

## RESEARCH ARTICLE

# Comparison of The Effects of Remifentanyl and Fentanyl Combined with Desflurane on Intraoperative Hemodynamic Parameters and Postoperative Recovery Period in Anesthesia for Day Case Surgery

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## Abstract

**Objective:** We aimed to compare the effects of two different opioids, fentanyl and remifentanyl with short-acting inhalation agent, desflurane on intraoperative hemodynamics and recovery quality in the postoperative period in anesthesia for day case surgery.

**Methods:** A prospective randomized case control study was carried out at Anesthesia and Reanimation Clinics of The Istanbul Education and Research Hospital with the approval of the local ethics committee between 2001-2002. The study population (n=100) who has arthroscopic knee surgery was composed of patients between the ages of 18-65 classified as ASA-II. The cases were randomized and divided into two groups. After giving fentanyl to patients in the first group and remifentanyl infusion to patients in the second group, induction has administered by propofol and mivacurium was given as a muscle relaxant in both groups. After endotracheal intubation, systemic blood pressure, heart rate and peripheral oxygen saturation (SpO<sub>2</sub>) values were recorded every five minutes. When the surgery was completed, eye opening, following commands, saying her name, saying her birthday, sitting without help and getting the correct answer to the DSS test was recorded for both groups. Visual Pain Scale (VAS) and Modified Aldrete Score were evaluated and recorded at 0, 15, 30, and 60 minutes. Patients were observed and recorded in terms of side effects such as increased secretion, bradycardia, nausea, vomiting, dizziness, headache, and tremors in both groups.

**Results:** In terms of demographic features there was no statistically significant difference between the two groups. Generally, systemic blood pressures were significantly higher in the fentanyl group. Heart rate was significantly higher in fentanyl group during intubation and intraoperative periods. There was no statistically significant difference between groups in terms of SpO<sub>2</sub>. Time until spontaneous breathing, extubating, eye opening, following commands, saying the name, DSST and unassisted sitting were significantly longer in the fentanyl group. The mean values of VAS scores at the 15th and 30th minutes were significantly higher in the remifentanyl group. Similarly, the mean Aldrete recovery scale scores at 15th and 30th minutes were significantly higher in the remifentanyl group. When postoperative pathological findings were evaluated, the frequency of bradycardia was significantly higher in the remifentanyl group, there was no difference in terms of other side effects.

**Conclusion** According to the our study results; we concluded that it is a better alternative to use remifentanyl together with desflurane which is preferred short-acting inhalation agent in ambulatory anesthesia; in terms of hemodynamic stability during the intubation, peroperative and extubation periods and rapid postoperative recovery.

**Key words:** Remifentanyl, Fentanyl, Day Case Surgery, Recovery, VAS, Aldrete

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**Introduction**

Ambulatory anesthesia includes admission of the patient to the hospital, surgery, recovery period and delivery to the home. The frequency of ambulatory anesthesia has increased from 10% to 55% since the 1980s, and at least 17% has been applied under polyclinic conditions (American Hospital Association,2014). Day case surgery procedures are increasingly preferred in eligible patients due to lower costs, reducing length of hospital stay and shortening of waiting patient lists (Lapetina EM and Armstrong, 2002, Vila H et al. 2003, Coldiron B et al. 2004, Clayman MA et al. 2006). In addition to that, the increase of the role of anesthesiologists during the perioperative process, beginning to use of many short-acting anesthetic drugs, and increased use of minimal invasive surgical techniques are the other reasons. The presence of fast and short-acting anesthetic, analgesic and muscle relaxant agents allows many surgical interventions to be performed daily, thanks to this recovery will be easier and faster (Lapetina EM and Armstrong, 2002; Coldiron B et al. 2004; Shapiro et al,2014; Hüppe et al,2018; Barbier et al, 2019;). Propofol, which is one of the most preferred intravenous agents in ambulatory anesthesia induction, is one of the most suitable choices since it provides very fast recovery due to its short elimination half-life and early redistribution (Doze et al,1998). Since it isn't preferred to antagonize muscle relaxants, today the most popular agent in this respect is mivacurium, whose half-life is quite short, like 10-20 minutes (Cook et al,1989; Viby-Mogensen et al, 1995). Desflurane, one of the inhalation agents that frequently used in maintenance; by reason of its rapid induction and recovery and ensuring cardiovascular stability, it has become more often and widely used than other agents (White et al,2009). Remifentanyl and fentanyl which have rapid onset of action are widespread used as a narcotic agent, titratable, metabolised by non-

specific esterases. Like other opioids, they can cause dose-dependent analgesia, respiratory depression, and muscle stiffness (Glass,1995; Mulas et al,1998). Recent years, many researches have been conducted to find the most appropriate combination among agents that have rapid onset of action, short recovery time and few side effects, provides amnesia and analgesia (Doris and Frances, 1999; Peacock,1999; Mulas et al,1998; Joo, 2000; Gelb AW et all, 2018). In our study, we used propofol as a hypnotic agent, mivacurium as a muscle relaxant, and desflurane in maintenance for ambulatory anesthesia of patients who have arthroscopic knee surgery. By comparing the effects of two different opioids, fentanyl and remifentanil with short-acting inhalation agent, desflurane on intraoperative hemodynamics and recovery quality in the postoperative period, we aimed to reveal whether they have superiority to each other.

**Methods**

A prospective randomized study planned as a thesis was carried out at Istanbul Education and Research Hospital with the approval of the local ethics committee between 2001-2002. 100 patients between the ages of 18-65, classified as American Society of Anesthesiologists Classification (ASA)I-II, who has arthroscopic knee surgery were included in the study. The patients were informed about the procedures to be performed before the operation; their approvals were obtained. Vascular access was obtained from the forearm veins with 22 Gauge (G) intravenous (iv) cannula. Crystalloid infusion with the dose of 2 ml / kg / hour was started. Before induction, for the digit symbol substitution (DSS) test, we were informed that we would give a verbal warning such as a sentence or word, and that we would want it to repeat after the operation. No medication was used for premedication. Then DSS test was conducted to all patients. The cases were randomized and divided into two groups. After giving 1 microgram / kilogram ( $\mu\text{g} / \text{kg}$ ) fentanyl to patients in the first group, we preoxygenated patients with a mask for 3 minutes. In the second group of patients, subsequent to remifentanil  $1\mu\text{g} / \text{kg}$  bolus,  $0.25\mu\text{g} / \text{kg} / \text{min}$  infusion was started. Induction has administered by 2 milligrams / kilogram ( $\text{mg} / \text{kg}$ ) propofol in both groups. As a muscle relaxant, mivacurium was given in two steps, as priming dose before propofol,  $0.15\text{mg} / \text{kg}$  and then  $0.10\text{mg} / \text{kg}$ . After ventilating with a mask for 2.5 minutes, endotracheal intubation was performed. After endotracheal intubation, maintenance was supplied with 50% Nitroprotoxide (N<sub>2</sub>O) + 50% oxygen and

4% desflurane and mechanical ventilation was initiated. Systemic blood pressure (systolic, diastolic, mean), heart rate and peripheral oxygen saturation (SpO<sub>2</sub>) values were recorded every five minutes. An additional dose of 0.5 µg / kg fentanyl was administered to the patients in group 1, whose operation lasted more than 30 minutes. Remifentanyl infusion rate was reduced to 0.05 µg / kg / min after the 30th minute in patients in group 2. When the surgery was completed, remifentanyl infusion was terminated and desflurane was reduced to 2%. Desflurane inhalation was stopped after skin suturization. Then N<sub>2</sub>O was ceased and switched to 100% oxygen. Duration of anesthesia was defined as the time from the moment of induction until the desflurane was ceased; the duration of the surgery was defined as from the moment of skin incision to removal of the trocars. The time from cessation of desflurane to extubation, eye opening, following commands, saying her name, saying her birthday, sitting without help and getting the correct answer to the DSS test were recorded for both groups. Visual Pain Scale (VAS) and Modified Aldrete Score were evaluated and recorded at 0, 15, 30, and 60 minutes (Aldrete,1995; Katz and Melzack,1999). Patients were observed and recorded in terms of side effects such as increased secretion, bradycardia, nausea, vomiting, dizziness, headache, and tremors in both groups.

**Statistical Analyses**

SPSS 10.0 software (IBM, SPSS 10.0; Chicago, Illinois, USA) was used in the analysis. The mean, standard deviation, median minimum, median maximum, frequency and ratio values were used as descriptive statistics of the data. The distribution of variables was checked with the Kolmogorov–Smirnov test. The t-test and the Mann–Whitney U-test were used in the analysis of quantitative data for independent samples. The demographic data and intraoperative variables such as duration of surgery, between the two groups were analyzed using the Student’s t -test for continuous variables. Chi-squared test was used for categorical variables and the analysis of qualitative data. Hemodynamic parameters and scores at a particular point of time between two groups were compared, using unpaired t -test. p- value < 0.05 was regarded as statistically significant.

**Results**

Our study was planned as a randomized controlled study. In all, 100 patients between the ages of 18-65, classified as ASA I-II, had arthroscopic knee surgery in Istanbul Education Hospital between 2001-2002, were included in the study with the approval of the ethics committee. The mean age of the patients was 41.11. In terms of demographic features like age, average height and weight, gender, duration of anesthesia and surgery; there was no statistically significant difference between the two groups. (p> 0.05) (Table 1).

**Table 1.** Comparison of demographic characteristics of the study groups.

	REMIFENTANYL		FENTANYL		p value
	Mean	SD	Mean	SD	
Age <sup>a</sup>	41.72	11.86	40.50	12.99	.625
Weight <sup>a</sup>	75.98	11.71	74.68	10.84	.566
Length <sup>a</sup>	170.30	7.98	167.40	8.31	.078
Duration of anesthesia (min) <sup>a</sup>	34.18	6.10	35.24	7.90	.428
Duration of surgery (min) <sup>a</sup>	24.18	4.94	25.28	7.38	.347
	<b>n</b>	<b>%</b>	<b>n</b>	<b>%</b>	
Gender <sup>b</sup>					.147
Women	15	30	28	56	
Men	35	70	22	44	

<sup>a</sup> Student t-test and <sup>b</sup> Chi-square, \* statistically significant p<0.05

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**Table 2:** Hemodynamic parameters during outpatient anesthesia

	REMIFENTANYL		FENTANYL		p value
	Mean	SD	Mean	SD	
<b>SBP(mmHg)</b>					
Preoperative	143.26	15.83	148.12	18.14	.157
Induction	116.26	14.45	119.08	15.09	.342
Intubation	136.24	17.96	<b>145.42</b>	<b>22.04</b>	<b>.025*</b>
Intraoperative	111.62	11.15	<b>124.41</b>	<b>13.29</b>	<b>.000*</b>
Pre-extubation	129.74	13.79	<b>139.84</b>	<b>17.42</b>	<b>.002*</b>
Post-extubation	143.70	13.61	<b>151.42</b>	<b>18.60</b>	<b>.020*</b>
Postoperative 15 minute	139.82	13.03	143.06	15.49	.260
Postoperative 30 minute	138.20	11.62	137.70	16.08	.859
Postoperative 60 minute	137.06	12.04	138.78	16.26	.549
<b>DBP (mmHg)</b>					
Preoperative	82.28	10.97	86.00	13.40	.132
Induction	65.70	10.50	69.58	12.62	.098
Intubation	78.90	12.71	<b>85.66</b>	<b>15.80</b>	<b>.020*</b>
Intraoperative	63.30	9.00	<b>71.77</b>	<b>11.95</b>	<b>.000*</b>
Pre-extubation	73.42	11.19	<b>79.44</b>	<b>15.61</b>	<b>.029*</b>
Post-extubation	83.04	11.51	87.40	14.05	.093
Postoperative 15 minute	79.60	9.76	81.28	12.36	.453
Postoperative 30 minute	76.22	9.92	<b>80.48</b>	<b>11.35</b>	<b>.048*</b>
Postoperative 60 minute	75.64	10.62	<b>80.46</b>	<b>12.09</b>	<b>.037*</b>
<b>MBP (mmHg)</b>					
Preoperative	105.37	14.95	108.78	15.54	.268
Induction	86.16	12.33	87.68	12.54	.543
Intubation	99.58	14.23	<b>108.90</b>	<b>18.91</b>	<b>.006*</b>
Intraoperative	82.46	12.02	<b>93.50</b>	<b>14.29</b>	<b>.000*</b>
Pre-extubation	95.54	14.96	101.92	18.84	.065
Post-extubation	104.98	12.89	<b>113.30</b>	<b>17.48</b>	<b>.008*</b>
Postoperative 15 minute	99.72	9.44	102.38	12.80	.240
Postoperative 30 minute	96.42	9.35	99.64	12.19	.142
Postoperative 60 minute	95.06	10.25	<b>99.58</b>	<b>12.29</b>	<b>.049*</b>
<b>HR/min</b>					
Preoperative	84.62	12.34	89.20	12.11	.064
Induction	76.78	10.69	79.34	11.74	.257
Intubation	85.26	11.73	<b>90.84</b>	<b>11.88</b>	<b>.020*</b>
Intraoperative	68.69	7.57	<b>73.29</b>	<b>7.81</b>	<b>.004*</b>
Pre-extubation	79.80	9.82	82.40	9.46	.181
Post-extubation	92.08	10.03	93.00	10.76	.659
Postoperative 15 minute	85.06	7.05	86.78	10.69	.345
Postoperative 30 minute	82.54	6.14	84.54	8.79	.190
Postoperative 60 minute	80.94	5.99	82.90	9.98	.237
<b>SP02 (%)</b>					
Preoperative	97.40	1.17	96.14	4.20	.370
Induction	98.50	1.08	98.43	1.16	.880
Intubation	99.20	1.03	99.29	1.07	.846
Intraoperative	99.46	.74	99.42	.86	.913
Pre-extubation	99.50	.71	99.46	.88	.911
Post-extubation	98.00	.82	98.54	1.27	.256
Postoperative 15 minute	97.90	.57	97.92	1.26	.958
Postoperative 30 minute	97.89	.60	97.77	1.30	.800
Postoperative 60 minute	97.78	.67	97.92	1.19	.744

Student t-test, \*statistically significant p<0.05, SBP: systolic blood pressure, DBP:diastolic blood pressure, MAP: mean arterial pressure, HR: heart rate per minute, SpO2: peripheral oxygen saturation

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Systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP), Heart rate (HR), oxygen saturation (SPO2) values were recorded preoperatively, in the course of induction and intubation, every five minutes during the intraoperative period, before and after extubation, and also at the 15th, 30th and 60th minutes in the postoperative period. As presented in Table 2; during intubation, in the perioperative period, before and after extubation, mean SBP were significantly higher in the fentanyl group ( $p < 0.05$ ,  $p < 0.001$ ,  $p < 0.01$ ). There was no significant difference between the two groups at 15, 30 and 60 minutes postoperatively ( $p > 0.05$ ). Mean DBP were significantly higher in the fentanyl group in the course of intubation, during intraoperative period, before extubation, at 30 min and 60 min postoperatively ( $p < 0.05$ ,  $p < 0.001$ ,  $p < 0.01$ ). There was no statistically significant difference between the two groups at preoperatively,

at time of induction, post-extubation and postoperative 15th minutes ( $p > 0.05$ ). Mean MAP was significantly higher in the fentanyl group during intubation, intraoperatively, post-extubation and postoperative 60th minutes. ( $p < 0.05$ ,  $p < 0.001$  and  $p < 0.01$ ). There was no statistically significant difference preoperatively, at time of induction, pre-extubation, 15th and 30th minutes postoperatively ( $p > 0.05$ ). When the two groups were compared in terms of mean heart rate, there was no statistically significant difference preoperatively, at induction, before and after extubation, postoperative 15, 30 and 60 minutes ( $p > 0.05$ ). However, heart rate was significantly higher in fentanyl group during intubation and intraoperative periods ( $p < 0.05$ ,  $p < 0.001$ ,  $p < 0.01$ ). There was no statistically significant difference between groups in terms of SpO2 ( $p > 0.05$ ) (Table 2).

**Table 3:** Findings of postoperative recovery period

	REMIFENTANYL		FENTANYL		p value
	Mean	SD	Mean	SD	
Spontaneous breathing	3.57	.67	5.73	.77	.000*
Extubation	4.26	.59	7.29	1.03	.000*
Eye opening	4.37	.81	9.07	10.12	.001*
Complying with command	7.27	1.07	15.53	3.44	.000*
Answering questions	5.68	.95	10.74	2.45	.000*
DSST	6.17	.92	12.17	2.48	.000*
Unaiding sitting	12.25	1.47	24.12	5.44	.000*

Student t-test, \*statistically significant  $p < 0.05$ , DSST: digit symbol substitution test

**Table 4:** VAS score averages

	REMIFENTANYL		FENTANYL		p value
	Mean	SD	Mean	SD	
0. minute	4.10	2.31	3.68	2.07	.341
15. minute	<b>6.28</b>	<b>1.98</b>	5.08	1.98	.003*
30. minute	<b>7.14</b>	<b>1.48</b>	6.08	1.85	.002*
60. minute	6.28	1.51	6.48	1.79	.547

Student t-test, \*statistically significant  $p < 0.05$ , VAS: Visual analog scale

On the other hand, there was no statistically significant difference between the two groups in terms of mean values of systolic, diastolic, mean arterial pressure, and heart rate at time of induction, intubation, before and after extubation ( $p > 0.05$ ). However, when both groups are analyzed separately; compared with values at induction, systolic, diastolic, mean arterial pressures and heart rate values were significantly increased during intubation and before extubation, except SpO2 ( $p < 0.001$ ,  $p < 0.05$ ). SpO2 values were significantly low ( $p < 0.001$ ,  $p < 0.05$ ). As presented in Table 3, time until spontaneous breathing, extubation, eye opening, following commands, saying the name, DSST and unassisted

sitting were significantly longer in the fentanyl group ( $p < 0.001$ ). The mean values of VAS scores at the 15th and 30th minutes were significantly higher in the remifentanyl group ( $p < 0.01$ ) (Table 4). Similarly, the mean Aldrete recovery scale scores at 15th and 30th minutes were significantly higher in the remifentanyl group ( $p < 0.01$ ) (Table 5). When postoperative pathological findings were evaluated, the frequency of bradycardia was significantly higher in the remifentanyl group, there was no statistically significant difference between the two groups in terms of other side effects ( $p < 0.01$ ,  $p > 0.05$ ) (Table 6)

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**Table 5:** ALDRETE recovery scale score averages

	REMIFENTANYL		FENTANYL		P value
	Mean	SD	Mean	SD	
<b>0. minute</b>	8.36	.78	8.16	.65	.166
<b>15. minute</b>	<b>9.68</b>	<b>.51</b>	8.88	.82	.000*
<b>30. minute</b>	<b>9.88</b>	<b>.33</b>	9.54	.73	.004*
<b>60. minute</b>	9.96	.20	9.86	.35	.082

Student t-test, \*statistically significant p<0.05

**Table 6:** Pathological findings of postoperative recovery period

	REMIFENTANYL		FENTANYL		p value
	n	%	n	%	
<b>Increased secretion</b>	4	8.0	3	6.0	-
<b>Laryngospasm</b>	3	6.0	4	8.0	-
<b>Nausea</b>	1	2.0	7	14.0	0.059
<b>Vomiting</b>	0	-	0	-	-
<b>Headache</b>	3	6.0	6	12.0	0.487
<b>Dizziness</b>			3	6.0	0.242
<b>Shake</b>	1	<b>2.0</b>	1	<b>2.0</b>	-
<b>Bradycardia</b>	17	34.0	5	10.0	0.007*

Student t-test, \*statistically significant p<0.05,

### Discussion

Nowadays, the common features of the agents used in modern anesthesia practice are that their duration of action is short and therefore the anesthetic depth can be easily controlled, and they ensure the shorter and safer postoperative recovery period. With the widespread use of these agents, outpatient surgery has preferred and performed more frequently as a popular technique. We compared the effects of remifentanil and fentanyl in outpatient anesthesia. We didn't find any difference in SpO2 values between these opioids at any stage of anesthesia. However, in the fentanyl group, values of systolic, diastolic and mean blood pressures were detected higher, especially during intubation, intraoperative period, pre- and post-extubation periods, compared to remifentanil. In support of our data, some authors found SBP, DBP and MAP higher values in fentanyl group during intubation, intraoperative and extubation periods (Albertin et al,2001; Twersky et al, 2001; Lang et al, 2019). In contrast, some other authors reported that they could not find any significant difference between SBP, DBP and MAP in preoperative, peroperative and postoperative periods between administration of remifentanil 0.5 mcg /kg bolus, 0.2 mcg/kg/min infusion and fentanyl 1 mcg/kg bolus and 2mcg/kg/hour infusion (Doyle et al,2001; Choi et al, 2016 ).It was thought that these results may be due to using different dosage and way of remifentanil and fentanyl.

When HR was evaluated in our study, it was found increased in the fentanyl group compared to the remifentanil group in the intubation and

intraoperative period. Many authors were also found to similar results. In the remifentanil group, bradycardia was detected more frequently during intubation, preoperative and extubation period. When values were found below the 50 beat /min, intervened with atropine and these data were consistent with the literature (Cafiero et al,2000; Doyle et al,2001; Twersky et al, 2001; Choi et al, 2016).

When the findings of the postoperative recovery period are evaluated; in the fentanyl group, onset time of spontaneous breathing, extubation, eye opening, following commands, saying the name, DSST, and unaided sitting were found to be significantly longer. These values were found to be compatible with other remifentanil-fentanyl comparative studies (Mulas et al,1998; Doyle et al,2001, Dy et al, 2001; Grundmann et al, 2001). Similarly, some authors compared combination desflurane-remifentanil to desflurane-fentanyl; in remifentanil group, they found that onset time of spontaneous breathing, extubation, eye opening, saying the name, and following the commands are significantly shorter. They also reported that they found DSST duration significantly shorter in the remifentanil group (Wilhelm et al,2001). But the others were found no difference between them (Choi et al, 2016). While the VAS scores that we used to evaluate postoperative pain were statistically significantly higher in the remifentanil group at 15th and 30th minutes, we didn't find any significant difference at the 60th minute. In their study with 16 patients from the remifentanil and fentanyl groups, some authors reported that 7 patients in the remifentanil group and

4 patients in the fentanyl group had analgesic requirements in the early post-operative period (Doyle et al,2001). But the others found no difference VAS scores between fentanyl and remifentanil group in their studies (Haytural, 2015). On the other hand; some other authors found higher VAS scores in the fentanyl group (Monsef et al, 2019). We didn't administer additional analgesics in our study, but when the VAS scores were evaluated, it was concluded that pain control was better achieved in patients treated with fentanyl in the early period.

The average of Aldrete score used for assessment of the cooperation of the patients in remifentanil group at the 15th and 30th minutes during the recovery period were found significantly higher . At 0 and 60 minutes, the score results were similar. When the pathological findings were evaluated, 4 patients in the remifentanil group had increased secretion, 3 patients had laryngospasm, 1 patient had nausea and 3 patients had headache. Increased secretion in 3 patients, laryngospasm in 4 patients, nausea in 7 patients, and headache in 6 patients were detected in the fentanyl group. However, there was no significant difference between the two groups in terms of these parameters. These findings were consistent with the literature. Similar findings are declared between the two groups in the many studies (Mulas et al,1998; Doyle et al,2001; Haytural, 2015, Monsef et al, 2019).

### Conclusion

According to the results we obtained from our study; we concluded that it is a better alternative to use remifentanil together with desflurane which is preferred short-acting inhalation agent in ambulatory anesthesia; in terms of hemodynamic stability during the intubation, peroperative and extubation periods and rapid postoperative recovery.

**Ethics Committee Approval:** Ethics committee approval was received for this study from Clinical Research Ethics Committee of Istanbul Teaching and Research Hospital.

**Peer-review:** Externally peer-reviewed.

**Author Contributions:** Concept – M.D Design M.D; Supervision M.D; Materials – M.D; Data Collection and/or Processing – M.D; Analysis and/or Interpretation – M.D; Literature Review – M.D,E.G; Writing - M.D,E.G; Critical Review -M.D

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