A Comparison of Propofol and Ketamine as Induction Agents for Cesarean Section

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Objective : *To compare the neonatal and maternal effects of propofol and ketamine as induction agents for elective cesarean section*
Design : *Randomized, double-blind study.*
Setting : *Inpatient Obstetrics Department of Sappasitthiprasong Ubonratchatani Hospital, Ubonratchatani province, Thailand.*
Intervention : *2 groups of 50 patients each receiving either 2mg/kg propofol or 1mg/kg ketamine for the induction of anesthesia.*
Results : *The time from the induction to cord clamping (I-C), the time from the uterine incision to cord clamping (U-C), the hemodynamic changes, sleep' quality, dream, recall, awareness, Postoperative nausea & vomiting (PONV), and Apgar scores were studied. In the ketamine group Systolic Blood Pressure and Diastolic Blood Pressure rose about10-25% of the baseline after the induction, intubation, skin incision, and cord clamping ($p < 0.001$) while in the propofol group only the Heart Rate rose ($p < 0.036$) after the induction, the intubation, the skin incision, and cord clamping. Apgar scores, the I-C time, the U-C time, the age, the weight and total amount of methergin and oxytocin were not significantly different in both groups. No incidence of awareness, nightmare and ketamine's phychomimetic side effects was found. The incidence of unpleasant light sleep, dreams and PONV was low. Most patients were willing to have the same anesthetic technique for the next cesarean section (81.3% of the propofol group& 86% of the ketamine group).*
Conclusion : *Both propofol and ketamine can be used as alternative induction agents to thiopental. The addition of sevoflurane immediately after the induction, together with the use of midazolam and morphine after delivery shall prevent awareness and ketamine's phychomimetic side effects.However ketamine was cheaper and although Systolic Blood Pressure and Diastolic Blood Pressure were elevated they were within an acceptable range.*

Keywords : *Ketamine General anesthesia, Cesarean section, Low resource*

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About half of all cesarean sections as well as emergencies and some patients with contraindications for regional anesthesia are performed with general anesthesia in Sappasitthiprasong Ubonratchatani hospital. One important factor concerning general anesthesia for cesarean section is the choice of induction drugs, which ideally should induce maternal unconsciousness rapidly with a minimum of undesirable side effects as well as avoiding as much as possible concomitant direct or indirect neonatal depression.

Thiopental sodium is the standard and routine induction drug, but at Sappasitthiprasong Ubonratchatani Hospital the authors did not have

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thiopental sodium for 2 years. Both propofol and katamine have been recommended as an alternative to thiopental sodium for the induction of general anesthesia[1-11].

Propofol has been proposed but controversies exist as to the ideal dose and neonal effect[1-8]. Ketamine has been recommended as an alternative to thiopental sodium for the induction of general anesthesia in patients undergoing elective cesarean section. Compared to thiopental sodium induction, ketamine induction yields a significantly lower intraoperative maternal awareness and better neonatal outcome[9-11].

In this randomized, double-blind study the authors evaluated neonatal and maternal effects of propofol and ketamine as induction drugs for elective cesarean section.

Material and Method

The subjects of this study the patients consisted of one hundred healthy pregnant women aged 21-42 years old, with no underlying diseases, no medical or obstetric complications, at term with a single and healthy fetus (37-40 week gestation, confirmed by ultrasound analysis) undergoing an elective cesarean section. The study was approved by The Ethical Review Committee for Research in Human Subjects, Ministry of Public Health, Thailand. Informed consent was obtained from each patient.

Two anesthetic nurses and one anesthesiologist were assigned to each patient. One nurse prepared the induction drugs and the other anesthetized the patient. The anesthesiologist administed the induction drugs and the anesthesia. One experienced circulating nurse evaluated the neonatal Apgar scores at 1 and 5 minutes, respectively.

The patients were randomized by the use of a computerized randomization code to one of the two groups of 50, each to receive either 2mg/kg propofol and 1mg/kg ketamine. Premeditation by 50mg Ranitidine was administered intravenously 30 minutes before the induction. The patients were induced in supine with left uterine displacement, following preoxygenation of 6 L/min 100 percent oxygen for 3-5 minutes before the induction via a facemask. A rapid sequence with cricoid pressure induction of anesthesia was performed in all patients. Both the anesthesiologist and anesthetic nurse did not know what induction drug was used. 2mg/kg Succinylcholine was given to facilitate endotracheal intubation with a cuffed tube. After the injection of the induction drug and Succinylcholine, 4 percent of sevoflurane in 6 L/min 100 percent oxygen was administered immediately. After successful intubation, fifty percent of N_2O in oxygen total flow 4 L/min and 0.04-0.06 mg/kg pancuronium were administered. The ventilation was controlled by a ventilator with the tidal volume of 10-12 ml/kg to keep normocarbia of end tidal CO_2, and sevoflurane was adjusted to 1 percent end tidal until the umbilical cord was clamped. After delivery the N_2O was increased to 60 percent, and the sevoflurane was discontinued, 0.01mg/kg morphine,0.04-0.06mg/kg midazolam, and 0.2mg methergin were injected intravenously. 20 IU Oxytocin in 1,000 ml NSS was thereafter continuously infused.

To avoid neonatal hypothermia, the air condition in the operating room was only turned on after the neonate was out of the operating room. Apgar scores at 1 and 5 minutes were used to assess the neonatal outcome by an experienced circulating nurse who had been well trained by a pediatrician.

The electrocardiogram was put on continuously displayed mode. The pulse oximetry, capnography, systolic blood pressure (SBP), diastolic blood pressure (DBP), and heart rates were recorded automatically every minute before delivery, using Phillip Agilent V24CT Datex Ohmeda, Aestiva Compact plus and Ventilator7100 were used as anesthetic machines with a ventilator to control ventilation and anesthesia.

The time from the induction to delivery (cord clamping), the time from the uterine incision to delivery, and the total amount of oxytocin and methergin in the operating room were recorded.

24 hours after cesarean section the other anesthetic nurse performed a follow up interview on all the patients about recall, quality of sleep, dreams, postoperative nausea & vomiting (PONV), postoperative uterine atony, and satisfaction of anesthesia by using questionnaires.

Data are presented as mean $\pm$ SD. Statistic evaluation was performed by using SPSS for baseline characteristics; Continuous data were performed by student t-test, and category data were performed by Chi-square test. For vital sign performed repeated measure ANOVA with adjusted covariate (baseline) was used. A *p*-value of 0.05 or less was considered significant.

Results

The maternal characteristics were comparable in the two groups (Table1). No significant

Table 1. Maternal characteristics

	Propofol (n = 50)	Ketamine (n = 50)	P value
Age Years	28.54 ± 5.89	27.16 ± 4.73	0.200
Weight Kg	65.55 ± 9.60	63.26 ± 9.12	0.224

differences were noted in age and weight in both groups.

The time from the induction of anesthesia to cord clamping (I-C),the time from the uterine incision to cord clamping (U-C), and the neonatal Apgar scores at 1 and 5 minutes of the 2 groups were not significantly different (Table2).

Cardiovascular responses 1minute after the induction, intubation, and skin incision and at cord clamping are reported in Table3, respectively. The patients in the ketamine group showed a significant increase in systolic blood pressure (SBP), diastolic blood pressure (DBP) after the induction, intubation, incision and delivery ($p < 0.001$). The propofol group showed a significant increase in heart rates to ($p < 0.036$).

Table4 shows a non-significant difference of the total amount of intra-operative methergin and oxytocin. No postoperative uterine atony 24 hours after the cesarean section was noted. The quality of sleep during and after the cesarean section is given in Table 4. There was no significant difference in both groups. The incidence of recall is shown in Table 4. There was no incidence of awareness in both groups. The dream pattern in the propofol group, 8% (4) had a good dream showing a higher incidence than the ketamine group. The incidence of Postoperative nausea & vomitng (PONV) was the same. The willingness to have the same anesthetic technique again is shown in Table 5.

Table 2. The time from the induction to cord clamping (I-C),the time from the uterine incision to cord clamping (U-C) and Apgar scores in both groups

	Propofol (n = 50)	Ketamine (n = 50)	P value
I-C time, sec	425.40 ± 146.63	410.86 ± 161.57	0.985
U-C time, sec	129.68 ± 99.71	122.02 ± 108.55	0.992
Apgar 1 min	8 26% (13)	22% (11)	
	9 74% (37)	76% (38)	0.554
	10 0% (0)	2% (1)	
Apgar 5 min	9 2% (1)	2% (1)	0.753
	10 98% (49)	98% (49)	

Discussion

The Apgar scores of the neonates did not differ significantly in both groups like previous studies[1-11]. The present study has shown that the addition of 1% sevoflurane (end-tidal) immediately after the administration of the induction drug has an acceptable Apgar score like other sevoflurane studies in elective cesarean section[12], The total amount of intra-operative methergin and oxytocin was not significantly different, and no evidence of uterine atony was found one day after the operation.

In the present study, there was no report of discomfort during the injection of the induction drugs, because 1ml of 1% xylocain was used with the induction drugs.

Maternal cardiovascular responses were significantly higher, especially the Systolic Blood Pressure(SBP) and Diastolic Blood Pressure(DBP) in

Table 3. Systolic blood pressure (SBP), Diastolic blood pressure (DBP), Heart rates (HR), and SPO_2

	Propofol (n = 50)	Ketamine (n = 50)		Propofol (n = 50)	Ketamine (n = 50)
SBP			DBP		
Induction	127.94 ± 14.82	136.44 ± 16.38*		69.52 ± 17.56	89.12 ± 17.87*
Intubation	149.84 ± 21.64	158.62 ± 16.82*		90.38 ± 15.28	103.12 ± 12.83*
Incision	143.20 ± 18.77	150.36 ± 12.40*		83.26 ± 16.75	92.34 ± 14.97*
Delivery	130.26 ± 14.26	141.30 ± 13.12*		68.74 ± 14.39	82.48 ± 17.17*
HR			SPO_2		
Induction	102.96 ± 13.65	94.90 ± 16.27**		99.76 ± 0.56	99.84 ± 0.42
Intubation	111.60 ± 13.71	104.68 ± 15.73**		99.66 ± 0.69	99.64 ± 0.72
Incision	109.44 ± 15.91	106.20 ± 13.54**		99.56 ± 0.76	99.48 ± 0.89
Delivery	97.30 ± 12.70	102.94 ± 12.85**		99.44 ± 0.86	97.68 ± 12.68

Note: Data are mean ± SD, *Significant difference ($p < 0.001$), **Significant difference ($p < 0.036$)

Table 4. Mean ± SD of total amount of methergin and oxytocin and postoperative uterine atony, quality of sleep, recall, dream and post operative nausea and vomiting

	Propofol (n = 50)	Ketamine (n = 50)
Tota amount of methergin and oxytocin		
Methergin mg	0.22 ± 0.07	0.21 ± 0.05
Oxytocin IU	19.00 ± 12.66	17.40 ± 4.43
Atony	-	-
Quality of sleep		
Deep sleep, pleasant	98% (49)	96% (48)
Light sleep, unpleasant	2% (1)	4% (2)
Recall		
Preparation room	10% (5)	4% (2)
Operating table	84% (42)	92% (46)
Operation(Awareness)	-	-
Recovery room	4% (2)	2% (1)
Ward	2% (1)	2% (1)

Note: Atony = Postoperative uterine atony 24 hours after cesarean section
PONV = Postoperative nausea and vomiting
* Significant difference, ($p < 0.005$)

Table 5. Willingness to use the same anesthetic again

	Propofol (n=50)	Ketamine (n=50)
Yes	81.3% (39)	86% (43)
No	18.8% (9)	14% (7)

the ketamine group, with an increase of about 10-25% similar to previous studies[17]. This can be attributed to the sympathomimetic effect[13]. An increased HR in propofol was significant because of the difficulty in maintaining an adequate depth of anesthesia[8].

Many studies approved the use of propofol and ketamine as alternative and safe induction drugs for general anesthesia in cesarean section[1-11]. The frequency of awareness with propofol may be very high, especially when used in a low dose[1]. A higher dose has been proposed to reduce this problem[14], however, significant neonatal depression occurred in the latter case. All the studies with ketamine (1mg/kg) as an induction agent reported low intraoperative awareness and acceptable Apgar, scores however there are high incidences of ketamine's phychotomimetic side effects. This effect can be reduced by diazepam or midazolam[11]. The present study showed that propofol (2mg/kg) and ketamine (1mg/kg), as induction agents, combined with 1% sevoflurane (end-tidal), midazolam (0.040.06mg/kg), and morphine (0.1mg/kg) can be used to prevent awareness and hallucination. This has been already confirmed by previous studies[18]. Capogna G, et al proposed that the addition of a volatile drug immediately after propofol prevented any maternal recall and awareness[19]. In the present study, the immediate addition of sevoflurane prevented light anesthesia and awareness in both groups.

Almost all patients in both group had pleasant deep sleep and low incidences of dream. The present study shows very low incidences of dream and awareness when compared with other studies which used the same dose of ketamine[15,16].

The incidence of Postoperative nausea & vomiting (PONV) in the present study was 8% and recovered without any treatment. Lying on the operating table before the induction was recalled by most patients (84%) in the propofol group and 92% in the ketamine group. Both groups of patients showed high willingness to have the same anesthetic technique again (86%) in ketamine 81.3% in the propofol group.

Comparing the anesthetic techniques to previous General anesthesia 75% of patients thought the propofol technique was equal or superior, only 46% patients thought the ketamine technique was equal or superior. As for Regional anesthesia 14.3% thought the propofol technique was superior 33.3% thought the ketamine technique was equal or superior.

When the cost was compared, propofol was approximately 4 times more expensive than ketamine. In the present study, propofol average of 13 ml (130 mg/65.55kg.) costs 200 (or 5 US dollars) and 1.2ml ketamine (60mg/63.26 kg.) costs 50 (1.25 US dollars).

In conclusion, both propofol and ketamine can be a used as alternative induction agents to thiopental for elective cesarean section with maternal acceptability with no significant neonatal effect as measured by apgar scores after 1 minute. No awareness, low incidence of dreams and postoperative nausea & vomiting (PONV), low incidences of unpleasant sleep in the mother were found. The addition of sevoflurane immediately after the induction, and the injection of midazolam and of morphine after delivery prevented hallucination, awareness and light anesthesia without neonatal depression and uterine atony. The maternal cardio-

vascular response increased 10-25% but was still within the acceptable range. Interestingly, in previous ketamine studies it was proposed that ketamine can be used not only for special indications but also as a routine method for induction of general anesthesia for cesarean section[11]. Ketamine can also lower postoperative analgesia requirement[20]. Ketamine is also cheaper.

In the context of many Thai rural hospitals with limited resourses the authors suggest ketamine be used as an induction agent for Cesarean section.

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การนำสลบด้วย Propofol เปรียบเทียบกับ Ketamine สำหรับการผ่าท้องคลอด

โอภาส หว่านนา, เทวารักษ์ วีระวัฒกานนท์, สนธยา พิริยะกิจไพบูลย์, บุษกร แต้ศิริ

วัตถุประสงค์ *: เพื่อศึกษาผลของการนำสลบด้วย propofol และ ketamine ต่อมารดาและทารกแรกคลอดจากการดมยาสลบสำหรับการผ่าท้องคลอดแบบนัดล่วงหน้า*

วัสดุและวิธีการ *: เป็นการศึกษาแบบ randomized double-blind study ทำการศึกษาในมารดา อายุระหว่าง 21-42 ปี สุขภาพสมบูรณ์แข็งแรง ไม่มีโรคประจำตัว ไม่มีภาวะแทรกซ้อนทางสูติกรรม และอายุครรภ์ ตั้งครรภ์ครบกำหนด (37-40 สัปดาห์) มีทารกในครรภ์เพียง 1 คน สุขภาพดี ครบกำหนดคลอด(ยืนยันด้วย ultrasound) ที่กลุ่มงานสูติกรรม โรงพยาบาลสรรพสิทธิประสงค์ อุบลราชธานี จำนวน 100 ราย สุ่มแยกเป็น 2กลุ่มๆละ50คน ได้รับ propofol 2mg/kg หรือ ketamine 1mg/kg นำสลบแบบ rapid sequence induction with cricoid pressure เสริมด้วย 4%sevoflurane ทันทีหลังฉีดยานำสลบหมด ควบคุมให้ได้ 1% sevoflurane end-tidal ปิดเมื่อทารกคลอด ฉีด midazolam 0.04-0.06 mg/kg และmorphine 0.1 mg/kg ศึกษาเปรียบเทียบ cardiovascular effects, time from induction to cord clamp (I-C), time from uterine to cord clamp (U-C), sleep's quality, dream, recall, awareness, PONV และ Apgar scores ที่ 1 และ 5 นาที*

ผลการศึกษา *: พบว่า อายุ, น้ำหนัก, I-C time, U-C time, ปริมานการใช้ oxytocin, methergin ในห้องผ่าตัด และ Apgar scores ไม่แตกต่างอย่างมีนัยสำคัญทางสถิติทั้ง 2 กลุ่มในกลุ่ม ketamine ค่า SBP, DBP เพิ่มขึ้นอย่างมีนัยสำคัญทางสถิติหลัง induction, intubation, skin incision และ delivery ($p < 0.001$) คิดเป็น 10-25% ของ base line กลุ่ม propofol HR เพิ่มขึ้นอย่างมีนัยสำคัญทางสถิติ ($p < 0.036$) เช่นกัน ไม่พบ awareness, ketamine's phychomimetic side effects, intraoperative และ postoperative uterine atony อุบัติการณ์การหลับไม่ลึก, ฝัน, PONVต่ำ มารดาส่วนใหญ่ต้องการเลือกเทคนิคการดมยาสลบเดิมสำหรับการผ่าท้องคลอดครั้งต่อไป (propofol 81.3% & ketamine 86%)*

สรุป *: ทั้ง propofol และ ketamine สามารถนำมาใช้เป็นยานำสลบสำหรับการผ่าท้องคลอดแบบนัดล่วงหน้า นอกจาก thiopental การเสริมด้วย sevoflurane ทันทีหลังฉีดยานำสลบ และฉีด midazolam, morphine หลังทารกคลอด สามารถป้องกัน awareness, ketamine's phychomimetic side effects, ฝันร้ายได้ ทำให้หลับลึก ไม่เกิด uterine atony ทั้ง intraoperative และpostoperative. Ketamine มีราคาถูกกว่า 1 ใน 4 ของ propofol แม้ว่า SBP, DBP เพิ่มขึ้นแต่อยู่ในช่วงที่ยอมรับได้*