

## Comparative study of Ketamine and Diazepam with Meperidine and Diazepam in laparoscopic femal sterilization

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*From February to June 1990, 176 healthy females (aged 18-45 years) undergoing laparoscopic sterilization were divided randomly into two groups: A and B. Diazepam (0.2-0.3 mg/kg of body weight [Bw.]) was administered intravenously to group A acceptors. Diazepam (0.2-0.3 mg/kg. Bw) and Meperidine (2 mg/kg. Bw) were administered intravenously and supplemented with a local anaesthetic in group B acceptors. Mean operative times were not significantly different ( $p > 0.05$ ). The anaesthetist evaluated the results to be significantly ( $p > 0.05$ ) better in group A. Ketamine and Diazepam had a tendency to increase blood pressure and stimulate respiration, while Meperidine and Diazepam had the opposite effect in the Ketamine group, 29.55% of the cases experienced emergence phenomena. There was not much difference with regard to findings during operation and complications. It was concluded that Ketamine is one of the anaesthetics of choice for women undergoing laparoscopic sterilization.*

*Key word: Ketamine, Diazepam, Meperidine, Laparoscopic female sterilization.*

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สุวิทย์ บุญยะเวชชีวิน. การศึกษาเปรียบเทียบการใช้ยาเคตามีน ร่วมกับไดอะซีแพม เปรียบเทียบกับเมอเพอริดีน ร่วมกับไดอะซีแพม ในการทำหัตถุผ่านกล้องแลบปาโรสโคป. จุฬาลงกรณ์เวชสาร 2534 พฤษภาคม; 35(5): 255-263

ได้ทำการศึกษาเปรียบเทียบการใช้ยา *Ketamine* กับ *Meperidine* เมื่อใช้ร่วมกับ *Diazepam* ในผู้รับบริการทำหัตถุด้วยกล้อง *Laparoscope* ที่มีสุขภาพแข็งแรง และมีอายุระหว่าง 18-45 ปี จำนวน 176 ราย แบ่งผู้รับบริการเป็น 2 กลุ่ม โดยกลุ่ม A ได้รับยา *Diazepam* 0.2-0.3 มก. ต่อ นน.ตัว กก. และ *Ketamine* 1 มก. ต่อ นน.ตัว กก. ทางหลอดเลือดดำ กลุ่ม B ได้รับยา *Diazepam* 0.2-0.3 มก. ต่อ นน.ตัว กก. และ *Meperidine* 2 มก. ต่อ นน.ตัว กก. ทางหลอดเลือดดำ และยาระงับความรู้สึกที่แผลผ่าตัดพบว่าเวลาเฉลี่ยที่ใช้ในการทำผ่าตัด ไม่แตกต่างกันอย่างมีนัยสำคัญทางสถิติ ( $P > 0.05$ ) ยกเว้นกลุ่ม A ให้ผลทางวิสัญญีดีกว่าอย่างมีนัยสำคัญทางสถิติ ( $P < 0.05$ ) *Ketamine* และ *Diazepam* มีแนวโน้มที่จะเพิ่มความดันโลหิต และกระตุ้นการหายใจ ในขณะที่ยกเว้นกลุ่ม *Meperidine* และ *Diazepam* มีผลตรงข้าม พบ *Emergence Phenomena* ในกลุ่ม *Ketamine* 29.55% สิ่งที่พบขณะทำผ่าตัด และภาวะแทรกซ้อนใกล้เคียงกันทั้งสองกลุ่ม *Ketamine* เป็นข้อเลือกทางวิสัญญีอีกวิธีหนึ่ง ซึ่งสามารถใช้ได้อย่างเหมาะสมในการทำหัตถุผ่านกล้อง *Laparoscope*

Ketamine is a popular anaesthetic drug used in general and community hospitals because of its many advantages:<sup>(1)</sup> it is convenient to use; can be used as a sole anaesthetic; is a potent analgesia; is colourless, water-soluble and stable in solution; and is painless and non-irritating following parenteral injection. But there are some undesirable side-effects, especially emergence phenomena the occurrence of, which varies from less than 5% to more than 30% of the cases.<sup>(2-4)</sup> Several investigators have reported a decrease in post-hypnotic emergence phenomena when Ketamine is used with drugs in the benzodiazepine group.<sup>(5, 6)</sup> Diazepam (0.15-0.3 mg/kg, I.V.) has been reported to decrease significantly the incidence of dreams and to eliminate post-operative illusion when administered before induction of Ketamine anaesthesia.<sup>(5, 6)</sup> Others have shown that Ketamine-induced cardiovascular stimulation and the concomitant rise in plasma noradrenaline (norepinephrine) levels may be decreased significantly by premedication with Diazepam (0.2-0.5 mg/kg, I.V.)<sup>(7, 8)</sup>

Many hospitals use Ketamine as the sole anesthesia for a number of minor operations including laparoscopy. Since there seems to be a lack of research or reports about the benefits of this drug when combined with benzodiazepines in performing laparoscopic female sterilization, we conducted a study to compare its use with that of the conventional regimen involving Meperidine.

The purpose of this study is to compare hemodynamic and respiratory changes, operative time, outcome of operation and anesthesia and complications associated with both regimens.

## Materials and methods

Enrolled in this study were 176 female acceptors of sterilization in a family planning project in Uthai-thani province during 1990. A mobile laparoscopic female sterilization team from the Maternal and Child Hospital (subcenter 61) provided female sterilization service at three community hospitals in Uthai-thani. All the acceptors were healthy women aged 18-45 years, American society of anesthesiologist physical status (ASA) I, not pregnant, having no contraindication either for undergoing the operation or for being given the anesthetic drug. The acceptors were informed in detail of the anesthetic effects and they all signed informed consent forms. Acceptors were randomly allocated to two treatment groups as follows:

**Group A.** Diazepam (0.2-0.3 mg/kg.Bw.) was given intravenously followed by Ketamine (1

mg/kg.Bw.) 5 minutes later. If there was inadequate anaesthesia, Ketamine (0.2-0.4 mg/kg.Bw.) was administered intermittently.

**Group B.** Diazepam (0.2-0.3 mg/kg.Bw.) and Meperidine (2 mg/kg) were given intravenously, followed by plain 1% Xylocaine (10 ml) infiltrated at the site of the incision.

During the operation, the depth of anesthesia was evaluated using these criteria:

Excellent = Patient motionless.

Good = Movement unrelated to pain.

Fair = Movement related to pain.

Poor = Inoperable.

Blood pressure, pulse and respiratory rate were recorded at 0, 3, 5, 10, 15, 30 minutes after drug administration and thereafter every 30 minutes. Immediately after completion of the procedure, the patients were transferred to the wards for further observation by the ward nurses.

## Statistical analysis

1. Unpaired student t-test for characteristics of acceptors.
2. Paired student t-test and repeated measures analysis of variance in changes of vital signs.
3. Unpaired student t-test for operative times.
4. T-test proportion for anesthetic evaluation.
5. T-test proportion for complications during the operation. (statistical significance at  $\alpha = 0.05$ )

## Results

The women in the Ketamine and Meperidine groups did not differ significantly with regard to patients' characteristics nor did the mean operative times, as indicated in table 1. More than 80 percent of the 176 patients interviewed preoperatively wished to be unaware of the surgical manipulations, i.e. 80.68 and 89.77 per cent of those in the Ketamine and the Meperidine groups, respectively. The same anesthetist viewed that analgesia at the excellent level produced by Ketamine was significantly ( $P < 0.05$ ) Meperidine was significantly ( $P < 0.05$ ) better than that produced by Meperidine; and that the analgesia at the good and fair levels produced by Meperidine was significantly ( $P < 0.05$ ) better than that produced by Ketamine (table 2.)

Table 3 shows that, in four cases in the Ketamine group and three cases in the Meperidine group, the procedures could not be accomplished owing to intraabdominal adhesions (table 3.)

In the Ketamine group, there were two cases who had tearing of the fallopian tubes and

mesosalpinx. Uterine perforations occurred in four cases (one in the Meperidine group and three in the Ketamine group. The author had to remove the hulka elevator clamp and apply a new technique for interval sterilization<sup>(9)</sup> to continue the operation. Laparotomy was not done (table 4).

Changes in vital signs during the operation, when compared between the two groups using the paired student-t-test, were significantly different 3, 10 and 15 minutes after the drugs were administered (table 5).

A comparison of the time-course of changes in vital signs in each group (before and after administration of the drugs), using repeated measures analysis of variance, showed that in the Ketamine group the values at three minutes were higher than the baseline of both the systolic and diastolic readings, but at 30 and 60 minutes only the systolic values were lower. On the other hand, a significant pressure drop was observed in systolic

values at 10, 15, 30 and 60 minutes; there was no difference in diastolic values throughout for the Meperidine group. A slight increase in the pulse rate was found in the Meperidine group immediately after injection. The heart rate decreased significantly ( $P < 0.05$ ) when compared with the baseline values in both groups. With regard to respiratory effect, the readings of those in the Meperidine-treated group declined until recovery, while those in the Ketamine group increased significantly ( $P < 0.05$ ) within three minutes of injection.

Emergence phenomena were found in 26 cases (29.55%) in the Ketamine group and in five cases (5.68%) in the Meperidine group.

Post-operative complications were: incisional bleeding, one and four cases in the Ketamine and Meperidine groups respectively; vaginal bleeding from uterine elevator insertion, four and seven cases in the Seven patients receiving Ketamine experienced nausea and vomiting.

Table 1. Patient's characteristics.

	Group A. (Ketamine) (n = 88) $\bar{X} \pm SD$	Group B. (Meperidine) (n = 88) $\bar{X} \pm SD$
Age (yr)	32.2 $\pm$ 5.9	31.5 $\pm$ 5.3
Body weight (kg)	54.2 $\pm$ 8.0	54.2 $\pm$ 8.4
Height (cm)	154.5 $\pm$ 4.6	153.3 $\pm$ 5.3
Hematocrit (%)	38.9 $\pm$ 3.3	38.0 $\pm$ 14.0
Systolic BP** (mmHg)	112.6 $\pm$ 11.5	111.8 $\pm$ 12.3
Diastolic BP (mmHg)	75.2 $\pm$ 8.7	75.8 $\pm$ 16.5

\*Statistical significance  $\alpha = 0.05$

\*\*BP = blood pressure

Table 2. Anaesthetic requirements, operative time and anesthetist's evaluation.

	Group A (Ketamine) (n = 88)	Group B (Meperidine) (n = 88)
Anaesthetic requirement (%)		
Awake intraoperatively	19.32	10.23
Unaware of procedures	80.68	89.77
Operative time (minutes)		
Mean $\pm$ SD	7.78 $\pm$ 2.94	7.23 $\pm$ 2.28
Anaesthetist's evaluation (%)		
Excellent	87.50*	44.32
Good	7.95	29.55*
Fair	3.41	25.00*
Poor	1.14	1.14

\*Statistical significance  $\alpha = 0.05$

Table 3. Findings.

	Group A (Ketamine) (n = 88)		Group B (Meperidine) (n = 88)	
	No.	%	No.	%
1. Normal pelvic organ	84	95.46	85	96.59
2. Few adhesive bands around adnexa (fimbrial ends could be visualized)	—	—	3	3.41
3. Adhesions around adnexa (fimbrial ends could not be visualized)	2	2.27	—	—
4. Severe adhesions (fallopian tubes could not be visualized)	2	2.27	—	—

Note: In cases described under Nos. 3, 4 above, it was not possible to perform laparoscopic tubal sterilization.

Table 4. Complications during operation.

	Group A (Ketamine) (n = 88)		Group B (Meperidine) (n = 88)	
	No.	%	No.	%
None	83	94.32	87	98.86
Bleeding from tearing of fallopian tubes or mesosalpinx	2	2.27	—	—
Uterine perforations	3	3.41	1	1.14

\*statistical significance = 0.05

Table 5. Changes in vital signs.

Time (min)	Parameters	Group A (Ketamine) (n = 88)	Group B (Meperidine) (n = 88)
		$\bar{X} \pm SD$	$\bar{X} \pm SD$
0	SBP	126.7 ± 11.0	127.3 ± 13.4
	DBP	81.8 ± 7.5	82.1 ± 10.2
	PR	83.3 ± 9.6	86.7 ± 13.6
	RR	22.5 ± 5.9	23.0 ± 2.3
3	SBP	136.4 ± 18.7*, **	124.1 ± 11.4
	DBP	88.9 ± 13.4*, **	81.4 ± 10.9
	PR	81.4 ± 11.6*	88.9 ± 14.5
	RR	23.5 ± 1.8**	23.3 ± 2.1

Time (min)	Parameters	Group A (Ketamine)	Group B (Meperidine)
		(n = 88) $\bar{X} \pm SD$	(n = 88) $\bar{X} \pm SD$
5	SBP	128.3 ± 18.2	123.8 ± 15.6
	DBP	84.2 ± 12.8	81.6 ± 11.8
	PR	78.2 ± 10.9**	86.1 ± 13.8
	RR	23.4 ± 1.8	23.6 ± 2.2
10	SBP	123.3 ± 15.5	121.6 ± 27.1**
	DBP	83.3 ± 12.2	81.8 ± 11.7
	PR	76.2 ± 10.2*, **	82.9 ± 8.3**
	RR	23.4 ± 2.0*	22.0 ± 2.2**
15	SBP	121.5 ± 16.6	123.1 ± 15.9**
	DBP	82.5 ± 12.3	81.4 ± 10.7
	PR	75.9 ± 8.8**	72.3 ± 8.3**
	RR	22.8 ± 2.4*	21.9 ± 2.3**
30	SBP	121.5 ± 13.1**	122.5 ± 12.1**
	DBP	81.9 ± 10.4	81.6 ± 10.2
	PR	76.1 ± 7.1**	77.9 ± 7.9**
	RR	22.1 ± 2.3	21.5 ± 2.1**
60	SBP	119.7 ± 13.3**	119.9 ± 11.2**
	DBP	79.9 ± 9.5	79.8 ± 9.5
	PR	74.9 ± 8.0**	77.8 ± 7.0**
	RR	21.7 ± 2.5	21.5 ± 2.0**

\* K vs M (Using paired t-test) Statistical significance at  $\alpha = 0.05$

\*\* K0 vs K3, K5, K10, K15, K30, K60

M0 vs M3, M5, M10, M15, M30, M60 (Using repeated measures analysis of variance) Statistical significance at  $\alpha = 0.05$

**Table 6.** Emergence phenomena\*.

	Group A (Ketamine)		Group B (Meperidine)	
	(n = 88)		(n = 88)	
	No.	%	No.	%
Without	62	70.45	83	94.32
With	26	29.55	5	5.68

(\*Emergence phenomena includes: disorientation, dreaming, excitement, hallucination, illusion)

Table 7. Post operative complications.

	Group A (Ketamine) (n = 88)		Group B (Meperidine) (n = 88)	
	No.	%	No.	%
Without	76	86.36	83	94.31
With:				
Incisional bleeding	1	1.14	4	4.55
Bleeding per vagina	4	4.55	1	1.14
Nausea, vomiting	7	7.95	0	—

## Discussion

Laparoscopic female sterilization can be performed as day care surgery on an out-patient basis; anaesthesia takes only a short time to perform and massive fluid or blood transfusions are not needed. Acceptors need no hospitalization. However, emphasis must be given to the anaesthetic method to be used in making the operation go smoothly and quickly. The drug, administration route, side-effects and, most importantly, the impression of the acceptors must be considered. Based on this study, most of the acceptors preferred to be unaware of the operative procedures and feel no pain.

Intravenous Meperidine is not adequate as a sole agent because its analgesic effect is inadequate and if it is used in high doses, its undesirable side-effects will increase. However, in combination with benzodiazepine and in conjunction with local anesthesia,<sup>(10, 11)</sup> the doses of Meperidine can be minimized as is now widely practiced in medical schools. Nonetheless this technique has some limitations and is not considered the best. Laparoscopic procedures are different from those of other operations since the patient is placed in the Trendelenburg position. If the abdominal cavity is insufflated, it is harmful to the patient if the arterial carbon dioxide tension is high.<sup>(12, 13)</sup>

With an anesthetic technique, in which spontaneous ventilation takes place while the patient sleeps, respiratory depressants such as Meperidine make the situation worse.

Limpongsanurak S. et al. (1983) reported the use of Ketamine in post-partum tubal ligation in Thai females with a dosage of only 1 mg/kg.Bw.<sup>(14)</sup> The same dosage of Ketamine was also used in this study and found to suffice for laparoscopic tubal sterilization. The anesthetist viewed it as providing good to

excellent operative conditions in nearly 100 per cent of the cases (95.5%).

According to this study, the effects of Meperidine and Ketamine on hemodynamic changes are different. In the Meperidine group, following injection, the systolic and diastolic blood pressure dropped significantly after 10 minutes which may be a result of the histamine-releasing effect of Meperidine.<sup>(15)</sup> When the blood pressure drops, autoregulation of the baroreceptor will increase the pulse rate to support the lowered blood pressure. Thus a slight increase in the pulse rate at three minutes was noticed.

In the Ketamine group, both the systolic and diastolic blood pressure levels increased promptly after injection. The rise in the blood pressure at 3 and 5 minutes came from direct stimulation of the central nervous system and catecholamine release.<sup>(16)</sup> The rise in the pulse rate of the Ketamine group in this study was not detectable as it would be usually. The rise in the pulse rate in the Ketamine group is not the effect of baroreceptor autoregulation like it is in the Meperidine group. Premedication with Diazepam has been found to counteract the effect of noradrenaline,<sup>(7, 8)</sup> which is in agreement with the findings of this study.

The decrease in the respiratory rate was found significantly in the Meperidine group. This supports the findings concerning the respiratory depression effect of Meperidine and its metabolite, Normeperidine, which has a longer half-life and continue to have an effect after an operation. This undesirable effect was not found in the Ketamine group, which is in agreement with the findings of this study.

The analgesic effect of Meperidine is not very potent, since it works mainly by binding to opioid receptors, one of many pain pathways. Ketamine's action has been described as "dissociative

anesthesia'' characterized by complete analgesia with only superficial sleep. It blocks afferent signals associated with some components of pain perception in the spinoreticular tracts and binds to opiate receptors.<sup>(16)</sup> The analgesic property produced by Ketamine is potent, which mean that it can be used as the sole agent in minor operations.<sup>(17)</sup>

Ketamine also increases muscle tone which could becomes a problem in abdominal operations. In this study, the operative times were not different. Moreover, the increase in muscle tone was advantageous for the insertion of the sharp trocar through the abdominal wall and for lessening any trauma to the visceral organs.

The incidence of emergence phenomena associated with the use of Ketamine in this study was 29.55%, which is in agreement with that of other reports.<sup>(2,5,6,18)</sup> By contrast, the incidence of emergence phenomena in the Meperidine group was only 5.68%.

Theoretically, narcotics directly stimulate the chemoreceptor trigger zone, playing the role of emetics.<sup>(19)</sup> In this study, it is of interest to note that none of the Meperidine-treated subjects developed nausea or vomiting, while in the Ketamine group seven cases experienced those effects. This reaction was not definitely explained by long food abstinence, individual susceptibility,<sup>(20)</sup> etc.; it should be noted that Ketamine itself has an emetic action.

In the content of cardiovascular and respiratory stimulation, Ketamine can be used safely. Emergence phenomena, an untoward side-effect, can be counteracted by pre-operative briefing of the patient and the administration of a low dose of benzodiazepine. Ketamine has fast onset, is short acting, involves no drug abuse, is easy to use and is a potent analgesia. These qualities encourage the use of Ketamine as the anesthetic choice o in laparoscopic female sterilization, especially, operations performed by mobile units in community hospitals.

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## Conclusion

Ketamine and Diazepam together provide good anaesthesia for laparoscopic sterilization compared with Meperidine and Diazepam. Ketamine and Diazepam have a tendency to increase blood pressure and stimulate respiration, while the effect of Meperidine and Diazepam is the opposite. The incidence of emergence phenomena with Ketamine is 29.55%. The operative time, findings during operation and complications were not different from those of other former of anaesthesia. Ketamine may there be considered one of the anaesthetics of choice for laparoscopic female sterilization.

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# แก้ไขเพิ่มเติม

จุฬาลงกรณ์เวชสารปีที่ 35 ฉบับที่ 5 เดือนพฤษภาคม 2534 เรื่อง **Comparative study of Ketamine and Diazepam with Meperidine and Diazepam in laparoscopic female sterilization.** ของ นพ.สุวิทย์ บุญยะเวชชีวิน

- หน้า 225 บรรทัดที่ 9 คำว่า or แก้เป็น of
- หน้า 225 บรรทัดที่ 4 (หัวข้อเรื่อง ตัวยพิมพ์เข้มใหญ่) Laparoscopic femal sterilization แก้เป็น Laparoscopic female sterilization.
- หน้า 255 บรรทัดที่ 8 Diazepam (0.2–0.3 mg/kg of body weight/Bw./) แก้เป็น Diazepam (0.2–0.3 mg/kg.Bw) and Ketamine (1 mg/kg.Bw)
- หน้า 257 บรรทัดที่ 11 นับจากล่าง คอลัมน์ขวา ตัดคำว่า Mepericine was significantly ( $P < 0.05$ ) ออก
- หน้า 258 บรรทัดที่ 3 คอลัมน์ซ้ายคำว่า Ketamine group the author แก้เป็น Ketamine group). The author
- หน้า 261 บรรทัดที่ 12 นับจากล่าง คอลัมน์ขวา คำว่า decrease แก้เป็น decrease
- หน้า 262 บรรทัดที่ 36 (นับจากบน) คอลัมน์ซ้าย คำว่า enceurage แก้เป็น encourage
- หน้า 262 บรรทัดที่ 37 (นับจากบน) คอลัมน์ซ้าย คำว่า choice o แก้เป็น choice
- หน้า 262 บรรทัดที่ 6 (นับจากบน) คอลัมน์ขวา คำว่า pressuse แก้เป็น pressure

ขอภัยมา ณ ที่นี้ด้วย

บรรณาธิการ