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COMPARISON OF PROPOFOL-REMIFENTANYL AND PROPOFOL-DEXMEDETOMIDINE USE IN OUTPATIENT ENDOMETRIAL BIOPSIES AND/OR CURETTAGES

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ABSTRACT

Introduction: Using single anesthetic agent in endometrial biopsy sampling and/or probe curettage (EBS and/or PC) may lead to inadequate analgesia and sedation. To achieve the adequate analgesia and sedation the single anesthetic agent doses must be increased which causes unwanted side effects. For avoiding high doses of single anesthetic agent nowadays combination with sedative agents is mostly a choice for analgesia and sedation for EBS and/or PC. **Aim:** The aim of this study is to investigate the effects of propofol + remifentanil, and propofol + dexmedetomidine combinations on the total dose of propofol to be administered during EBS and/or PC and on the pain scores after the process. Materials and Method. This randomized study was performed with 108 patients (ASA I-II-III) ranging between 18 and 70 years of age who underwent sedation/analgesia for elective . The patients were administered remifentanil (1 µg/kg) + propofol (1,5 mg/kg) in Group I, dexmedetomidine (1 µg/kg) + propofol (1,5 mg/kg) combination in Group II. All the patients' sedation levels were assessed with the Ramsey Sedation Scale (RSS). Their recovery was assessed with the Aldrete and Numerical Rating Scale Score (NRS) at 10 min intervals. Results. The total doses of propofol administered to the patients in the two groups in this study were as follows: 150 mg in Group I, and 245 mg in Group II. Conclusion: Propofol-dexmedetomidine combination is as effective as propofol-remifentanil combination but with fewer side effects for conscious sedation during EBS and/or PC sugery. It was observed that, in the patients undergoing EBS and/or PC, administration of propofol in combination with an opioid or α2 receptor agonist provided effective and reliable sedation, reduced the total dose of propofol, increased the practitioner satisfaction, decreased the pain level, and provided hemodynamic stability . Sedation Score, patients' satisfaction, surgeons' satisfaction, heart rate, mean arterial blood pressure, and oxygen saturation were recorded. Side effects such as respiratory depression, nausea, vomiting, airway obstruction, and oxygen desaturation were also recorded.

KEYWORDS: Probe curtaj - Conscious sedation - Narcotics - Adrenergic alpha2 receptor agonists.

1. INTRODUCTION

Anesthesia support during EBS and/or PC is widely accepted and it has become almost a standard practice. Since administering a single-agent during EBS and/or PC leads to inadequate sedation and analgesia and thus to excessive drug use and increases in undesirable side effects, using sedative agents in combination has become more widespread.[1,2] Although there are several studies in the literature reporting that administering propofol in combination with an opioid or dexmedetomidine leads to early awakening from sedation[3,4], the number of studies on the effects of on the propofol dose is limited.[5]

Dexmedetomidine is an α2 receptor agonist with potent sedative, anxiolytic and analgesic properities which is commonly used for intraoperative and intensive care sedation.5 The present study aims at evaluating the effects of propofol-dexmedetomidine versus propofol-remifentanil conscious sedation during awake EBS and/or PC.

2. MATERIALS AND METHODS

The permission for the study was received from the Education Planning Department of Sadikonuk Education and Research Hospital in İstanbul, Turkey. The study was performed with 108 patients (ASA I-II-III) who were scheduled to undergo elective EBS and/or PC. The participants were between the ages of 18 and 70 years Those younger than 18 and older than 70 years old; pregnant, epileptic, allergic to the medicine to be administered; taking chronic opioids, sedatives, and analgesics; having had a condition requiring emergency intervention; having undergone surgery within the last 72 hours; having psychiatric problems; and/or taking drugs affecting central nervous system (CNS) were excluded from the study.

After peripheral venous access was established in the patients to be treated in the EBS and/or PC unit, the patients had intravenous infusion of 0.9% saline and they were followed with noninvasive interventions such as blood pressure (NIBP), electrocardiogram (ECG), blood oxygen saturation, and respiratory rate monitorization. The patients who received O2 (4–6 L/min) via oxygen mask of face throughout the process were not given any premedication before the process.

The patients were randomly divided into 2 groups of 54 people each. The patients in Group I were given propofol loading dose of 1.5 mg/kg and 1 µg/kg remifentanil . The patients in Group II were administered propofol loading dose of 1.5 mg/kg and 1 µg/kg dexmetamodine intravenously (i.v) 5 min before the process. The patients in Group I and Group II were administered 40 mg of lidocaine intravenously before propofol administration in order to prevent injection pain. In order to maintain Ramsey Sedation Scale (RSS) between 3 and 4, all the patients were given 1.5 mg/kg bolus of propofol.

Data about all the patients' systolic arterial pressure (SAP), diastolic arterial pressure (DAP), mean arterial pressure (MAP), heart rate, saturation of peripheral oxygen (SpO2), RSS, and ECG were recorded at 5 min intervals.

Complications such as SpO2 level lower than 95%, hypocapnia, apnea, nausea and vomiting, hypotension, hypertension, and bradycardia observed during the process were recorded, the process was suspended, and the necessary interventions were performed.

When the RSS level was 2 after the process, the patient was taken to the recovery room. In the recovery room, Aldrete and NRS (numerical rating scale score) were assessed at 10 min intervals and the total length of stay in the recovery unit was recorded. When the Aldrete score was 9 points, the patient was transferred to the ward from the recovery room.

Statistical analyses were performed with SPSS 23. Normality assumption of data was checked using the Kolmogorov-Smirnov test. Continuous variables are presented as Median (IQR) or M ± SD, while categorical variables are presented frequency and percentage. Parametric and non-parametric data were analyzed by Independent Samples t test and Mann Whitney U respectively. The relationships between categorical variables were examined using Chi-squared test. A p value less than .05 were considered significant.

3. RESULTS

The present study included 154 patients (ASA I-II-III) who underwent EBS and/or PC.

Demographic and medical characteristics of all patients were presented in Table 1.

Table 1: Demographic and medical characteristics of all patients.

Variables	Median (IQR) or M ± SD
Age	47.00 (42.00 - 50.00)
Weight	70.00 (62.25 - 80.00)
Height	160.00 (155.00 - 165.00)
Duration of anesthesia (minutes)	10.50 (7.25 - 15.00)
Duration of operation (minutes)	8.00 (5.00 - 12.00)
Total dose of propofol (mg)	100.00 (80.00 - 110.00)
Dexsmetamodin (mcgr)	35.00 ± 7.19
Remifentanyl (mcgr)	40.00 (39.25 - 45.00)
Pulsation baseline	79.15 ± 15.23
Pulsation at 5 minutes	68.50 (64.00 - 77.00)
Pulsation at 10 minutes	70.75 ± 10.56
Pulsation at recovery room	70.00 (65.00 - 78.75)
SpO2 baseline	99.00 (98.00 - 100.00)
SpO2 at 5 minutes	99.50 (99.00 - 100.00)
SpO2 at 10 minutes	99.00 (98.00 - 100.00)
SpO2 post-treatment	99.00 (98.00 - 100.00)
SpO2 at recovery room	99.00 (98.00 - 100.00)
Systolic artery pressure baseline	135.00 (122.25 - 147.75)
Diastolic artery pressure baseline	74.00 (69.00 - 80.00)
Systolic artery pressure at 5 minutes	116.00 (107.00 - 131.75)
Diastolic artery pressure at 5 minutes	68.90 ± 10.26
Systolic artery pressure at 10 minutes	113.50 (101.00 - 128.75)
Diastolic artery pressure at 10 minutes	67.30 ± 12.10
Systolic artery pressure post-treatment	113.00 (106.00 - 126.75)
Diastolic artery pressure post-treatment	65.00 (60.00 - 74.00)
Systolic artery pressure at recovery room	113.00 (103.25 - 120.00)

Diastolic artery pressure at recovery room	70.00 (62.00 - 77.50)
RASS score	.00 (.00 - .00)
VAS at recovery room	.00 (.00 - 1.00)
Delirium	.00 (.00 - .00)
Discharge time	2.50 (2.00 - 3.00)
Use of Atropine	
No	94 (87.0%)
Yes	14 (13.0%)
Use of Parol flakon 1000 (mg)	
No	96 (88.9%)
Yes	12 (11.1%)

As seen Table 2, the weight was significantly higher in the 'Remifentanyl' group than the 'Dexsmetamodin' group (p=.014). The use of Parol flakon 1000 (mg) more frequent in the 'Remifentanyl' group than the 'Dexsmetamodin' group (p=.014). However, there were no significant differences between the 2 groups regarding to age, height and use of atropine (p > .05).

Table 2: Demographic characteristics and drug use according to groups.

	Remifentanyl (n=54)	**Dexsmetamodin (n=54)**	
	Median (IQR)	**Median (IQR)**	**p**
Age*	45.50 (42.00 - 50.00)	47.00 (41.75 - 50.00)	.580
Weight*	75.00 (64.50 - 86.50)	68.00 (60.00 - 76.00)	.014
Height*	160.00 (154.50 - 163.25)	161.00 (156.00 - 165.25)	.110
	n (%)	**n (%)**	
Use of Atropine**			1.00
No	47 (87.0%)	47 (87.0%)	
Yes	7 (13.0%)	7 (13.0%)	
Use of Parol flakon 1000 (mg)**			.014
No	44 (81.5%)	52 (96.3%)	
Yes	10 (18.5%)	2 (3.7%)	
*Mann Whitney test, **Chi square			

Table 3 shows the Median (IQR) or M ± SD of the some medical variables according to groups. The systolic artery pressure at 10 minutes (p=.012), systolic artery pressure post-treatment (p=.001), diastolic artery pressure çıkış (p=.017), systolic artery pressure at recovery room (p<.001), diastolic artery pressure at recovery room (p=.025) and VAS at recovery room (p=.043) were significantly higher in the 'Remifentanyl' group than the 'Dexsmetamodin' group. However, there were no significant differences between the 2 groups regarding to other variables (p > .05).

Table 3: Some medical characteristics according to groups.

	Remifentanyl (n=54)	**Dexsmetamodin (n=54)**	
	Median (IQR) or M ± SD	**Median (IQR) or M ± SD**	**p**
Duration of anesthesia (min.)*	11.00 (7.75 - 15.00)	10.00 (7.00 - 15.00)	.702
Duration of operation (min.)*	8.00 (5.00 - 12.50)	7.50 (5.00 - 12.00)	.703
Total dose of propofol (mg)	100.00 (80.00 - 112.50)	95.00 (80.00 - 110.00)	.516
Pulsation baseline**	80.69 ± 14.68	77.61 ± 15.75	.297
Pulsation at 5 minutes*	67.50 (63.00 - 77.00)	60.00 (58.00 - 78.50)	.013
Pulsation at 10 minutes**	72.67 ± 10.39	68.83 ± 10.48	.059
Pulsation at recovery room*	70.00 (66.00 - 80.00)	70.00 (62.00 - 77.25)	.172
SpO2 baseline*	99.00 (98.00 - 100.00)	99.00 (98.00 - 100.00)	.831
SpO2 at 5 minutes*	99.00 (98.00 - 100.00)	100.00 (99.00 - 100.00)	.536
SpO2 at 10 minutes*	99.00 (97.75 - 100.00)	100.00 (99.00 - 100.00)	.137
SpO2 post-treatment*	99.00 (97.00 - 100.00)	99.00 (98.00 - 100.00)	.105
SpO2 at recovery room*	99.00 (98.00 - 100.00)	100.00 (98.00 - 100.00)	.214
Systolic artery pressure baseline*	140.00 (123.00 - 153.50)	131.50 (122.00 - 146.25)	.150
Diastolic artery pressure baseline *	75.00 (69.00 - 83.00)	72.00 (67.00 - 77.00)	.102

Systolic artery pressure at 5 minutes*	121.50 (108.25 - 135.00)	115.00 (106.75 - 127.75)	.311
Diastolic artery pressure at 5 minutes**	69.35 ± 9.81	68.44 ± 10.76	.648
Systolic artery pressure at 10 minutes*	120.00 (105.75 - 130.00)	109.00 (100.00 - 120.00)	.012
Diastolic artery pressure at 10 minutes**	68.74 ± 13.90	65.85 ± 9.92	.217
Systolic artery pressure post-treatment*	120.00 (109.00 - 130.25)	108.50 (101.00 - 120.00)	.001
Diastolic artery pressure post-treatment*	69.00 (60.00 - 75.25)	62.50 (58.75 - 71.00)	.017
Systolic artery pressure at recovery room*	120.00 (108.00 - 130.00)	108.00 (100.00 - 116.25)	<.001
Diastolic artery pressure at recovery room*	70.00 (65.00 - 80.00)	65.50 (59.75 - 73.00)	.025
RASS score*	.00 (.00 - .00)	.00 (.00 - .00)	.993
VAS at recovery room*	.00 (.00 - 1.00)	.00 (.00 - .00)	.043
Delirium*	.00 (.00 - .00)	.00 (.00 - .00)	.317
Discharge time*	2.50 (2.00 - 3.00)	2.50 (2.00 - 3.00)	.539
*Mann Whitney test; **Independent samples t test			

4. DİSCUSSİON

In our study, we considered remifentanil as the most appropriate opioid agent because it led to maximum reduction in the pain level and in the amount of propofol to be administered and its side effects were not different from those of the others. Ince et al. divided hematooncological pediatric patients into two groups, administered remifentanil + propofol combination to the first group and propofol + fentanyl combination to the second group for sedation, and determined better sedation in the first group during early awakening.[3] Kramer et al. divided oral and dental surgery patients into two groups, administered propofol + ketamine combination to the first group and propofol + remifentanil combination to the second group for sedation, and determined more effective results in the second group.[4]

The total doses of propofol administered to the patients in this study were as follows: 180 mg in Group I, 150 mg in Group II. The group in which the highest dose of propofol was administered was Group I to which propofol was administered with dexsmetamodine. In Lee et al.'s study in which the patients underwent ERCP, the patients in the first group were administered only propofol whereas the patients in the other group were administered midazolam, fentanyl, and/or meperidine in addition to propofol. The total dose of propofol administered was significantly higher in the first group which was administered only propofol than that in the other group to which propofol was administered in combination with other agents.[5]

There was a significant difference between the pain levels of Group I and Group II. In Group II, while 38 patients had no pain, the pain level was mild in 10 patients, severe in 5 patients, and extremely severe in 1 patients. In Group I, to which remifentanil and propofol were administered, there was no pain in 44 patients, but 10 patients had mild pain. No patients reported severe or extremely severe pain. In the literature, there are studies indicating that the patients administered propofol-dexmedetomidine suffered poor pain compared to the patients administered propofol in combination with an opioid.[6] In our study too, the patients in the propofol only group suffered pain most.

Since there could be a significant decrease in oxygen saturation in patients receiving anesthesia support during curetaj procedures, 4 to 5 liters of face oxygen mask was administered to each patient as indicated in the literature.[5,7]

Under conscious sedation, patients are able to maintain protective airway reflexes and can recover quickly. Rapid recovery is an advantage not only for the patient but also for hospitals and day surgery units where rapid patient circulation is desired. Conscious sedation lays the grounds for some interventions and ensures the patient's collaboration with the physician; therefore, it is more advantageous than general anesthesia is. Reducing anxiety and creating amnesia make the patient feel more relaxed and thus ensure favorable conditions necessary for the intervention. Medication used in conscious sedation should have minimum side effects, should depress the patient's consciousness level in a controlled manner, should prevent airway reflexes from being suppressed, should not cause respiration suppression, should ensure early and high quality recovery after the process, should have inactive metabolites, and should not necessitate resedation.[8,9]

In our study too, through the administration of propofol and opioids in given doses, adequate depth of anesthesia was obtained, the comfort necessary for the process was ensured, and no problem was encountered regarding patient recovery. In our study, the modified Aldrete recovery scoring was used and no significant differences were determined between the groups. In one study, the researchers compared sevoflurane and propofol in patients who had outpatient surgery under anesthesia and reported no differences between the groups regarding the patients' early recovery and cognitive functions (remembering and telling their names, ages, dates of birth, etc.).[10]

When the side effect profiles were compared, no side effects were observed in any of the three groups. In studies conducted with propofol, the most common side effect is propofol injection pain. The incidence of pain on injection of propofol ranges between 30% and 70% in case lidocaine or fentanyl is not administered.[11] In our study, in order to prevent pain on injection of propofol,

the patients in Group I were administered 40 mg of lidocaine intravenously prior to injection of propofol, and thus the patients suffered no pain. Administration of opioids in the other two groups before the injection of propofol may have prevented the formation of injection pain.[12]

Another side effect seen in patients receiving sedation is nausea and vomiting. However, in our study, neither nausea nor vomiting was observed in any patient. Patients' not experiencing nausea and vomiting may have been due to the antiemetic properties of propofol. Amornyotin et al. used propofol as a sedation agent during ERCP and observed neither nausea nor vomiting. They also attributed this result to the antiemetic properties of propofol.[13,14]

The depth of sedation was at such a level as to maintain Ramsey Sedation Scale (RSS) between 3 and 4 which was in all patients during the process. Comparison of Ramsey scores obtained during follow-up (monitorization) indicated no significant differences between the groups. In our literature review, we could not find any other study using Ramsey Sedation scoring. Sedation was assessed using Ramsay Sedation Score 8 as follows: 1) if anxious, agitated or restless; 2) if cooperative, oriented and tranquil; 3) responsive to command only; 4) brisk response to light glabellar tap or loud auditory stimulus; 5) sluggish response to light glabellar tap or loud auditory stimulus; or 6) no response. Score (1) implies inadequate sedation. Score (2 to 4) implies acceptable sedation. Score (5) or (6) implies excessive sedation.

During ERCP, stimulation, discomfort, and pain levels may vary. Achieving an optimum level of sedation may also be hindered by patient-specific sensitivity. ERCP procedure usually takes longer and is technically more challenging than other gastrointestinal endoscopy procedures; therefore, it requires deep sedation level.[15] Depending on their own preferences and the type of anesthesia monitorization, clinicians may administer boluses at different doses.

In our study, there were no statistically significant differences between the groups in terms of the satisfaction of the gastroenterologist who performed the process. However, the gastroenterologist's satisfaction was higher in Group II than in Group I and Group III. The fact that all the interventions were performed by the same gastroenterologist who did not know what agent was administered and that the assessments were made by the same person eliminated the possibility of person-related differences. In their study of 61 patients who underwent ERCP, Mazanikov et al. administered propofol, remifentanil, and alfentanil and observed no differences between the groups in terms of patient and endoscopist satisfaction.[16]

The most significant cardiovascular effect of propofol during the induction of anesthesia is a drop in the arterial blood pressure. In our study, differences between the groups were not statistically significant either although there was a decrease in MAP, DAP, and SAP values in all the three groups after the administration of the loading dose of propofol. In their study, Gazdag et al. administered etomidate and propofol to the patients during electroconvulsive therapy and reported that MAP values decreased significantly with propofol administration.[17] In their study, Falk and Zed administered etomidate, propofol, thiopental, etomidate, and midazolam for sedation during cardioversion procedures and determined significant decreases in blood pressure levels with all the medicines except for etomidate.[18]

DEX, a new selective alpha 2-agonist, has sedative, anxiolysis, and analgesia effects. Above all else, it has the advantage of causing mild respiratory depression even at higher doses. Previous studies have reported that DEX can both decrease the incidence of desaturation and reduce the secretions.[19,20]

As a result, practitioners should avoid excessive sedation while providing adequate sedation during EBS or/and PC and try to minimize the side effects associated with excessive sedation. In line with the findings of our study, the application of propofol in combination with an opioid or α2-adrenoreceptor agonist instead of a single agent in EBS and/or PC patients provides effective and reliable sedation, reduces the total dose of propofol, increases physician satisfaction and pain. level and hemodynamic stabilization were achieved. We think that remifentanil and dexmetamodine are the most appropriate agents because they greatly reduce the severity of pain and the amount of propofol to be administered, and are not different from other agents in terms of side effects. The dexmetamodine-propofol (DP group) group had a stronger analgesic effect than the remifentanil-propofol (RP group) group, but there was more propofol consumption in the dexmetamodine group.

Conflict of Interests

All authors stated that they have no conflict of interests.

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