

## A Randomized Clinical Assessment of the Efficacy and Hemodynamic Stability of Ketamine / Fentanyl Along With Propofol in Patients Undergoing Dilatation and Curettage

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Received: 10-01-2024 / Revised: 13-02-2024 / Accepted: 23-04-2024

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Conflict Of Interest: Nil

### Abstract

**Aim:** The aim of the present study was to evaluate and compare the efficacy and hemodynamic stability of ketamine / fentanyl along with propofol and also assess recovery profile, post-operative analgesia and complications in patients undergoing Dilatation and Curettage.

**Methods:** The present study was carried out in the Department of Anaesthesia, Anugrah Narayan Magadh Medical College and Hospital, Gaya, Bihar, India from December 2019 to November 2020 the study was conducted in 100 patients, aged 18-35 years of ASA Grade 1&2 scheduled for Dilatation and Curettage procedures lasting up to 30 minutes.

**Results:** Pre-induction heart rate, systolic blood pressure, diastolic blood pressure, mean arterial pressure, spo2 were comparable in both the groups with a statistically no significant difference between them ( $p < 0.05$ ).

**Conclusion:** It may be concluded from our present study that propofol with ketamine as an adjuvant in the dose of 0.75 mg/kg compared to propofol with fentanyl as adjuvant in the dose of 2 mcg/kg provides deep sedation. But propofol-ketamine group is more efficacious and provides better peri-operative hemodynamic stability during anaesthesia as compared to propofol-fentanyl group. Also the propofol-ketamine combination produces good analgesia with less requirement of rescue drug in post-operative period with fewer peri-operative complications than propofol-fentanyl combination. We have not encountered any psychotomimetic effects of injection Ketamine in the 0.75mg/kg dose. Hence propofol-ketamine combination is a better choice especially when hemodynamic stability is of great importance in patients undergoing dilatation and curettage.

**Keywords:** Propofol, Ketamine, Fentanyl, Sedation, Hemodynamic stability, Dilatation, Curettage.

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### Introduction

Dilatation and curettage (D & C) is one of the mechanical methods used for abortion. In this operation, opening the cervix or dilatation is far more painful than curettage. [1] The anesthetic method for this operation can be general (GA) or regional, GA is the most common anesthetic approach based on the surgeon and patients' wish. Because bleeding is common in this operation, maintaining the hemodynamic during anesthesia is very important. The duration of the stay in the hospital is often short, and the patient can be discharged if they do not develop any complications. [2]

So, it's best to use a method to get the patient to wake up and recover faster. Therefore, the choice type of drug in the general anesthesia should be carefully investigated and the best medicine be

chosen. [3] Thiopental induces anesthesia by bonding to the position of ionophore chloride in the Gaba aminobutyric acid receptor (GABA) and inhibiting this receptor about 30 seconds after injection. It has no analgesic effect, but its effect on the cardiovascular system and the reduction of vascular resistance leads to hypotension and sometimes, reflex tachycardia. [4] Propofol is a drug with rapid onset and hepatic clearance after intravenous administration. It has direct antinociceptive effects but no analgesic effect. On the other hand, Ketamine acts on the NMDA via antagonistic effects, which increases the systolic blood pressure (SBP), diastolic blood pressure (DBP), and heart rate (HR). Ketamine has dose dependent effects of inaccuracy and analgesia. [5] Ketofol is a combination of two drugs (propofol and ketamine) and is used in anesthesia.

Combining propofol with other drugs such as opioids or ketamine is recommended for improving the quality of sedation, analgesia and minimizing the potential adverse effects with maintenance of a stable cardiovascular and respiratory status in the perioperative period. [6] Ketamine, a NMDA receptor agonist, in subanesthetic doses with propofol has gained attention in total intravenous anesthesia because of its powerful analgesic action without causing myocardial and respiratory depression. Ketamine also causes some degree of sympathetic stimulation, which tends to counterbalance the cardiovascular effects of propofol. [7] Fentanyl on the other hand is synthetic opioid analgesic which has rapid onset and short duration of action and has been used in combination with propofol satisfactorily.

Ketofol (propofol-ketamine admixture) is a combination of ketamine and propofol that is an agent of choice for various procedures. [8] The safety and efficacy of ketofol as a sedoanalgesic agent depend on the dose and the ratio of the admixture. [9] The ratios of 1:2, 1:3 and 1:4 [sub dissociative dose] ratios were very effective for the day case procedure. [10] Dilation and curettage (D C), a brief and painful procedure, is performed for the diagnosis and treatment of endometrial and intrauterine disorders. The procedure is one of the most frequently performed gynecological surgical procedures. It causes considerable pain during cervical dilation and tissue extraction. [11]

The aim of the present study was to evaluate and compare the efficacy and hemodynamic stability of ketamine / fentanyl along with propofol and also assess recovery profile, post-operative analgesia and complications in patients undergoing Dilatation and Curettage.

### Materials and Methods

The present study was carried out in the Department of Anaesthesia, Anugrah Narayan Magadh Medical College and Hospital, Gaya, Bihar, India from December 2019 to November 2020 the study was conducted in 100 patients, aged 18-35 years of ASA Grade 1&2 scheduled for Dilatation and Curettage procedures lasting up to 30 minutes.

The patients were randomly allocated using sealed envelope method in 2 groups (30 of each). Patients

with respiratory, cardiovascular, neurological, liver diseases, patients on narcotic therapy were excluded from study. Pre-anaesthetic evaluation including history and a thorough general and systemic examination and all relevant investigations were done for all the patients.

Patients were kept fasting for at-least 8 hours prior to anaesthesia. Pre-operative baseline heart rate, systolic blood pressure, diastolic blood pressure, mean blood pressure, spo2 was recorded. A peripheral iv line was established. All patients were pre-medicated with Inj. Glycopyrrolate 0.004 mg/kg and Inj. Midazolam 0.02 mg/kg. Group A received Inj. Ketamine 0.75 mg/kg body weight IV slowly over 2 minutes, after 5 minutes Inj. Propofol given at rate of 1ml/3 seconds till loss of consciousness. Group B received Inj. Fentanyl 2 mcg/kg body weight as slow IV injection, after 5 minutes Inj. Propofol given at rate of 1ml/3 seconds till loss of consciousness.

Intra-operatively heart rate, blood pressure, oxygen saturation and Ramsay sedation score was recorded at different time intervals of 5, 10, 15, 20, 25, 30 minutes following induction of anaesthesia in both groups. Throughout the procedure patients were allowed to breathe spontaneously on room air and oxygen supplementation was given to some patients during apnoea.

Top-up dose of Inj. Propofol 0.5 mg/kg was given when patient became light during anaesthesia as indicated by rise in heart rate, blood pressure or any other movement to surgical stimulus. Total dose of propofol required for the patients was noted.

Post-operatively all vital parameters like heart rate, blood pressure, oxygen saturation and visual analogue score was recorded every 30 minutes for first 2 hours then every 2 hours till 12 hours. Any complication like nausea, vomiting, delirium, sedation, pain was noted.

### Statistical Analysis

Continuous variables were compared at different time intervals between ketamine and fentanyl groups by performing unpaired t-test,  $p < 0.05$  was considered as statistically significant.

### Results

**Table 1: Comparison of Heart Rate In Both Groups**

Heart rate	Baseline	1 min	5 min	10 min	15 min	20 min	25 min	30 min
Group A Mean $\pm$ SD	83.57 $\pm$ 3.37	82.22 $\pm$ 4.94	86.64 $\pm$ 5.3	83.32 $\pm$ 6.34	82.0 $\pm$ 5.5 5	81.49 $\pm$ 6.03	80.24 $\pm$ 6.2	80.8 $\pm$ 6.2
Group B Mean $\pm$ SD	86.82 $\pm$ 3.87	88.06 $\pm$ 6.06	83.67 $\pm$ 6.00	78.22 $\pm$ 5.25	78.34 $\pm$ 4.86	76.45 $\pm$ 6.63	80.65 $\pm$ 6.16	79.55 $\pm$ 6.31
P- value	0.01	0.0001	0.0007	0.0003	0.0007	0.03	0.763	0.482

**Table 2: Comparison of Systolic Blood Pressure (SBP) In Both Groups**

SBP	Baseline	1 min	5 min	10 min	15 min	20 min	25 min	30 min
Group A	123.64	119.14	120.60	119.14±9	116.35	114.10	114.78	115.07
Mean ± SD	±5.48	±12.17	±11.30	.90	±10.97	±11.87	±10.56	±10.23
Group B	123.35	119.85	117.21	116.57	111±7.44	108.42	109.85	107±18.7
Mean ± SD	±4.52	±9.67	±8.35	±9.19		±8.21	±8.68	7
P-value	0.823	0.803	0.191	0.301	0.030	0.04	0.05	0.001

**Table 3: Comparison of Diastolic Blood Pressure (DBP) In Both Groups**

DBP	Baseline	1 min	5 min	10 min	15 min	20 min	25 min	30 min
Group A	72.47	69.65±	69.38±	67.42±	67.22±	67.35±	67.47±	69.25±
Mean± SD	±4.91	7.04	2.95	5.56	5.34	5.97	4.39	3.78
Group B	73.37	69.77±	69.47±	64.75±	64.45±	65.58±	67.37±	25
Mean± SD	±4.51	4.88	3.51	3.59	3.59	4.71	4.39	
P-value	0.370	0.858	0.802	0.013	0.017	0.060	0.033	0.926

**Table 4: Comparison of Ramsay Sedation Score in Both Groups**

RSS	Base-line	1 min	5 min	10 min	15 min	20 min	25 min	30 min
Group A	1.92	1.92±	4.40±	4.82±	5.46±	5.86±	5.96±	5.95±
Mean± SD	±0.27	0.27	0.57	0.56	0.57	0.35	0.19	0.20
Group B	1.94±	1.94±	3.94±	4.06±	5.10±	5.72±	5.9±	5.97±
Mean± SD	0.23	0.23	0.74	0.72	0.57	0.49	0.30	0.14
P-value	0.70	0.70	0.009	<0.0001	<0.0001	0.20	0.35	0.65

**Table 5: Comparison of VAS in Both Groups**

VAS	30 min	1 hour	1 hour 30 min	2 hour	4 hour	6 hour	8 hour	10 hour	12 hour
Group A	2.87±1.22	2.33±1.12	1.57±0.9	1.33±0.76	1.17±0.53	1.1±0.4	1±0	1±0	1±0
Mean±SD									
Group B	4.37±1.54	3.27±1.34	2.8±1.13	2.3±0.84	1.63±0.85	1.23±0.5	1±0	1±0	1±0
Mean±SD									
P-value	0.0001	0.004	<0.0001	<0.0001	0.013	0.262	-	-	-

Pre-induction heart rate, systolic blood pressure, diastolic blood pressure, ramsay sedation score, VAS were comparable in both the groups with a statistically no significant difference between them ( $p < 0.05$ ).

### Discussion

Day care gynecological procedures require the use of anesthetic agents which ensure rapid induction and recovery. [12] Total intravenous anesthesia (TIVA) is a combination of hypnotic agents, analgesic drugs and may be muscle relaxants, excluding simultaneous administration of any inhaled drugs. Therefore, it can be an effective alternative to inhalational anesthesia and for ambulatory surgery when the speed and completeness of recovery are important. Drugs used for TIVA should have quick onset, smooth induction, easy maintenance, quick recovery and minimal side effects. [6] Ideal drug for sedoanalgesia should have rapid onset and fast recovery time. However, there is still no consensus for best sedoanalgesic management for short-term procedures. [11]

Pre-induction heart rate, systolic blood pressure, diastolic blood pressure, ramsay sedation score, VAS were comparable in both the groups with a statistically no significant difference between them ( $p < 0.05$ ). The minimal fall in SBP, DBP and MBP in group PK as compared to group PF is due to the sympathomimetic activity of ketamine which counteracts with the cardiovascular depressant action of propofol, thus maintaining a stable hemodynamic profile as compared to fentanyl. These findings are correlated well with the study done by Pawar et al [13], Phillips et al [14] and Khutia et al. [15] The opposing effect of ketamine and propofol on arterial pressure tended to cancel each other out resulting in improved cardiovascular stability. The propofol ketamine group experienced a smaller percentage decrease in SBP, which is comparable with other studies. [7,8,16]

The ketamine-propofol combination is thought to act by counteracting the cardiovascular side-effects of each other, preserving the sedative efficacy. Also the amount of propofol needed to achieve a deep sedation level was much lower in case of PK group than PF group, which contributed to the lower incidence of hypotension and apnea. Also, no

patients in present study required airway manipulation. The post operative complications were also higher in group PF than in group PK. There were no incidences of psychedelic effects of ketamine like hallucination, dysphoria and psychotomimetic emergence reactions when ketamine is used in combination with a sedative-hypnotic (e.g., benzodiazepines, propofol) or a general anesthetic (e.g., halothane, nitrous oxide) is minimal or negligible. Hypnotic doses of propofol are reported to block these hallucinations. These findings are concordance with the study done by Arikani et al [7] Brajesh et al [8] Mahajan et al. [16]

### Conclusion

It may be concluded from our present study that propofol with ketamine as an adjuvant in the dose of 0.75 mg/kg compared to propofol with fentanyl as adjuvant in the dose of 2 mcg/kg provides deep sedation. But propofol-ketamine group is more efficacious and provides better peri-operative hemodynamic stability during anaesthesia as compared to propofol-fentanyl group. Also the propofol-ketamine combination produces good analgesia with less requirement of rescue drug in post-operative period with fewer peri-operative complications than propofol-fentanyl combination. We have not encountered any psychotomimetic effects of injection Ketamine in the 0.75mg/kg dose. Hence propofol-ketamine combination is a better choice especially when hemodynamic stability is of great importance in patients undergoing dilatation and curettage.

### References

- Mehdizadeh A, Akbarian A, Ghasemi A, Ardjomand F. Comparison of lidocaine and saline effect in cervical anesthesia on level of pain during curttage. *RJMS*. 2000; 7 (21):220-222.
- Sahin L, Sahin M, Aktas O, Kilic E, Mandollu E. Comparison of propofol/ketamine versus propofol/alfentanil for dilatation and curettage. *Clin Exp Obstet Gynecol*. 2012;39 (1):72-5.
- MacKay HT, Schulz KF, Grimes DA. Safety of local versus general anesthesia for second-trimester dilatation and evacuation abortion. *Obstet Gynecol*. 1985 Nov; 66 (5):661-5.
- Liu H, Yao S. Effect of thiopental sodium on the release of glutamate and gamma-aminobutyric acid from rats prefrontal cortical synaptosomes. *J Huazhong Univ Sci Technolog Med Sci*. 2004;24(6):602-4.
- Miller R, Eriksson L, Fleisher L, Wiener-Kronish J, Cohen N, Young W. *Miller's Anesthesia*. 8th ed, Elsevier Health Sciences. 920.
- Babita R, Dinesh K, Sangita R, Gurdeep S. A comparative evaluation of Propofol-Ketamine and Propofol-fentanyl as TIVA techniques in terms of haemodynamic variables and recovery characteristics in minor surgeries. *IOSR Journal of Dental and Medical Sciences (IOSRJ DMS)*. 2015;14(4):19-26.
- Arikani M, Aslan B, Arikani O, But A, Horasanli EY. Comparison of propofol-remifentanyl and propofol-ketamine combination for dilatation and curettage: a randomized double blind prospective trial. *European Review for Medical and Pharmacological Sciences*. 2015 Sep 1;19(18):3522-7.
- Kaushal B, Dhawale Y, Gupta D. Comparative evaluation of propofol ketamine and propofol fentanyl in day care surgeries. *Journal of evolution of Medical and Dental Sciences*. 2014 Sep 4;3(41):10325-36.
- Daabiss M, Medhat E and Rashed A.: Assessment of different concentration of ketofol in procedural operation. *British Journal of Medical Practitioners*, 2009;2(1)27-31.
- Wang Y, Jiang X, Pang L, Dong S, Feng Y, Prajapati SS, Yuan C, Ma H. A randomized double-blind controlled study of the efficacy of ketofol with propofol-fentanyl and propofol alone in termination of pregnancy. *Afr J pharm pharmacol*. 2012 Sep 15;6(34):2510-4.
- Yuce H, Kucuk A, Altay N, Bilgic TE, Karahan M, Buyukfirat E, Havlioglu I, Yalcin S, Camuzcuoglu A, Incebiyik A, Hilali G. Propofol-ketamine combination has favorable impact on orientation times and pain scores compared to propofol in dilatation and curettage. A randomized trial. *Acta Medical Mediterranean*. 2013 Jan 1;29:539-44.
- Ahuja H, Abraham V, Abraham J, Liddle D. Ideal anesthetic agents for day-care gynecological procedures: A clinical trial comparing thiopentone with ketamine as adjuncts to propofol. *Advanced Biomedical Research*. 2015 Jan 1;4(1):81.
- Pawar D, Bhole P, Pandey S, Khobragade S. Comparative evaluation of propofol-ketamine and propofol-fentanyl for minor surgical procedures. *International Journal of Research in Medical Sciences*. 2015; 3(12): 3795-3801.
- Phillips W, Anderson A, Rosengreen M, Johnson J, Halpin J. Propofol versus propofol/ketamine for brief painful procedures in the emergency department: clinical and bispectral index scale comparison. *J Pain Palliat Care Pharmacother* 2010; 24: 349-355.
- Khutia SK, Mandal MC, Das S, Basu SR. Intravenous infusion of ketamine-propofol can be an alternative to intravenous infusion of fentanyl-propofol for deep sedation and analgesia in paediatric patients undergoing emergency short surgical procedures. *Indian J Anaesth*. 2012; 56:145-50.
- Mahajan R, Swarnkar N, Ghosh A. Comparison of ketamine and fentanyl with propofol in total intravenous anesthesia: a double blind

randomized clinical trial. The Internet Journal of Anesthesiology. 2009;23(2):1-7.