Propofol and Methohexitone for Elective Caesarean — A Comparative Study

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Summary

Two identical groups of females underwent caesarean operations. One group was induced with propofol 2.04 (SD 0.023) mg per kilogram and the other group induced with methohexitone 1.05 (SD 0.15) mg per kilogram body weight. Maintenance of anaesthesia was identical in both groups. Post-intubation blood pressure in the methohexitone group was significantly raised whereas with propofol the changes were not significant. There were no significant differences in the Apgar scores, uterine contractility and umbilical venous or arterial blood gases. There was a significant difference in the analgesic requirement in the first hour of the post-operative period; in the propofol group, patients needed less analgesia compared to the methohexitone group. There was no maternal awareness in both groups.

Key words: Propofol, Methohexitone, anaesthesia for caesarean

Introduction

One of the challenges of obstetric anaesthesia for a caesarean operation is to guarantee maternal unconsciousness without cardiovascular depression and foetal depression[1]. The administration of 50% nitrous oxide in oxygen with an inhalation agent reliably eliminates maternal awareness, at the same time maintaining adequate uterine perfusion and oxygenation in the non-stressed foetus[2]. Methohexitone has been used for caesarean operations with no cardiovascular depression and no depression of the foetus[3]. In this study, we planned (a) to compare propofol (diisopropyl phenol 1% emulsion in soya bean oil) with methohexitone and evaluate its cardiovascular effect on induction, analgesic requirement in the post-operative period (first hour after extubation), awareness and uterine contractility (b) to compare Apgar minus colour score with the umbilical venous, umbilical arterial and the maternal arterial blood gases. Informed consent from patients and permission from the hospital ethical committee were obtained before the study.

Patients and Methods

All healthy women of 36 weeks gestation and above of physical status ASA (American Society of Anaesthesiologist) class 1, coming for elective caesarean section under general anaesthesia were included in this study. Those with pregnancy induced hypertension or placentofetal insufficiency were excluded. Patients were randomised into 2 groups, 1 group to receive methohexitone 1% and the other group to

Table I
Mean (SD) values of obstetric and physical characteristics of the patients and mean dosages of drugs

	Propofol	Methohexitone
Age (years)	33.2 (5.7)	31.45 (5.35)
Gestation (weeks)	38.4 (0.91)	38.0 (0.84)
Parity	2.73(1.22)	2.26 (0.88)
Weight (kg)	52 (10.22)	56.3 (9.51)
Dosage (mg/Kg)	2.04 (0.23)	1.05 (0.15)

receive propofol 1% as the induction agent. There were 30 patients, the mean age was 32 years, the mean weight (NPW-non-pregnant weight) was 54 kilograms, and mean gestation was 38 weeks (Table I).

Premedication was ranitidine (150 mg orally 12 hours before the operation); 50 mg ranitidine and meta–clopropamide 10 mg intramuscularly half hour before the operation. Patients were transported to the operation theatre in the lateral position - preferably the left lateral. In the operation theatre, patients were placed with a left lateral tilt, an 18 gauge intravenous line was set up. Patients were pre-oxygenated for 5 minutes while blood pressure, pulse and ECG were monitored. Blood pressure and pulse were recorded automatically by using the Dinamap, a non-invasive automatic blood pressure monitor. Basal systolic and diastolic pressures and pulse rates were recorded after the patient had been in the lateral position for 15 minutes. Subsequently, blood pressure and pulse rate were taken 1 minute, 5 minutes and 10 minutes after intubation and then at 15 minute intervals till the end of the operation.

The patients were either induced with propofol or methohexitone after randomisation into 2 groups. Induction dose was titrated to the loss of eyelash reflex or loss of verbal contact. The trachea was intubated with suxamethonium 1 mg per kilogram while cricoid pressure was applied. Maintenance was with nitrous oxide 60% in 40% oxygen and enflurane 1% w/v. Neuromuscular blockade was maintained with atracurium 0.4 mg per kilogram body weight. Inspired oxygen was continuously monitored with an oxygen analyser. The patients were initially hand-ventilated and then connected to the Ohio 7000 using a tidal volume of 10 ml per kilogram body weight and respiratory rate of 12 per minute. At delivery the umbilical cord was double-clamped and the umbilical arterial, umbilical venous and maternal arterial blood were taken and analysed within 30 minutes for pH, PCO_2, and PO_2.

After delivery the mother was given syntocinon 10 units and fentanyl 3 microgram per kilogram. The following indices were recorded: the induction delivery time (ID) in minutes and uterine incision delivery time (UD) in seconds. The contractility of the uterus was assessed by the obstetrician who was 'blinded'. Uterine contractility was graded into 4 grades (Table II). The Apgar score minus colour of the baby was noted by the paediatric medical officer at 1 minute and at 5 minutes on a scale of 1-8. The medical officer was not aware of the induction agents used. The method of resuscitation was recorded. The haemoglobin and haematocrit pre-operatively and 24 hours post-operatively were analysed.

Recovery was timed from the time of extubation. Analgesic requirement during the first hour after extubation was noted by the recovery staff and checked by the doctor. The time of the first dose of analgesic given was noted. Both the recovery staff and the doctor at the recovery were 'blinded' as regards to the induction agent. In the recovery bay, patients were observed for any nausea or vomiting. On the following day the patients were visited and interviewed for any recall, awareness or dreams during surgery. The

Table II
Contractility score of the uterus

Very flabby even after 30 seconds, requiring infusion of oxoytocin in addition to usual steps	0
Flabby but responds briskly by contracting to direct massage of the uterus or repeat ergot alkaloids i.v.	1
Contracts with usual dose of ergometrine (1 ampoule)	2
Contracts spontaneously without need for additional measures (15 seconds)	3

patients were also asked whether they were prepared to accept this technique of anaesthesia a second time if there was a need. Results are given in mean and SD unless stated.

Statistical analyses for parametric data were performed using the paired 't' test and for non-parametric data the Mann Whitney U test was performed. $P<0.05$ was taken as significant.

Results

Thirty healthy females were included in this study. There were 15 in each group. The biodata and obstetric and physical characteristics were comparable (Table I).

The rise in systolic and diastolic blood pressure at 1 minute after intubation in the propofol group was minimal compared to the pre-induction blood pressure. The systolic and diastolic pressures at 1 minute post-intubation in the methohexitone group were significantly elevated when compared with the pre-induction blood pressure. The systolic and diastolic pressure at 5 minutes and 10 minutes post-intubation were lower in both groups (Table III).

The average Apgar score minus colour and the range in both groups are given in Table IV. There were 2 infants in the propofol group who had Apgar score minus colour of 5; and both these had prolonged induction delivery time (ID), of more than 15 minutes; in 1 case the ID interval was 25 minutes.

The average induction delivery time and uterine incision delivery time are shown in Table IV. The maternal arterial, umbilical venous and umbilical arterial blood pH, PCO_2 and PO_2 in both groups were comparable. The median uterine contractility for the propofol group was 3 and for the methohexitone group was 2.5. The difference was not significant ($p=0.27$).

The mean haemoglobin and haematocrit pre-operatively and post-operatively are shown in Table V. The blood loss was under 500 ml and no patient was given intra-operative blood transfusion.

In the propofol group 11 patients did not request analgesic, 4 requested analgesic drugs in the first hour after extubation. In the methohexitone group, 14 needed analgesics, 1 did not request analgesia.

Table III
Changes in blood pressure at 1, 5 and 10 minutes post intubation

Drug	Blood pressure	Relation to intubation (mmHg)	Mean (SD) blood pressure	p value
Propofol				
	Systolic Pre Pressure		118.7 (11.5)	
		1 minute	121.0 (28.2)	p=0.34
		5 minutes	109.0 (18.3)	p<0.02*
		10 minutes	110.1 (14.9)	p=0.02*
	Diastolic Pre Pressure		76.9 (10.8)	
		1 minute	74.1 (12.8)	p=0.20
		5 minutes	68.5 (13.4)	p<0.02*
		10 minutes		p=0.036*
Methohexitone				
	Systolic Pre Pressure		122.5 (10.3)	
		1 minute	146.9 (14.5)	p<0.001*
		5 minutes	121.2 (21.5)	p>0.21
		10 minutes	114.3 (18.3)	p=0.21
	Diastolic Pre Pressure		77.00 (9.8)	
		1 minute	92.2 (12.6)	p<0.001*
		5 minutes	77.3 (13.3)	p>0.21
		10 minutes	75.3 (13.0)	p=0.39

*Significant Difference

There was no incidence of recall or dreams and all patients were willing to undergo a similar anaesthetic technique if there was a need. The mean (SD) dose of propofol was 2.04 (0.23) mg per kilogram and for methohexitone 1.05 (0.15) mg per kilogram body weight.

Discussion

The qualities of general anaesthesia for caesarean section are very demanding. The mother should be asleep without awareness and with adequate oxygenation. There should be minimal cardiovascular depression and no metabolic acidosis. This is to ensure minimal interference with the newborn baby. The widely accepted technique of anaesthesia for caesarean operations is 50% nitrous oxide in 50% oxygen with a potent inhalation agent like halothane 0.5% w/v. Pre-calculated dose of induction dose may not be satisfactory as the patients' requirements may vary.

In this study, the induction dose was assessed by the loss of eyelash reflex or loss of verbal contact. The induction dose for methohexitone was 1.05 (SD 0.15) mg per kilogram body weight and the range was 0.8 mg-1.1 mg per kilogram. This was within the recommended dose of 1 mg to 1.4 mg per kilogram body[3]. The dose of propofol in this study was 2.04 (SD 0.23) mg per kilogram with a range of 1.83 mg-2.27 mg per kilogram body weight. The recommended dose for young patients is 2.0 mg to 2.5 mg per kilogram body weight[4]. In non-premedicated and lightly anaesthetised obstetric patients, the hypertensive response to intubation can be very critical, especially in those patients who have pregnancy induced hypertension

Table V
Mean (SD) values of Apgar score* minus colour and the induction delivery (ID) time, and uterine incision (UD) delivery time.

	Propofol	Methohexitone	p Value
1 minute	6.86 (1.06)	7.8 (0.4)	p=0.044**
Range	5 - 8	5 - 8	
Median	7	8	
5 minutes	7.46 (0.86)	7.87 (0.35)	p=0.38
Range	7 - 8	7 - 8	
Median	8	8	
ID interval (in minutes)	14.86 (4.88)	12.26 (1.94)	p<0.03**
Range	10 - 25	10 - 15	
UD interval	109 (63)	90 (58)	p>0.05
Range	40 - 240	30.240	

*Scale 1-8, ** Significant difference

Table V
Mean (SD) haemoglobin (Hb), haematocrit (Hct) and uterine contractility

	Propofol	Methohexitone
Pre-operative		
Hb gm/dl.	10.5 (1.4)	11.23 (1.14)
Hct	31.69 (3.19)	33.4 (3.65)
Post-operative		
Hb gm/dl	10.5 (1.0)	10.76 (1.13)
Hct	31.0 (4.12)	32.3 (1.14)
Uterine contractility		
Median	3	2.5 (p=0.27)

or intracranial vascular anomalies. This hypertensive response has been attributed to a sudden surge in plasma levels of adrenaline and nonadrenaline following intubation[5].

At 1 minute, the post-intubation systolic and diastolic pressures were higher compared with the pre-induction measurements in the methohexitone group and this rise in blood pressure was significant (P<0.001). In the propofol group, there was a rise in the systolic and diastolic pressure at 1 minute post-intubation. However, compared to the pre-intubation values, the rise was not significant (P=0.34). This is of clinical importance especially when one has to anaesthetise patients with high-blood pressure for caesarean operations. The pressures at 5 minutes, 10 minutes and subsequently at 15 minute intervals

during the ID interval were lower in both groups but it was lower in the propofol group compared to the methohexitone group. There were 4 patients who had low systolic pressures of 90 mmHg but responded to fluids and reduction of the enflurane concentration. These hypotensive episodes were after the delivery of the newborn. The ID intervals were prolonged in 2 cases to 25 and 24 minutes. These 2 cases had uterine incision delivery times of 240 and 220 seconds respectively. The 1 minute Apgar minus colour scores for these 2 infants were 5; but at 5 minutes the Apgar scores were 7. Suction and oxygen-by-mask application were carried out and no intubation was required. The low Apgar score may be attributed to prolonged ID and UD intervals. The mean overall ID interval for the propofol group was 14.86 (SD 4.8) minutes and for the methohexitone group was 12.26 (SD 1.94) minutes. The difference in mean values between the 2 groups was significant ($P<0.05$). The uterine incision delivery time (UD) for the propofol and methohexitone groups were comparable. In this study, there was a slightly lower Apgar minus colour score for the propofol group compared to the methohexitone group and this may be attributed to the slightly prolonged ID interval in the propofol group. Even then the mean Apgar minus colour score in the propofol group mean was 6.86 at 1 minute and 8 at 5 minutes. There was thus no foetal depression in spite of the prolonged ID interval. With a tidal volume of 10 ml per kilogram, the maternal arterial blood PCO_2 was low. With hypocapnia, one would have expected a lower umbilical venous PO_2[6]. The umbilical venous PO_2 was, however, within normal limits. The uterine contractility was not affected by both the agents nor was there any excessive bleeding. Of the patients in the propofol group, 11 did not request for analgesic in the first hour after extubation. In contrast, 14 in the methohexitone group requested for pain relief in the first hour after extubation. This difference between the groups was significant ($P<0.01$), thus showing that propofol has some analgesic properties. This property of propofol has been reported[7] and requires further study. This analgesic effect would be beneficial especially in the immediate post-operative period. None of the patients had recall or dreams. The patients were all satisfied and were willing to accept this technique of anaesthesia again if the need arose.

Conclusion

This study showed that propofol, compared to methohexitone, has the following advantages: post-operative analgesia and minimal hypertensive response to intubation which is of clinical importance particularly in patients with hypertension who have to undergo caesarean operations. Compared with methohexitone; propofol consistently produced lower blood pressures during the induction delivery period, yet the Apgar minus colour score at 5 minutes was comparable to methohexitone. Uterine contractility was not affected nor was there an increase in bleeding. There was an analgesic effect with propofol. There were no recall or dreams. Patient acceptance was good.

Propofol is therefore a quick induction agent and represents a good alternative to methohexitone with the added advantages of minimal post-intubation hypertensive response and analgesia persisting in the post-operative period.

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References

1. Harvey C. Anaesthesia for caesarean delivery. International Anaesthesiology clinics 1990;28 : 25-9.
2. Warren TJ, Datta S, Ostheimer GW et al. Comparison of maternal and neonatal effects of halothane, enflorane and isoflorane for caesarean delivery. Anesth Analg 1983;62 : 516-20.
3. Anita Holdcroft, Robinson MJ, Gordon H, Whitwam JG. Comparison of effects of two induction doses of methohexitone on infants delivered by Caesarean section. Brit Med J 1974;2 : 472-5.
4. Dundee JW, Robinson FP, McCollum J & C, Patterson CC. Sensitivity to propofol in the elderly. Anaesthesia 1986;41 : 482-5.
5. Russel WJ, Morris RG, Frewin DB, Dren SE. Changes in catecholamine concentration during endotracheal intubation. Brit J Anaesthesia 1981;53 : 837-9.
6. Peng ATC, Blancato LS, Motoyama EK. Effect of maternal hypocapnia vs encapnia on the foetus during caesarean section. Brit J Anaesthesia 1972;44 : 1173-8.
7. Briggs P, Dundee JW, Bahar M, Clarke RSJ. Comparison of the effect of diisopropyl phenol (IU 35868) and thiopentone response to somatic pain. Brit J Anaesthesia 1982;54 : 307-11.