European Review for Medical and Pharmacological Sciences 2015; 19: 3522-3527

Comparison of propofol-remifentanil and propofol-ketamine combination for dilatation and currettage: a randomized double blind prospective trial

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Abstract. – OBJECTIVE: The purpose of this study was to compare the propofol-remifentanil combination and propofol-ketamine combination for Dilatation and Curettage (DC) procedure.

PATIENTS AND METHODS: This prospective, double blind, and randomized study comprised 81 female patients undergoing diagnostic DC. Patients were randomly allocated to one of two groups; propofol-remifentanil (Group PR, n= 44) or propofol-ketamine (Group PK, n= 37). The level of sedation was assessed with the Ramsay Sedation Score (RSS). The patients' RSS scores were maintained at 4-5 with an additional 0.5 mg/kg bolus dose of propofol. Heart rate (HR), mean blood pressure (MBP), peripheral oxygen saturation (SpO_2), and RSS were recorded. The Modify Aldrete Score (MAS) was used for postoperative recovery evaluation, and the time to reach MAS score of 10 was recorded. Total dose of propofol, procedure time, side effects, and satisfaction scores of patient and surgeon were also recorded.

RESULTS: The mean HR and MBP values of Group PR were lower than those of Group PK, at all recording times. Sedation levels were significantly higher in Group PK. The total dose of propofol consumed was significantly higher in Group PR. The recovery time of Group PK was significantly longer than that of Group PF ($p<0.05$). Nausea-vomiting and bradycardia were more frequent in the Group PR. There was no difference in patient and surgeon satisfaction between the two groups.

CONCLUSIONS: Ketamine-propofol combination provides better hemodynamic stability and better quality of sedation than propofol-remifentanil combination. Ketamine still seems as an advantageous and safe drug for such procedure.

Key Words:
Dilatation and curettage, Propofol, Ketamine, Remifentanil.

Introduction

Dilatation and Curettage (DC), 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 dilatation and tissue extraction[1].

Therefore, drugs that are used for this procedure, should ensure a rapid onset of action, an adequate level of sedation, analgesia, and muscle relaxation for a short period of time, as well should also provide rapid recovery. The most important objectives, in such operations, are maintaining the hemodynamic-respiratory stability and minimizing the side effects of drugs[2].

Propofol is a short-acting intravenous hypnotic, and provides rapid onset and complete recovery from anesthesia[3]. It is commonly used during brief surgical intervention. However, it has not an analgesic effect. The use of high-doses propofol may cause severe complications, such as hypotension, respiratory depression and bradicardia[4].

Combining propofol with opioids or ketamine is recommended for improving the quality of sedation and analgesia, and minimizing the potential adverse effects of drug-related events, and maintaining a stable cardiovascular and respiratory status[3,4].

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Ketamine, a neuroleptic anesthetic agent, provides excellent amnesia and analgesia without affecting spontaneous respiration[4]. On the other hand, it may cause significant adverse effects including sympathomimetic effects and vomiting when administered in sedating doses. The combination of propofol and ketamine has several benefits because of hemodynamic stability and lack of respiratory depression. It may be an appropriate option for painful procedures[5].

Remifentanil, a potent short-acting opioid, provides both analgesia and sedation[6-8]. It also ensures a rapid recovery profile due to its brief half-life. The drug may be a good option for brief and painful procedures like DC. However, remifentanil may cause nausea-vomiting, hypotension, and respiratory depression[9].

Various combinations, such as remifentanil-propofol, fentanyl-propofol, alfentanil-propofol or ketamine-propofol, were shown to provide a safe and effective hypnosis and analgesia for DC procedures[1,2,6,7].

However, there are only a limited number of studies concerning the use of ketamine, and the use of bolus-dose remifentanil for DC procedures[1,2,6].

We designed this randomized, double-blind study to evaluate the administration of remifentanil versus ketamine when combined with propofol during DC procedures. We compared hemodynamic effects, propofol consumption, sedation scores, recovery time, side effects, and the satisfaction of the patients as well as the surgeon. To our knowledge, the present study is the first that compares the use of remifentanil bolus doses with ketamine for the DC procedure.

Patients and Methods

This double-blind, prospective randomized trial was performed after approval of the Ethic Committee. This study was conducted at the Department of Anesthesiology and Obstetrics and Gynecology, Zekai Tahir Burak Training and Reaserch Hospital, Ankara, Turkey, from November 2009 to August 2010.

Eighty-one, American Society of Anesthesiologist Physical Status Classification I or II (ASA) patients, age between 18 and 40, subjected to DC procedure were included into the investigation.

Exclusion criteria were ASA ≥ III, BMI ≥ 35, history of allergic reaction to study drugs, chronic use of sedatives or opioid analgesics, and presence of a psychiatric disorder with chronic medical treatment, presence of liver or kidney dysfunctions, cardiac and endocrine diseases and non-cooperative patients. The participants, whose operations exceeded 15 minute, were excluded.

After informed consent form was obtained, patients were randomly divided into two groups by closed envelope method as Group PR: propofol plus remifentanil group (n = 44), and Group PK: propofol plus ketamine group (n = 37).

All patients fasted for at least 6 hours before the procedure. In the operation room, a peripheral intravenous (iv) line was provided by 18G cannula on patients, and 6-8 mL/kg/h crystalloid solition was started. Electrocardiogram, noninvasive blood pressure, and pulse oxymeter were monitored and recorded. Patients were premedicated with midazolam (0.03 mg/kg, iv) before starting the procedure, and received supplementary oxygen (6 L/min) with a facemask during the procedure.

Group PR: patients who received 1 μg/kg remifentanil over a period of 30 sec.

Group PK: patients who received 0.5 mg/kg ketamine. Then, induction was maintained with 1 mg/kg propofol in both groups.

Depth of sedation was assessed with the Ramsay Sedation Score (RSS)[10]. The patients' RSS scores were maintained at 4-5 with an additional 0.5 mg/kg bolus dose of propofol when required.

The anesthesiologist, who administered the drugs, was not included in the study. Another anesthesiologist (who was blinded to the drug allocation) evaluated the depth of sedation, and administered additional doses of propofol. Patients and surgeons were also blind to the group application.

Heart rate (HR), mean blood pressure (MBP), peripheral oxygen saturation (SpO_2), and RSS values of all patients were recorded at baseline (before the induction), 1st, 3rd, 5th, 10th and 15th minute.

During the procedures, complications and side effects such as hypotension, bradycardia, nausea and vomiting, respiratory depression were recorded, and treated as required.

Recovery time was assesed with Modified Aldrete Score (MAS) (Table I)[11]. The time from the completion of the procedure to reach MAS of 10 was recorded. Patients were transported to the recovery room.

Surgeon and patient satisfaction were rated on a scale of 1 to 4 (1=perfect, 2=good, 3=moderate, 4=bad). The surgeons' satisfaction were assessed after completion of the operation. Patients were

Table I. Modified Aldrete Score[11].

Activity	Score
Able to move 4 extremities voluntarily or on command	2
Able to move 2 extremities voluntarily or on command	1
Able to move 0 extremities voluntarily or on command	0
Respiration	
Able to breathe deeply and cought freely	2
Dyspnea or limited breathing	
Apneic	0
Consciousness	
Fully awake	2
Arousable on calling	1
Not responding	0
Circulation	
Blood pressure ±20% of preanesthetic level	2
Blood pressure ±20% to 50% of preanesthetic level	1
Blood pressure ±50% of preanesthetic level	0
O_2 Saturation	
Maintains > 92% on room air	2
Needs O_2 inhalation to maintain O_2 saturation > 90%	1
Saturation < 90% even with supplemental oxygen	0

visited 2 hours later on the floor to assess their satisfaction. The patients' and the surgeons' satisfaction scores were recorded. The additional doses of propofol and procedure times were also recorded.

Statistical Analysis

Statistical analysis was performed using SPSS for Windows, version 11.5 (SPSS, Chicago, IL, USA), p values < 0.05 were considered significant. Data are presented as mean ± standard deviation (SD). Chi-square (χ^2) test was used for categorical data. Parametric continuous variables were analyzed using the Student's t-test. Based on a previous study, a priori power analysis was performed using two-sided analysis with an (alpha) error of 0.05 and a power of 0.8 to detect a difference of 60% for recovery times. Thirty patients were calculated to be needed for each group.

Results

Eighty-one patients successfully completed this study. The demographic characteristics including age, weight, ASA status, and procedure times of two groups are shown in Table II. There was no statistical difference between groups in terms of these parameters.

The baseline recordings of HR, MBP, and SpO_2 did not differ significantly between the groups. In Group PK, HR and MBP values were similar for all recording times. However, in Group PR, MBP and HR were significantly lower at all recording times compared to baseline. These parameters of Group PR were also significantly lower than those of Group PK for all recording times. The RSS scores of Group PK were higher than those of Group PR for all recording times (p<0.05, Table III).

Table II. Demographic characteristics and procedure times of the patients.

	Group PR (n=44)	Group PK (n=37)	p
Age (year)	28.3 ± 5.9	27.8 ± 5.9	0.708
Weight (kg)	67.1 ± 12.8	65.8 ± 10.6	0.922
ASA I/II (n)	36/8	31/6	0.816
Procedure time (min)	8.15 ± 2.8	9.25 ± 3.4	0.061

Data are expressed as mean ± SD, or number of patients. There were no statistically significant differences between the groups. ASA: The American Society of Anesthesiologists.

Table III. Hemodynamic parameters and RSS values of the groups.

	Baseline	1st	3rd	5th	10th	15th
MBP						
Group PR	92.1 ± 14.0	72.9 ± 11.5+*	76.7 ± 16.1+*	74.8 ± 11.2+*	72.5 ± 10.6+*	74.1 ± 12.3+*
Group PK	91.5 ± 6.5	89.2 ± 9.9	86.3 ± 11.5	85.5 ± 8.6	87.2 ± 12.2	88.4 ± 14.6
HR						
Group PR	83.0 ± 9.8	65.7 ± 9.1+*	67.4 ± 10.9+*	69.7 ± 11.1+*	70.2 ± 9.6+*	71.9 ± 10.8+*
Group PK	80.8 ± 7.8	78.2 ± 11.6	82.5 ± 7.0	82.6 ± 9.5	79.9 ± 10.2	80.1 ± 11.4
RSS						
Group PR		4.02 ± 0.4*	3.95 ± 0.5*	3.86 ± 0.4*++	3.68 ± 0.6*	2.96 ± 0.2*
Group PK		4.62 ± 0.6	5.02 ± 0.5	4.84 ± 0.5	4.26 ± 0.6	3.85 ± 0.4

Data are means ± SD. +p<0.05, significant changes compared to baseline values in the same group. *p<0.05, significant inter-group differences.
Bpm: beats per minute. MBP: mean blood pressure (mmHg). HR: heart rat (bpm). RSS: Ramsey Sedation Score.

The total propofol consumption of Group PR was significantly higher than that of Group PK (p <0.05). The mean recovery time of Group PK was significantly longer than that of Group PR (p<0.05) (Table IV).

The prevalence of hypotension (≥ 20% decrease from the baseline value), and apnea (SpO_2 <92%) were comparable in the two groups. However, the occurrence of nausea/vomiting, and bradycardia (heart rate <60 beats per minute) were higher in Group PR. For two groups, surgeons' and patients' satisfaction scores were similar (Table IV).

Discussion

The present report shows that remifentanil group had a significantly shorter recovery time than the ketamine group. However, ketamine provides more deeper sedation levels, and also ensures more stable hemodynamics. In ketamine group, the mean consumption of propofol, adverse effects such as, nausea/vomiting, and bradycardia were lower.

Ketamine produces dose-related unconsciousness and analgesia with minimal effect on the central respiratory drive while stable hemodynamics are maintained[12].

The combination of propofol and ketamine provides an adequate sedation and analgesia for brief painful procedures, and it has been used in various departments[13-15].

There are only a limited number of investigation concerning the use of propofol-ketamine for sedation in gynecological procedures[1,2].

Sahin et al[2] compared alfentanil (10 μg/kg) and ketamine (0.5 mg/kg) in combination with propofol (0.7 mg/kg) for DC procedures, and found the mean consumption of propofol was higher, and the orientation time was longer in ketamine group than in the alfentanil group. In the

Table IV. Side effects, total propofol consumption, recovery times, surgeon and patient satisfaction scores.

	Group PR (n=44)	Group PK (n=37)
Bradycardia	8 (18.2%)*	0
Hypotension	2 (4.5%)	0
Nausea/vomiting	1/6 (15.9%)*	1/0 (2.7%)
Apnea	2 (4.5%)	0
Surgeon satisfaction score	3.15 ± 0.8	3.95 ± 1.0
Patient satisfaction score	3.32 ± 0.8	3.65 ± 0.9
Total propofol consumption (mg) Propofol Dose (mg)	135.65 ± 40.2*	91.42 ± 23.7*
Recovery time (minutes)	10.2 ± 3.5*	17.3 ± 3.2*

Data are expressed as proportions and numbers (yes/no) or means ± SD. *Statistically significant, p<0.05.

current study, we found that the time to reach MAS score of 10 was earlier in the remifentanil group, which was consistent with Sahin et al's findings[2]. However; the mean consumption of propofol was lower in the ketamine group than that in the remifentanil group.

Akin et al[13] compared a combination of propofol and fentanyl with propofol and ketamine, in 40 adult patients undergoing endometrial biopsy. They observed that there was no difference in the recovery times, but the discharge was delayed in the ketamine group. They also reported that the frequency of patient satisfaction was 95% in the fentanyl group, and 60% in the ketamine group.

Yüce et al[1] reported that propofol-ketamine combination is associated with shorter orientation times than propofol alone, with similar hemodynamic stability without any important side effects in DC anesthesia.

Remifentanil is a new and short-acting drug with a half life of 9-11 minutes, and provides a fast recovery profile. The use of bolus-dose remifentanil may be an appropriate option for analgesia during short painful procedures like DC[6].

In gynecologic settings, Castillo et al[7] compared different bolus doses of remifentanil in dilatation and sharp curettage.

In Oğurlu et al's study[6], propofol (2 mg/kg) combined with remifentanil (1 mcg/kg) and fentanyl (0.5 mcg/kg) were compared in DC procedures. The study demonstrated that bolus administration of remifentanil was a safe and effective alternative to fentanyl with faster recovery times. Satisfaction scores for both patients and gynecologists, and adverse effects were found to be similar between the groups.

In our work, the satisfaction scores for both patients and gynecologists were similar, consistent with Oğurlu et al's study[6]. On the other hand; adverse effects such as, bradycardia and nausea-vomiting were more frequent in remifentanil group.

Ryu et al[8] compared the efficacy of remifentanil-propofol with that of fentanyl-propofol for monitored anesthesia care during hysteroscopy. They founded that the patients in remifentanil group had lower pain scores than the patients in fentanyl group, and more stable blood pressures. However, we found remifentanil group had lower HR and MBP values during the procedure than ketamine group.

We suggest that propofol-ketamine combination provides better hemodynamic stability and quality of sedation compared with propofol-remifentanil combination. It also reduces need for additional propofol doses. Despite its excellent properties, it has a long recovery time.

The potential limitations of our study are lack of postoperative follow-up of patients in terms of side effects and the pain, and not using bispectral index monitoring.

Conclusions

Ketamine-propofol combination is superior to propofol-remifentanil combination for such procedures in terms of hemodynamic stability and lesser incidence of side effects such as, bradycardia and nausea-vomiting. Ketamine still seems as a perfect drug for such procedures. Further studies concerning the comparison of different doses of it with opioids should be planned.

Conflict of Interest

The Authors declare that they have no conflict of interests.

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