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Original Article

Comparative Evaluation of Effects of Propofol and Ketamine versus Dexmedetomidine and Ketamine on Blood Pressure, Heart Rate and Recovery of Patients undergoing Dilatation and Curettage

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ABSTRACT

Cardiovascular stability and fast recovery are fundamentals of anesthesia for day care surgery. Dilatation and curettage is a commonly performed minor surgery in obstetrics and gynecology. Propofol is well-studied agent in short surgical procedures. Dexmedetomidine, popular for conscious and cooperative sedation is being used for minor gynecological procedures nowadays. **Objective:** To compare the effects of propofol and ketamine combination with dexmedetomidine and ketamine combination on cardiovascular parameters and recovery of patients undergoing dilatation and curettage. **Methods:** In a quasi-experimental study from March 2021 to August 2021, 136 patients admitted for dilatation and curettage under anesthesia were enrolled. Patients were divided into two groups. Group P+K received intravenous propofol and ketamine and Group D+K received intravenous dexmedetomidine and ketamine. During the procedure, blood pressure, heart rate, oxygen saturation, and recovery time were noted in both groups. **Results:** The demographic data were comparable in both groups. Group P+K had significantly higher heart rate at 5, 10, 15 min, and at the ending of the procedure as compared to group D+K. Group D+K had significantly higher systolic and diastolic blood pressure at 2 min, 5 min, 10 min, 15 min and at procedure end in comparison with group P+K. Bradycardia was observed in 62 (91.2%) patients in D+K group whereas, in P+K group, hypotension was observed in 16 (23.5%) patients. The mean time to attain MAS (modified aldrete score) of 10 in group P+K was 32.0 ± 2.1 minutes whereas in group D+K was 41.3 ± 2.6 minutes. **Conclusions:** It was concluded that the use of dexmedetomidine and ketamine in dilatational and curettage provides cardiovascular stability without respiratory depression as compared to propofol and ketamine.

INTRODUCTION

Cardiovascular stability and early recovery are the mainstays of any type of Anesthesia. A combination of sedatives, analgesics, and hypnotics are used to achieve rapid onset, potent anesthesia, and fast recovery. It is also associated with minimum adverse effects due to reduced doses. Dilatation and curettage is a routine surgery that is frequently performed in obstetrics and gynaecology as a daycare procedure [1]. Day-care surgery is cost effective and removes economic burden from hospital resources. At present combination of sedatives, hypnotics and analgesics are used in anesthesia for minimally invasive procedures [2, 3]. Propofol is regarded as an effective anesthetic drug for short-duration procedures and ambulatory surgeries because of its quick onset and fast recovery [4, 5]. Due to minimal analgesic properties, propofol is often combined with opioids like fentanyl, morphine, or nalbuphine. Opioids are notorious for undesirable respiratory outcomes which are often related to depression of central nervous system [6]. Propofol may cause bradycardia and hypotension in addition to

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respiratory depression [7]. Propofol is a well-studied anesthetic agent in short surgical procedures but cannot be used as only an anesthetic agent. Ketamine has historical use in dilatation and curettage. It provides dissociative anesthesia with properties of fast onset, potent analgesia, sedation, and hypnosis. Propofol is strengthened with analgesic properties of ketamine instead of opioids due to the lack of respiratory compromise by ketamine. A combination of ketamine and propofol is a suitable option in gynecological procedures of short duration [8]. Dexmedetomidine is more selective alpha-2 receptor adrenergic agonist as compared to clonidine, with properties of analgesia, amnesia, sympatholysis and sedation [9]. It provides cardiovascular stability [10], without any significant respiratory depression [11]. Moreover, its sedative properties are unique due to mild cognitive impairment [12]. It can be used for conscious sedation [13, 14]. It is also useful in getting discharged earlier from post-anesthesia recovery unit [15]. The foremost advantage of dexmedetomidine on propofol is that it is not associated with suppression of spontaneous breathing and airway reflexes or fall of systolic blood pressures. Combination of dexmedetomidine with ketamine not only limits psychological side effects of ketamine like hallucinations but also avoids potential harmful effects of dexmedetomidine on heart rate like bradycardia So, the use of ketamine with dexmedetomidine appears to be a superior choice for dilatation and curettage [16, 17]. Though the efficacy of propofol, ketamine and dexmedetomidine are compared in many studies but use of a combination of dexmedetomidine in dilatation and curettage seems to be a better combination in terms of cardiovascular stability, effective sedation, potent analgesia, and minimum time of recovery.

The main aim of this research is to study the effects on cardiovascular parameters and recovery of patients undergoing dilatation and curettage using propofol-ketamine and dexmedetomidine-ketamine combinations. There is insufficient data for the use of these combinations of anesthetic drugs in dilatation and curettage. Results of different studies comparing cardiovascular parameters and recovery characteristics of propofol and dexmedetomidine are equivocal. There is a need for further studies to elaborate properties of dexmedetomidine and propofol when used in combination with ketamine.

METHODS

It was a quasi-experimental study conducted at Dr. Faisal Masood Teaching Hospital, Sargodha. Upon approval from our Hospital Ethical Committee (IRB NO.528) and after getting informed consent from participants, 136 patients undergoing dilatation and curettage (therapeutic or diagnostic) on elective list meeting the inclusion criteria were registered in a study from operation theatre, Department of Obstetrics and Gynecology, Dr. Faisal Masood Teaching Hospital Sargodha over a period of six months from March 2021 to August 2021. Patients were divided into 2 groups, Group (P+K) or Group (D+K), with 68 patients in each group by non-probability purposive sampling. Upon arrival in operating room, patients were infused with lactated Ringer (10ml/kg). Supplemental oxygen was provided to all (both groups) by nasal cannula @4 liters /min. Group (P+K) was injected with Ketamine 0.6mg/kg diluted slow IV then in Propofol 1mg/kg IV bolus slowly over 10 min followed by titrated intravenous infusion of 75- 100micro-gram/kg/min till end of procedure. Group (D+K) received Ketamine 0.6mg/kg slow IV then Dexmedetomidine at a loading dose 1micro- gram/kg IV over 10 min then a maintenance dose of 0.4 - 0.6 micro-gram/kg/hour infusion until achievement of RSS 4 (Ramsay sedation score). If the surgeon or patient was uncomfortable, the rate of infusion was increased and ketamine 20mg IV top up bolus was given as rescue sedation. The need for rescue sedation was noted and compared in both groups. During the procedure heart rate (HR), systolic BP, and diastolic BP were recorded at 0 min, 2 min, 5 min, 10 min, and 15 min afterwards every 5 min till completion of procedure. Any intraoperative adverse event like hypoxia, hypotension, hypertension, bradycardia, or tachycardia was noted and managed. cardiovascular characteristics were measured in terms of Heart rate, Systolic BP, and Diastolic BP. This study included Pregnant and non-pregnant females who undergoing elective dilatation and curettage. Diagnostic and therapeutic dilatation and curettage in whom dilatation of cervix is required before uterine curettage. And the age between 18-55 who are hemodynamically stable. And the patients with uncontrolled diabetes mellitus, hypertension, cardiac, renal, hepatic, and endocrine disorders. Patients with BMI <18 or >35, and who do not require dilatation of cervix for uterine curettage.

Operational Definitions

Bradycardia: Heart rate less than or equal to 50 bpm or Fall of Heart rate ≤ 20% from baseline value.

Tachycardia: Heart rate greater than or equal to 110 bpm or Rise in Heart rate ≥ 20% from baseline value.

Hypotension: Decrease in Systolic and Diastolic BP ≤ 20% from baseline.

Hypertension: Increase in Systolic and Diastolic BP ≥ 20% from baseline.

Recovery characteristics were measured in terms of time to reach Modified Alderete Score of 9.

Following formula was used for calculating sample size using perioperative hemodynamic variables, mean SBP (mmHg) of 120 in Group P and mean SBP (mmHg) of 117 in Group D, taken from the reference study [3].

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$$n = \frac{(Z_{1-\beta} + Z_{1-\alpha/2})^2 (\sigma_1^2 + \sigma_2^2)}{(\mu_1 - \mu_2)}$$

(Sample Size determination in health studies version 2.0.21 WHO)
Desired Power of study = 80%
Desired Level of Significance = 5%
Mean value of systolic BP in group 1 = 120
Mean value of systolic BP in group 2 = 127
Standard Deviation of systolic BP in group 1 = 15
Standard Deviation of systolic BP in Group 2 = 14
n = Minimum Sample size for each group= 68
All patients were shifted to Post Anesthesia Recovery Unit (PACU) after the accomplishment of procedure. Modified Aldrete Scoring System (MAS) and Ramsay Sedation Score (RSS) was used as a tool to evaluate post-anesthesia recovery every 5 minutes (Table 1&2).

Table 1: MAS Score among Patients

Characteristics	Score
Breathing	
Able to Breathe Deeply	2
Dyspnea	1
Apnea	0
Circulation	
Systemic BP not Equal to 20% of Preanesthesia Level	2
Systemic BP B/W 20% and 49% of Preanesthesia Level	1
Systemic BP not Equal to 50% of Preanesthesia Level	0
Oxygen Saturation	
Maintaining O_2 Saturation > 90% at Room Air	2
Needs Inhalation to Maintain O_2 Saturation > 90%	1
O_2 Saturation < 90% Despite Supplemental Oxygen	0
Consciousness	
Fully Awake	2
Arousable	1
Not Responding	0
Mobility	
Able to Move 4 Extremities on Command	2
Able to Move 2 Extremities on Command	1
Able to Move 0 Extremities on Command	0

Table 2: Ramsay Sedation Score among Patients

Sedation Level	Score
Anxious, agitated, restless.	1
Co-operative, oriented, tranquil.	2
Responds to commands only.	3
Brisk response to light glabellar tap or loud noise	4
Sluggish response to light glabellar tap or loud noise	5
No response.	6

Patients were discharged from PACU after gaining MAS ≥ 9. The time to reach MAS score of 9 was noted in PACUS and was compared in both Groups.

RESULTS

Data were compiled and analyzed using SPSS version 23.0. The mean age of patients in group (P+K) was 30.5 ± 5.4 years and mean age of patients in group (D+K) was 31.0 ± 5.9 years. The mean BMI of patients in group (P+K) was 24.4 ± 2.6 Kg/m^2 and mean BMI of patients in group (D+K) was 24.0 ± 2.3 Kg/m^2. The mean duration of procedure of patients in group (P+K) was 24.4 ± 2.6 min and mean duration of procedure of patient in group (D+K) was 24.0 ± 2.3 min. Independent sample t test showed that mean age, mean BMI and duration of procedure between the groups were not significant. Independent sample t test was used to compare the mean difference in heart rate between both groups at 0, 2, 5, 10, 15 min and at the end of the procedure. Results indicated that the mean heart rate was higher significantly in (P+K) group as compared to (D+K) group at 5 min, 10 min, and 15 min and at the end of the procedure (Table 3).

Table 3: Comparison of the Mean Heart Rate Between both Groups

Variables	Group (P+K) Mean ± SD	Group (D+K) Mean ± SD	p- value
0 Min	88.0 ± 3.3	86.8 ± 3.3	0.092
2 Min	82.7 ± 2.7	81.9 ± 3.3	0.197
5 Min	79.0 ± 3.1	69.7 ± 3.4	<0.001
10 Min	76.0 ± 3.6	62.4 ± 3.8	<0.001
15 Min	79.4 ± 3.9	67.6 ± 3.2	<0.001
At End of Procedure	81.6 ± 4.0	70.9 ± 3.4	<0.001

Independent sample t test was used to compare the mean difference in systolic blood pressure between both groups at 0, 2, 5, 10, 15 min and at the end of the procedure. Results indicated that the systolic blood pressure was significantly higher in (D+K) group as compared to (P+K) group at 2, 5, 10, 15 min and at the end of the procedure (Table 4).

Table 4: Comparison of the Mean Systolic Blood Pressure Between both Groups

Variables	Group (P+K) Mean ± SD	Group (D+K) Mean ± SD	p- value
0 Min	130.0 ± 8.1	129.4 ± 8.7	0.610
2 Min	118.7 ± 7.2	124.8 ± 8.0	<0.001
5 Min	111.0 ± 5.8	120.7 ± 7.5	<0.001
10 Min	106.1 ± 5.6	118.0 ± 7.2	<0.001
15 Min	111.4 ± 4.7	121.1 ± 7.3	<0.001
At End of Procedure	114.5 ± 5.6	123.2 ± 7.3	<0.001

Independent sample t-test was used to compare the mean difference in diastolic blood pressure between both groups at 0, 2, 5, 10, 15 min, and the end of the procedure. Results indicated that the mean diastolic blood pressure was significantly higher in (D+K) group as compared to the (P+K) group at 2, 5, 10, 15 min and the end of the procedure (Table 5).

DOI: https://doi.org/10.54393/pjhs.v5i07.1626

Table 5: Comparison of the Mean Diastolic Blood Pressure between both Groups

Variables	Group (P+K) Mean ± SD	Group (D+K) Mean ± SD	p- value
0 Min	85.3 ± 5.8	84.5 ± 5.3	0.441
2 Min	77.0 ± 5.5	81.2 ± 5.3	<0.001
5 Min	71.5 ± 5.1	78.5 ± 5.4	<0.001
10 Min	68.0 ± 4.7	76.2 ± 5.1	<0.001
15 Min	72.0 ± 4.5	78.9 ± 4.8	<0.001
At End of Procedure	74.0 ± 4.8	80.3 ± 5.0	<0.001

Mann Whitney U test was used to compare the mean difference in oxygen saturation between both groups at 0, 2, 5, 10, 15 min and at the procedure end. Results indicated that the mean oxygen saturation was significantly higher in (D+K) group as compared to the (P+K) group at 0, 2, 5, 10, 15 min and at the end of the procedure (Table 6).

Table 6: Comparison of the Mean Oxygen Saturation between both Groups

Variables	Group (P+K) Mean ± SD	Group (D+K) Mean ± SD	p- value
0 Min	98.0 ± 0.68	97.8 ± 0.72	0.037
2 Min	92.6 ± 1.36	97.2 ± 0.73	<0.001
5 Min	88.7 ± 1.45	96.3 ± 0.82	<0.001
10 Min	93.3 ± 1.36	96.7 ± 0.91	<0.001
15 Min	94.6 ± 1.03	97.3 ± 0.80	<0.001
At End of Procedure	95.6 ± 0.65	97.6 ± 0.66	<0.001

The mean time to achieve MAS of 9 of patients in group (P+K) was 32.0 ± 2.1 min and mean time to achieve MAS of 9 of patient in group (D+K) was 41.3 ± 2.6 min (Table 5). Normality of data were assessed by Shapiro Wilk test which revealed that the data were not normally distributed. Therefore, Mann Whitney U test was used to compare the mean time to achieve MAS of 9 between the groups. Result shows that mean time to achieve MAS of 9 was significantly more in group (D+K) as compared to group (P+K) (Table 7).

Table 7: Showing Comparison of Time to Achieve MAS of 9 between both Groups

Variables	Group (P+K)	Group (D+K)	p-value
Time to achieve MAS of 9 (in minutes)	32.0 ± 2.1	41.3 ± 2.6	<0.001

DISCUSSION

In this study, there was a significant fall in heart rate in group dexmedetomidine-ketamine as compared to group propofol-ketamine group at 5 min, 10 min, 15 min. Dexmedetomidine is well known for causing bradycardia due to its more selective affinity towards α2 adrenergic receptors and vagomimetic property. Heart rate at 2 min after loading dose was comparable in both groups probably due to cardiovascular effects of ketamine. A study comparing propofol-ketamine with dexmedetomidine-ketamine sedation in DCR (dacryocystorhinostomy) found that although there was significant reduction in mean arterial pressure and heart rate from baseline in two groups but the difference of heart rate and mean arterial pressure between two groups was not significant [18]. Research work done in pediatric patients undergoing minor cardiological procedures also commends our findings. Heart rate was significantly decreased in initial readings and kept on falling till twenty-five minutes in the dexmedetomidine and ketamine group as compared to propofol and ketamine [19]. A fall of heart rate of more than 20 percent of baseline was labelled as bradycardia. 62 patients out of 68, in dexmedetomidine-ketamine group had more than twenty percent fall of heart rate from baseline while none in propofol-ketamine group experienced bradycardia. Bradycardia in dexmedeto midine-ketamine group neither caused cardiovascular instability in any patient nor demanded atropine administration. A statistically significant difference of systolic and diastolic blood pressure was found in two groups. A decrease in trend of systolic and diastolic blood pressures was found at 2 min, 5 min, 10 min, and 15 min in propofol and ketamine group. This finding of our study is contradictory to findings of that of Farrukh *et al.*, in which difference between mean arterial pressures of two groups was not significant [20]. This decrease in blood pressure was due to peripheral vasodilation caused by propofol. In propofol-ketamine group, 16 out of 68 patients had fall in systolic and diastolic blood pressure of more than 20 percent of baseline values. While in dexmedetomidine-ketamine group, none experienced hypotension. Hypotension in patients was managed with rapid administration of crystalloids and colloids in most of patients. Vasopressor bolus (phenylephrine 50-100 micro gram) was administered only in two patients. Relatively stable blood pressure readings were observed in dexmedetomidine-ketamine group throughout procedure. Study of Sethi *et al.*, showed similar results when comparing propofol and dexmedetomidine in dilatation and curettage. They reported a higher number of episodes of hypotension (52%) with propofol as compared to dexmedetomidine (8%) [3]. Patients given propofol had significantly less values of systolic BP and diastolic BP at 2 min, 5 min, 10 min and 15 min of procedure as compared to dexmedetomidine. A study conducted in hemodynamically stable ICU patients with sepsis by Benken *et al.*,. also mentioned that hypotension was pronounced with propofol as compared to dexmedetomidine (a fall of 47 mmHg versus 34 mmHg) [21]. In our study reduction in non-invasive blood pressure was not as higher because of addition of ketamine and non-critical, relatively healthy patients. However, our results differed from published work of Canopolat *et al.*, which reported that propofol-ketamine had similar hemodynamic profile (heart rate, non-invasive BP) as dexmedetomidine-ketamine in pediatric population undergoing dental procedures under

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sedation [22]. Difference in oxygen saturation recorded by pulse oximeter was found to be significant at 2 min, 5 min, 10 min, 15 min and at end of procedure. A fall in oxygen saturation was noted in propofol and ketamine group at 2 and 5 minutes which was managed by increasing flow of oxygen. None of patient went into apnea. Oxygen saturation gradually started increasing at 10, 15, and 20 minutes and till end of procedure. In comparison, dexmedetomidine-ketamine group-maintained oxygen saturation throughout procedure. Kandil and his coworkers also found that the use of ketamine and dexmedetomidine combination resulted in less fall of oxygen saturation (less than 85%) as compared to propofol group during drug induced sleep endoscopy [23]. Difference in time to attain MAS (Modified Aldrete score) of 9 was found significant between dexmedetomidine-ketamine and propofol-ketamine group (41.31 ± 2.57 vs 32 ± 2.13 min respectively). This is consistent with findings of a research that compared dexmedetomidine- ketamine and propofol-ketamine procedural sedation in gastrointestinal endoscopy for patients with hepatic disease (9 ± 1.41 min in KP group versus 19 ± 1.53 min in the KD group). The shorter mean recovery time in comparison with our study is probably due to use of different drug dosing regimens and a different criterion for recovery [24].

CONCLUSIONS

Dexmedetomidine and ketamine is an effectual substitute to propofol and ketamine in dilatation and curettage. Combination of dexmedetomidine with ketamine provides cardiovascular stability without any respiratory depression but at the cost of delayed recovery and more need for rescue sedation in comparison with propofol and ketamine combination in obstetrics and gynaecology procedures of short duration.

Authors Contribution

Conceptualization: RF, MM

Methodology: FO

Formal analysis: AR

Writing-review and editing: FQ, SA

All authors have read and agreed to the published version of the manuscript.

Conflicts of Interest

The authors declare no conflict of interest.

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