Comparison of the effects of remifentanil and fentanyl on awakening and hemodynamic parameters in probe curettage cases

Probe küretaj olgularında remifentanil ve fentanilin uyanma ve hemodinamik parametreler üzerine etkilerinin karşılaştırılması

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Abstract

Aim: We aimed to investigate the effects of two different opioids, fentanyl, and remifentanil, on waking parameters, hemodynamic effects, duration of stay in the post-anesthesia care unit (PACU), pain and nausea and vomiting in patients undergoing probe curettage surgery.

Methods: Sixty-six patients scheduled for probe curettage surgery were randomly divided into Fentanyl (Group F, n = 33) and Remifentanil (Group R, n = 33) groups. For induction of anesthesia, 2.5 mg/kg propofol was administered as a bolus in both groups, 2.5 mcg/kg fentanyl in Group F and 2-4 mcg/kg i.v. remifentanil in Group R. No muscle relaxant agent was used. The laryngeal mask size was selected according to the patient's body weight. For induction of anesthesia, 2.5 mg/kg propofol was administered as a bolus in both groups, 2.5 mcg/kg fentanyl in Group F, and 2-4 mcg/kg i.v. remifentanil in Group R. No muscle relaxant was used. The laryngeal mask size was selected according to the patient's body weight and the cuff pressure was adjusted to 60 cm H2O using a manometer.

Results: The demographic data of both groups were similar in our study. Extubation time was shorter in Group R. The difference between the groups was significant (p<0.001). The awakening time was also significantly shorter in Group R (p<0.001). Among the hemodynamic data, MAP values were lower in Group R at T1, T3, and T5 time intervals. HR values were significantly lower in Group R. There was a statistically significant difference between the groups in both time intervals (p: 0.014, p: 0.037)

Conclusions: In our study, remifentanil provided better hemodynamic stability, shorter extubation and awakening times, and lower incidence of nausea and vomiting than fentanyl in probe curettage cases. Therefore, we suggest that the use of remifentanil with supraglottic airway devices is a good alternative in anesthesia management.

Keywords: Awakening from anesthesia; curettage; day surgery; fentanyl; laryngeal mask airway; remifentanyl

ÖZ

Amaç: Supraglottik hava yolu cihazı ile havayolu güvenliğin sağladığımız çalışmamızda fentanil ve remifentanil gibi iki farklı opiodin probe küretaj ogularında uyanma parametreleri, hemodinamik etkiler, anestezi sonrası bakım ünitesi (PACU)' da kalış süresi, ağrı ve bulantı kusma üzerine etkilerini incelemeyi amaçladık.

Yöntemler: Probe küretaj cerrahisi planlanan 66 hasta Fentanil (Grup F, n = 33) ve Remifentanil (Grup R, n = 33) guruplarına randomize olarak dağıtıldı. Anestezi indüksiyonunda her iki grupta 2.5 mg/kg propofol i.v, Grup F' de 2.5 mcg/kg fentanil i.v, Grup R' de ise 2-4 mcg/kg i.v remifentanil bolus olarak uygulandı ve kas gevşetici bir ajan kullanılmadı. Hastanın vücut ağırlığına göre laringeal maske boyutu seçildi ve kaf basıncı bir manometre kullanılarak 60 cm H2O'ya ayarlandı. Anestezi indüksiyonunda her iki grupta 2.5 mg/kg propofol, Grup F' de 2.5 mcg/kg fentanil, Grup R' de ise 2-4 mcg/kg i.v remifentanil bolus olarak uygulandı ve kas gevşetici bir ajan kullanılmadı. Hastanın vücut ağırlığına göre laringeal maske boyutu seçildi ve kaf basıncı bir manometre kullanılarak 60 cm H2 O'ya ayarlandı.

Bulgular: Çalışmamızda her iki grubun demografik verileri benzerdi. Ekstübasyon ve uyanma süresi Grup R'de daha kısaydı. Gruplararası fark anlamlı idi (p<0,001). Hemodinamik verilerden ortalama arter basıncı (MAP) değerleri; T1, T3, T5 zaman aralığında Grup R' de daha düşüktü. Kalp atış hızı (HR) değerleri Grup R'de anlamlı olarak daha düşüktü. Her iki zaman aralığında gruplar arasında istatiksel olarak anlamlı fark vardı (p: 0,014, p: 0,037)

Sonuçlar: Çalışmamızda edilen probe küretaj olgularında remifentanilin fentanile göre daha iyi bir hemodinamik stabilite sağladığı, ekstübasyon ve uyanma sürelerini daha kısa olduğu, bulantı kusma insidansının daha az olduğu görüldü. Bu nedenle supraglottik hava yolu cihazlarıyla birlikte remifentanil kullanımının anestezi yönetiminde iyi bir alternatif olduğunu düşünmekteyiz.

Anahtar Sözcükler: Anesteziden uyanma; fentanil; günlük cerrahi; küretaj; laringeal maske havayolu; remifentanil

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INTRODUCTION

Day surgery is defined as the discharge of a patient who has undergone an interventional procedure on the same day or within 24 hours (1). Reducing the time spent in the hospital decreases wound infection, minimizes the loss of labor force and minimizes hospital costs (2). Recently, day surgery interventions have become increasingly common.

Patient groups undergoing day-case anesthesia have many comorbidities. This situation makes anesthesia management special. Postoperative pain, nausea-vomiting, and depth of sedation are important factors affecting the duration of hospitalization in surgical applications (3).

Therefore, the anesthesia method to be used in day surgery applications should provide a stable hemodynamic state, adequate depth of anesthesia, and rapid recovery (4). One of the goals of day surgery is the rapid return of patients to their daily activities (5).

Probe curettage is a surgical procedure that constitutes the most minimally invasive gynecologic intervention used in diagnosis and treatment for a long time. Probe curettage is also one of the daily surgical procedures (6).

The use of supraglottic airway devices in short-term minimal surgical procedures that do not carry the risk of regurgitation is seen as a good alternative to endotracheal intubation in probe curettage cases because it does not require the use of muscle relaxants and is less irritating to the airway. (7) .

Many anesthesia methods and anesthetic drugs have been used in anesthesia applications used in day surgery operations. There are not many studies in the literature comparing remifentanil and fentanyl in cases of probe curettage using laryngeal mask airway (LMA).

In our study in which we ensured airway safety with LMA, we aimed to investigate the effects of two different opioids such as fentanyl and remifentanil on waking parameters, hemodynamic effects, duration of stay in the post-anesthesia care unit (PACU), pain and nausea and vomiting in probe curettage cases.

MATERIAL AND METHODS

Protocol

This study was conducted in the Department of Anesthesiology and Reanimation, Inonu University, Faculty of Medicine, Turgut Özal Medical Center, with the approval of the Malatya Clinical Research Ethics Committee (date: 21.12.2022, decision no: 2022/105). The study was conducted according to CONSORT guidance (8).

Study Participants

Our study was conducted as a randomized, double-blind clinical trial. Subjects who voluntarily agreed to participate in the study were informed about the potential risks and predictable outcomes of the study. Written informed consent was then obtained. For randomization, patients were assigned to the study groups completely by chance. MedCalc, version-16 statistical software for Windows (medcalc.com.tr.) was used for this purpose. Sixty-six patients scheduled for probe curettage surgery were randomly assigned to Fentanyl (Group F, n = 33) and Remifentanil (Group R, n = 33) groups.

Patient Recruitment

ASA I-II patients aged 18-65 years who underwent probe curettage were included in our study. Patients with severe respiratory, hepatic, or renal dysfunction, neurological and psychiatric patients, history of allergy to anesthesia drugs, obese patients with body mass index (BMI) over 30, difficult airway findings (modified Mallampati class 4 or thyromental distance <65 mm), high risk of regurgitation or aspiration were excluded.

Preoperative Procedures

General anesthesia was standardized for all patients. Patients were given midazolam 0.05 - 0.1 mg/kg i.v. for premedication 20 minutes before the surgical procedure. The patients were taken to the operation room and pre-oxygenated with 100% O_2 for 5 min. Routine noninvasive blood pressure (NIBP), pulse oximetry (SpO_2), electrocardiogram (ECG), heart rate (HR), and end-tidal carbon dioxide ($EtCO_2$) monitoring were performed.

General Anesthesia

For induction of anesthesia, 2.5 mg/kg i.v propofol was administered as a bolus in both groups, 3-5 μg/kg fentanyl in Group F and 2-4 μg/kg i.v. remifentanil in Group R. No muscle relaxant agent was used. The laryngeal mask size was selected according to the pa-

Table 1. Characteristics of the groups

	Group F (Mean ± StD)	Group R (Mean ± StD)	p
Age, (year)	44,48 ± 13,38	41,81 ± 14,32	0,393
Weight, (kg)	67,06 ± 11,76	70,30 ± 10,61	0,136
ASA, n(%)			0,804
I	18 (54,5)	20 (60,6)	
II	15 (45,5)	13 (39,4)	
Mallampati, n(%)			0,621
1	19 (57,6)	17 (51,5)	
2	14 (42,4)	16 (48,5)	
Bradicardia, n(%)	1 (3,03)	2 (6,06)	0,403
Surgical duration, (min)	15,81 ± 2,78	17,21 ± 2,73	0,073
Anaesthesia duration, (min)	23,63 ± 4,52	21,96 ± 2,73	0,076
PACU duration, (min)	19,06 ± 3,82	13,03 ± 2,87	**<0,001***
Extubation duration, (min)	7,09 ± 1,37	4,81 ± 1,073	**<0,001***
Wake-up duration, (min)	6,72 ± 1,20	3,42 ± 0,83	**<0,001***

ASA: American Society of Anesthesiologists, PACU: Postanesthetic care unit, StD: Standart deviation, min: Minute, n: Number, %: Percentage

Table 2. Sedation values of the groups

	Group F n(%)	Group R n(%)	p
Sedation S5			<0,001*
1	5 (15,2)	0 (0)	
2	13 (39,4)	1 (3,0)	
3	11 (33,3)	14 (42,4)	
4	4 (12,1)	18 (54,5)	
5	0 (0)	0 (0)	
Sedation S15			<0,001*
1	0 (0)	0 (0)	
2	4 (12,1)	0 (0)	
3	9 (27,3)	2 (6,1)	
4	16 (48,5)	13 (39,4)	
5	4 (12,1)	18 (54,5)	

Sedation S5: PACU 5th minute, sedation; S15: PACU 15th minute, 1: Deep sleep; 2: Sleeping, slow response to verbal stimulation; 3: Prone to sleep; 4: Awake calm quiet; 5: Awake active .* Significant difference, min: Minute, n: Number, %: Percentage

tient's body weight and the cuff pressure was adjusted to 60 cm H_2O using a manometer.

After placement of the laryngeal mask, the position of the airway devices in both groups will be confirmed by the absence of leak sound, and chest expansion during ventilation, auscultation, and capnography.

Anesthesia maintenance was provided with 75 mcg/kg/min propofol and 50% O2/air mixture in each group, 1.5 mcg/kg/h fentanyl in Group F and 0.1-0.3 mcg/kg/min remifentanil in Group R. In both groups, the anesthesia device was set in volume-controlled mode with a tidal volume of 6-8 mL/kg and a respiratory rate of 35-45 mm Hg $EtCO_2$.

Hemodynamic parameters were recorded at the following time intervals: T0 before induction, T1 after LMA placement, T2 surgery at 5 min, T3 surgery at 10 min, T4 surgery at 15 min, T5 surgery at 25 min, and T6 surgery at 35 min. Demographic data, duration of anesthesia and surgery, recovery time, postanesthetic intensive care unit stay, pain, nausea and vomiting data were evaluated.

Postoperative Management

Patients who opened their eyes with warnings, whose spontaneous breathing was regular, respiratory rate was 14-20/min, and oxygen saturation was greater

Table 3. Pain values of the groups

	Group F n(%)	Group R n(%)	p
NRS			0,019*
0-1	12 (36,4)	7 (21,2)	
2-4	15 (45,5)	10 (30,3)	
5-7	6 (18,2)	14 (42,4)	
8-10	0 (0)	2 (6,1)	

NRS: Numerical rating scale, no pain (0-1 points), mild pain (2–4 points), moderate pain (5–6 points) and severe pain (7–10 points). * Significant difference, n: Number, %: Percentage

Table 4. PONV values of the groups

	Group F n(%)	Group R n(%)	p
PONV-5			0,110
0	12 (36,4)	20 (60,6)	
1	13 (39,4)	9 (27,3)	
2	5 (15,2)	2 (6,1)	
3	3 (9,1)	2 (6,1)	
PONV-15			**0,007***
0	16 (48,5)	28 (84,8)	
1	8 (24,2)	1 (3,0)	
2	4 (12,1)	4 (12,1)	
3	5 (15,2)	0 (0)	

PONV: Postoperative nausea and vomiting; PONV-5: Postoperative 5th minute; PONV-15: Postoperative 15'th minutes, n: Number, %: Percentage, * Significant difference

than 95% were extubated and taken to the recovery room. In the recovery unit, hemodynamically and respiratory stable patients with a Modified Aldrete score ≥ 9 were transferred to the relevant ward (9).

Outcome Measures

Anesthesia duration; the time from induction of anesthesia until extubation. Surgical time; the time from the first surgical incision until the end of the surgical procedure. Extubation time; the time from the completion of surgery and discontinuation of anesthetic drugs until extubation. Recovery time was defined as a meaningful response to simple verbal commands (open your eyes, etc.) given after extubation. Bradycardia (<50/min) was evaluated. PACU length of stay was defined as the time from admission of the patient to the recovery room to transfer to the relevant service.

Pain was assessed by a blinded anesthesiologist as postoperative pain on a numerical rating scale (NRS) (0-10 scale (0-1: mild, 2-4: moderate, 5-7: moderate, 8-10: severe). 15 mg/kg i.v. paracetamol was given as a rescue analgesic in cases with NRS ≥5.

Nausea and vomiting were assessed with a 4-point scale (0=no nausea, 1=moderate nausea, 2=severe nausea, 3= retching, vomiting or both). In cases of 'severe nausea', ondansetron 50 mcg/kg i.v. was administered as antiemetic. In our study, all outcome measures were assessed by a blinded observer.

Sample Size

While the type I error (alpha) is 0.05, the power of the test (1-beta) is 0.9, the effect size is 0.82 and the alternative hypothesis (H1) is two-way, the minimum sample size required to find a significant difference using this test should be 33 in each group and 66 in total (10). Power analysis was calculated with WSSPAS software (11).

Statistical analysis

PONV: Postoperative nausea and vomiting; PONV-5: Postoperative 5th minute; PONV-15: Postoperative

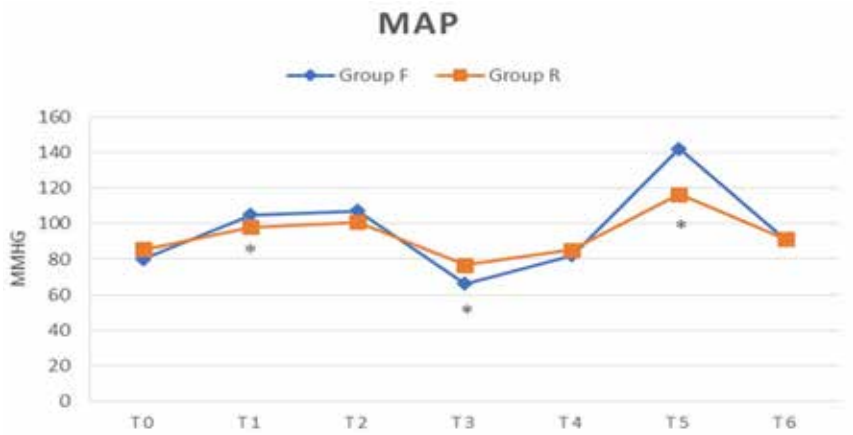

Figure 1. MAP values of the groups
MAP: Mean Arterial Pressure; T0: pre-induction; T1: after insertion of the LMA; T2: surgery 5'th min; T3: surgery 10'th min; T4: surgery 15'th min; T5: surgery 25'th min; T6: postextubation 5'th min.* Significant difference.

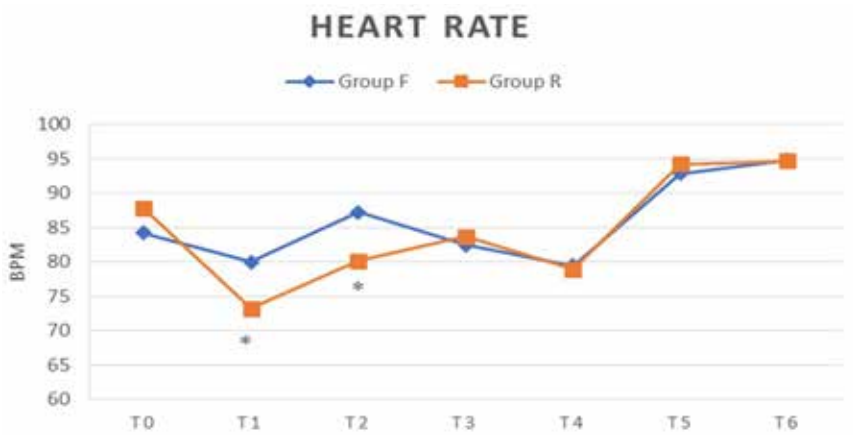

Figure 2. HR values of the groups
HR values of the groups. T0: pre-induction; T1: after insertion of the LMA; T2: surgery 5'th min; T3: surgery 10'th min; T4: surgery 15'th min; T5: surgery 25'th min; T6: postextubation 5'th min.* Significant difference, HR: Hearts rate, BPM: Beats per minute.

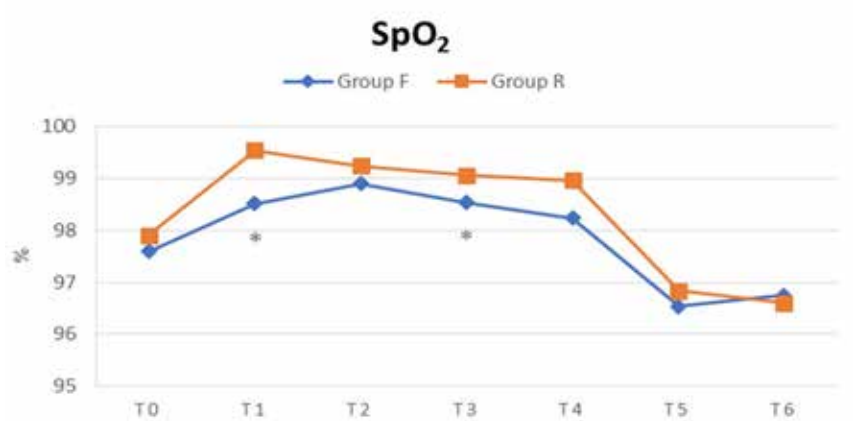

Figure 3. SpO_2 values of the groups
SpO_2: peripheral oxygen saturation; T0: pre-induction; T1: after insertion of the LMA; T2: surgery 5'th min; T3: surgery 10'th min; T4: surgery 15'th min; T5: surgery 25'th min; T6: postextubation 5'th min.* Significant difference.

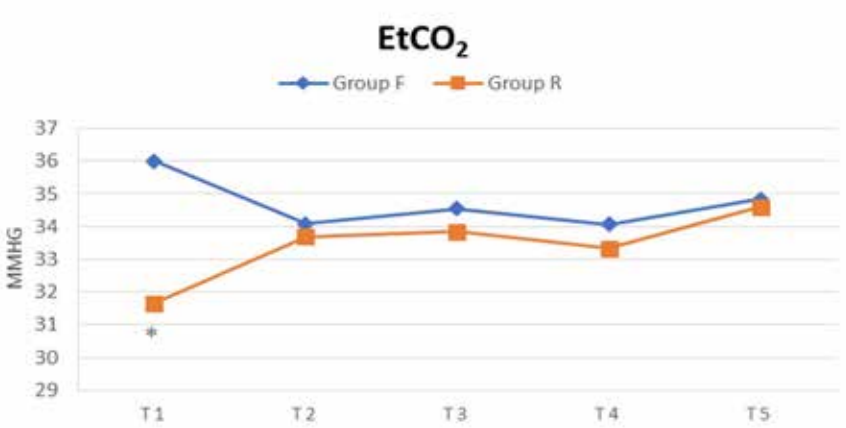

Figure 4. $EtCO_2$ values of the groups
$EtCO_2$: end-tidal carbon dioxide; T1: after insertion of the LMA; T2: surgery 5'th min; T3: surgery 10'th min; T4: surgery 15'th min; T5: surgery 25'th min; T6: postextubation 5'th min.* Significant difference.

15'th minutes, n: Number, %: Percentage, * Significant difference Shapiro-Wilk test, histogram distribution, and skewness-kurtosis parameters were used for normality analysis. Descriptive statistics are shown as mean ± standard deviation for variables with normal distribution, median (min-max) for variables with non-normal distribution, and the number of cases and (%) for nominal variables. The Chi-square and Fisher Exact tests were used to analyze the relationship between categorical variables. In evaluating the relationship between continuous variables, the Mann-Whitney U test was used if the variables were non-parametric, and Student's t-test was used if they were parametric. A p-value less than 0.05 was considered statistically significant.

RESULTS

The mean age of the patients in our study was 44.48 ± 13.38 years in Group F and 41.81 ± 14.32 years in group R. There was no significant difference between the groups (p>0,05). Weight, ASA and mallampati scores were similar between the groups and there was no statistically significant difference (p>0,05) . Bradycardia was observed in 1 patient in group F and 2 patients in Group R. The difference between the groups was not statistically significant. The duration of PACU stay was shorter in group R. The difference between the groups was statistically significant (p<0.001). Extubation time was shorter in Group R. The difference between the groups was significant (p<0.001). The awakening time was also significantly shorter in Group R (p<0.001). Demographic characteristics in our study are presented in Table 1.

Among the hemodynamic data, MAP values were lower in Group R at T1, T3 and T5 time intervals. There was a statistically significant difference between the groups (p: 0.024, p: 0.008, p: 0.006). There was no statistically significant difference between the groups at other time intervals (p>0,05) (Figure 1).

When HR values were analyzed, HR values were significantly lower in Group R at T1 and T2 time intervals. There was a statistically significant difference between the groups at both time intervals (p: 0.014, p: 0.037) (Figure 2).

When sedation values were measured at the 5th and 15th minute in PACU, sedation scores were higher in Group R at both time intervals. The difference between the groups was statistically more significant (p<0.001, p<0.001) (Table 2).

Postoperative pain scores were lower in Group F than in Group R when evaluated by NRS at 15 min in PACU. This difference was statistically significant (p: 0.019) (Table 3).

There was a statistically significant difference in SpO_2 values at T1 and T2 time intervals. There was no significant difference at other time intervals. EtCO2 values were significantly different between the groups

at T1. There was no significant statistical difference between the groups at other time intervals (Figure 3).

When postoperative nausea and vomiting scores were compared, there was no statistically significant difference in both groups at 5 minutes (p: 0.110). In the comparison of the other time interval of 15 minutes, the PONV values were lower in Group R. There was a statistically significant difference between the groups (p: 0.007).

DISCUSSION AND CONCLUSION

In this study, in which we applied TIVA, in daily probe curettage interventions using LMA We compared the effects of two different opioids (fentanyl and remifentanil) on hemodynamic data, awakening parameters, nausea, vomiting and pain. Extubation time and awakening time were significantly shorter in group R. Among hemodynamic parameters, MAP and HR values were more stable and lower at certain time intervals.

In PACU; pain intensity in NRS assessment was less in Group F. In PACU, nausea and vomiting were less in Group R in PONV-15th minute evaluation. The difference between the groups was statistically significant.

It is known that most of the surgical interventions are actually suitable cases for day surgery. Probe curettage cases are also considered in this group (12). In this study, we aimed to investigate important variables such as anesthesia awakening parameters of two different opioids and postoperative PACU stay time in probe curettage cases in which LMA was used for airway management.

Early discharge has many advantages in patients undergoing day surgery, and reduces the risk of infection, increases bed availability in hospitals and decreases the cost of treatment per patient (13).

Supraglottic airway devices are increasingly used as an alternative to endotracheal intubation in airway management in short-term day surgery applications requiring general anesthesia because they do not require the use of muscle relaxant agents, can be easily applied without the need for laryngoscopy which causes sympathetic discharge, cause less traumatic damage, provide better stability in hemodynamic data, less airway complications and provide better comfort in the postoperative period (14,15).

During endotracheal intubation, activation develops in the sympathoadrenal system due to supraglottic stimulation, and this leads to catecholamine discharge. This leads to unwanted increases in intracranial and intraocular pressure, especially arterial hypertension and tachycardia (16).

Tachycardia developing during the placement of supraglottic airway devices is one of the important hemodynamic parameters. This situation is especially important in terms of complications that may occur in patients with cardiac pathologies.

In a study by Zhang L. et al. comparing propofol-fentanyl and propofol-remifentanil combination for anesthesia in gastrointestinal endoscopy cases, HR values were lower in the remifentanil group (17). In another study comparing the effects of remifentanil and fentanyl on hemodynamic data, HR values were statistically significantly lower in the remifentanil group at all time intervals evaluated (18). In our study, in accordance with the literature, statistically significantly less tachycardia was observed in patients in whom remifentanil was used in the early period compared to patients in whom fentanyl was used.

Avoiding hypertensive episodes in airway management is critical in terms of morbidity. Suppression of hemodynamic response during intubation is one of the important parameters of a successful induction of anesthesia. In a study investigating cardiovascular response to intubation, MAP values were statistically significantly lower in the remifentanil group than in the fentanyl group at all time intervals determined, especially after induction (18). In our study, MAP values were similarly more stable in group R. MAP values were lower in group R at T1, T3 and T5 time intervals. There was no statistically significant difference between the groups at other time intervals.

Remifentanil has vagotonic and sympatholytic effects like other narcotics. radicardia is the most common side effect. Remifentanil is hydrolyzed by blood and tissue esterases independent of the liver and kidney. Therefore, it does not accumulate in tissues and its effect disappears rapidly (19).

Oğurlu M. et al. reported bradycardia in 4 (11.1%) patients in the remifentanil group and in 3 (8.3%) patients in the fentanyl group in probe curettage cases

(20). In our study, bradycardia was observed in 1 (3.03%) patient in group F and in 2 (6.06%) patients in group R. There was no statistically significant difference between the two groups.

Faster recovery time from anesthesia, earlier response to verbal commands and less time in the PACU are the desired outcomes in daily procedures such as probe curettage.

In a study comparing the effects of remifentanil and fentanyl in dilated curettage cases, the time to wake up, orientation and response to verbal commands after extubation was significantly shorter in the remifentanil group than in the fentanyl group (20).

In another study, in invasive hemato-oncologic procedures in which the efficacy of fentanyl and remifentanil were evaluated, it was shown that the time to open the eye with verbal stimuli and recovery time was statistically significantly shorter in the propofol-remifentanil group (21). In our study, extubation time, awakening time and PACU stay time were significantly shorter in the remifentanil group, consistent with the literature.

Postoperative nausea and vomiting are one of the most important complications in day surgery under general anesthesia, especially in gynecologic operations. In our study, the incidence of nausea and vomiting at 5-15 minutes in PACU was evaluated. While there was no significant difference in the incidence of nausea and vomiting in both groups at 5 minutes in PACU, nausea and vomiting was statistically significantly higher in the fentanyl group at 15 minutes. The effect of fentanyl lasts for 0.5 to 2 hours, depending on the dose. Remifentanil half-life is 3-6 minutes and terminal elimination half-life is 10-20 minutes (22). In this study, there was no statistical difference between the two agents in the evaluation of nausea and vomiting in the postoperative 6-24th hours. We think that late evaluation was effective in the formation of this picture (23).

Pain is one of the parameters affecting the length of hospital stay and patient comfort in patients undergoing day surgery. Analgesic properties of the agents used should be well evaluated (24). In a study comparing the effects of fentanyl and remifentanil in probe curettage cases, there was no significant difference in NRS values in the early postoperative period (5th min). However, NRS values were significantly higher in the remifentanil group at the 10th minute (25). In our study, pain intensity was found to be statistically higher in Group R at the NRS 15th-minute assessment. We think that the longer half-life of fentanyl was effective in the lower pain intensity in Group F in late pain scores.

In our study, remifentanil provided better hemodynamic stability, shorter extubation and awakening times, and lower incidence of nausea and vomiting than fentanyl in probe curettage cases accepted as day surgery. Therefore, we think that the use of remifentanil with supraglottic airway devices is a good alternative in anesthesia management.

Conflict-of-Interest and Financial Disclosure

The author declares that he has no conflict of interest to disclose. The author also declares that he did not receive any financial support for the study.

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