that the high infusion group had a higher MAP than the low propofol group ($P < 0.05$).

Trends in HR are shown in Figure 2. Heart rate increased ($P < 0.01$) in all groups after induction of anaesthesia, peaked after tracheal intubation and had returned to baseline values in the low propofol group by

five minutes, in the thiopentone group by seven minutes and in the high-dose group by ten minutes. Between groups, the HR over the first 20 min was consistently higher in the high-dose propofol group than in the other groups ($P < 0.05$).

Maternal recovery (Table III)

Total anaesthetic time was similar in all groups, ranging from 30 to 68 min. There were no differences among groups in the time from administration of morphine to the end of the anaesthetic. No patients complained of nausea or vomited postoperatively. Time to eye opening was faster in both propofol groups ($P < 0.05$) than the thiopentone group. The time to correct date of birth was faster in the low infusion group than in the other groups ($P < 0.05$). Postoperative postbox scores were less than preoperative values and there were no significant differences detected among groups.

Recovery times were not correlated to total anaesthetic time or total propofol dose.

Neonatal assessment (Tables IV and V)

There were no differences in gestational age or birth weight among the groups. Induction to delivery times were similar in all groups, ranging from 4.7 to 16.0 min. Uterine incision to delivery times were all less than 60 sec. Neonates of the mothers in the high propofol infusion group who received 100 per cent oxygen were expected to have higher oxygen tensions but this was not statistically significant.

Neonatal Apgar scores were satisfactory and there were no differences detected among the groups. The NACS at two hours were lower in the high-infusion group than the thiopentone group ($P < 0.05$). There were no differences at 15 min or 24 hr. Apgar scores and NACS were not related to induction to delivery times.

Blood loss was difficult to estimate accurately but there were no patients with excessive bleeding requiring trans-

FIGURE 1 Mean arterial pressure trends during induction and maintenance of anaesthesia. Mean value and only selected standard error bars displayed for clarity.

FIGURE 2 Trends in mean heart rate during induction and maintenance of anaesthesia. Most standard error bars have been omitted for clarity.

TABLE III Variables of maternal recovery

	Thiopentone		High infusion		Low infusion	
	mean	SD	mean	SD	mean	SD
Anaesthetic time (min)	43.1	7.5	44.6	12.4	41.9	6.5
Eye opening (min)	8.38	2.55	*5.90	1.79	*6.00	1.55
Date of birth (min)	11.23	2.46	11.61	3.24	*†8.95	1.90
PB 25 min/preop PB	0.40	0.26	0.35	0.32	0.47	0.21
PB 60 min/preop PB	0.68	0.14	0.84	0.26	0.80	0.21

PB = postbox score.

* $P < 0.05$ compared to thiopentone group.

† $P < 0.05$ compared to high infusion group.

TABLE IV Induction to delivery (I-D) times, umbilical venous (UA) and arterial (UA) blood gas analysis.

	Thiopentone		High infusion		Low infusion	
	mean	SD	mean	SD	mean	SD
I-D times (min)	11.5	2.6	11.4	2.1	10.5	1.6
UV $[H^+]$ (nmol $\cdot$ L $^{-1}$)	46.0	1.9	46.5	3.1	45.9	6.8
UV PCO $_2$ (kPa)	5.74	0.68	5.69	0.74	5.77	0.93
UV PO $_2$ (kPa)	4.01	1.27	4.35	0.96	3.82	0.93
UA $[H^+]$ (nmol $\cdot$ L $^{-1}$)	54.7	12.4	51.0	4.8	53.7	7.3
UA PCO $_2$ (kPa)	6.54	1.34	6.50	0.57	6.81	1.27
UA PO $_2$ (kPa)	2.14	0.64	2.70	0.69	2.21	0.73

TABLE V Apgar scores and neurologic and adaptive capacity scores (NACS)

	Thiopentone		High infusion		Low infusion	
	median	range	median	range	median	range
Apgar 1 min	9	6–9	8	6–9	9	8–9
Apgar 5 min	10	9–10	10	7–10	10	9–10
NACS 15 min	31	28–37	30	23–33	31	28–36
NACS 2 hr	*32	30–34	*30	29–32	31	28–35
NACS 24 hr	33	30–36	32	30–36	33	29–36

* $P < 0.05$, difference between thiopentone and high infusion.

fusion. There were no other obstetric complications. No patients admitted to any recall during anaesthesia.

Discussion

A propofol infusion coupled with nitrous oxide appears to be a satisfactory anaesthetic technique. Early maternal recovery in the low propofol group was faster than the thiopentone group with comparable neonatal outcome. Patients in the high propofol group without nitrous oxide showed the highest arterial pressure and heart rate and their neonates had the lowest NACS at two hours.

There had been no previous work published using propofol infusions in obstetric anaesthesia. We decided to evaluate this technique in small groups, keeping in mind the possible neonatal depression. However, trials with small sample sizes may fail to detect real differences. With a sample size of ten patients, there was a 73 per cent chance of detecting whether the propofol infusion regimens gave results at least one standard deviation better than the thiopentone group, allowing a five per cent chance of making a Type I error. If the real differences are small then there is little reason to change established practice. Our initial findings appear to warrant further evaluation of the low-infusion technique but we are less enthusiastic for the high-infusion regimen.

A valid comparison of induction agents should use equipotent doses. It has been estimated that the potency of propofol compared with thiopentone is 1:1.6.¹³ This would equate propofol $2.5 \text{ mg} \cdot \text{kg}^{-1}$ with thiopentone $4 \text{ mg} \cdot \text{kg}^{-1}$. However, propofol $2 \text{ mg} \cdot \text{kg}^{-1}$ and thiopentone $4 \text{ mg} \cdot \text{kg}^{-1}$ were equipotent for success of induction in unpremedicated patients⁸ and propofol $2 \text{ mg} \cdot \text{kg}^{-1}$ caused more hypotension than thiopentone $5 \text{ mg} \cdot \text{kg}^{-1}$. For Caesarean section, $2 \text{ mg} \cdot \text{kg}^{-1}$ appears to be a clinically acceptable dose although this is less than the dose at which 95 per cent of non-pregnant patients were unconscious ($2.2 \text{ mg} \cdot \text{kg}^{-1}$)¹³ and the dose required to induce anaesthesia in 95 per cent of unpremedicated non-pregnant patients ($2.5 \text{ mg} \cdot \text{kg}^{-1}$).¹⁴

There is a decreased anaesthetic requirement in pregnancy but this has not been documented for intravenous anaesthesia. Minimum alveolar concentrations (MAC) for inhalational agents are reduced in animal studies with pregnant ewes¹⁵ and rats.¹⁶ This may be related to increased levels of circulating endorphins.¹⁷ In pregnancy, there is decreased plasma binding of many drugs with increased free levels¹⁸ though this has not been established for propofol.

The infusion doses of propofol employed in this study were lower than those previously used in unpremedicated non-pregnant patients whose lungs were ventilated with oxygen and nitrous oxide.³ Propofol levels at delivery in the high-infusion group have been reported previously.¹⁹

Both propofol groups had higher levels at delivery (range: $1.9\text{--}3.8 \text{ } \mu\text{g} \cdot \text{ml}^{-1}$) than at the time of eye opening ($0.9\text{--}2.5 \text{ } \mu\text{g} \cdot \text{ml}^{-1}$) (unpublished observations). No patients experienced awareness and we feel justified in employing the chosen infusion regimes. However, with our sample size of ten, there is still a five per cent probability that the incidence of awareness is as high as 26 per cent.

Hypotension was not noted after induction of anaesthesia in any group in contrast to many previous studies⁷⁻⁹ and no differences were demonstrated between the thiopentone and propofol groups. The peak decrease in blood pressure in controlled studies usually occurs over two to three minutes and patients in this study were subjected to the coincident stimuli of cricoid pressure, intubation and succinylcholine administration. Additionally, our patients receive 500 ml lactated Ringer's solution over the first ten minutes and this may have compensated for the decreased systemic vascular resistance that has been noted with propofol.^{6,8}

After intubation, the low-dose propofol infusion/nitrous oxide group had the most stable cardiovascular system. The SAP and MAP returned to baseline levels faster than the other groups without development of significant hypotension. Propofol appeared to attenuate the cardiovascular response to laryngoscopy and intubation⁷ more than thiopentone.^{1,20} One possible contributory factor is that propofol is not antanalgesic compared with thiopentone.²¹

Trends in haemodynamic variables during maintenance of anaesthesia are difficult to evaluate during Caesarean section. The non-standardized influences on blood pressure and heart rate include circulatory changes at delivery, blood loss and fluid replacement. During other types of surgery, the cardiovascular changes during maintenance by propofol infusions are comparable to the use of volatile agents.^{1,2,4} The higher MAP and HR in the high propofol group probably reflected a lighter depth of anaesthesia due to the lack of nitrous oxide.

Propofol has been used during induction of anaesthesia for Caesarean section and comparative studies with thiopentone have shown variable neonatal outcome. Apgar scores may be similar²²⁻²⁴ or lower after propofol.^{25,26} No differences have been detected in umbilical cord blood gas analysis.^{23,24} Neurobehavioural assessment has been judged satisfactory after propofol ($2.5 \text{ mg} \cdot \text{kg}^{-1}$)²⁷ although other workers have found lower scores after propofol ($2.8 \text{ mg} \cdot \text{kg}^{-1}$) than with thiopentone ($5 \text{ mg} \cdot \text{kg}^{-1}$).²⁶ The NACS for the Chinese neonates in this study were less than those for non-Chinese.^{12,27,28} All NACS were evaluated by the same paediatrician and were comparable with NACS 24 hr after normal vaginal deliveries and elective epidural Caesarean sections at this

institution. In particular, Chinese neonates seemed to score poorly in response to sound and light, active contraction of neck flexors and response to traction following palmar grasp. The poor adaptive capacity scores may reflect habituation as the neonates are kept in a brightly lit and noisy room although testing is performed in relatively quiet surroundings. These findings may represent a racial difference but nevertheless comparisons among the three groups in this study should still be valid. Although the NACS scores were lower at two hours in the high-infusion group, the difference was small and had disappeared by 24 hr. No significant clinical effects could be attributed to this result.

Early maternal recovery was faster with propofol but a larger series may have shown this more conclusively with respect to psychomotor performance. Speed of recovery may be influenced by concomitant medications, other anaesthetic agents, general medical health and type of surgery. Propofol has not always shown faster recovery³ especially after major operations.¹

The total intravenous anaesthesia group appeared to be the least satisfactory. A greater infusion rate may provide better haemodynamic stability but this may delay recovery. Other studies in non-pregnant patients without additional analgesic drugs have also commented on the high propofol dose requirement.^{3,29} Recovery in this study was not improved over the low-dose propofol/nitrous oxide group and the use of 100 per cent oxygen did not appear to be beneficial to the neonate.

A propofol infusion coupled with nitrous oxide appears to be a satisfactory technique for Caesarean section. Induction and maintenance of anaesthesia was smooth with relatively stable haemodynamic variables. No adverse neonatal effects were detected and maternal recovery was faster than following thiopentone/nitrous oxide/enflurane.

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