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Effects of Fentanyl and Remifentanil on intraoperative hemodynamics and postoperative recovery in percutaneous nephrolithotomy cases

Fentanil ve Remifentanil'in perkütan nefrolitotomi vakalarında inraoperatif hemodinami ve postoperatif derlenmeye etkileri

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ÖZET

Amaç: Perkütan nefrolitotomi (PCNL) uygulanan hastalarda fentanil veya remifentanilin intraoperatif hemodinamik etkileri ve postoperatif derlenme üzerine etkilerini karşılaştırmak.

Gereç ve Yöntemler: Çalışmamız randomize, ve prospektif olarak yapıldı. Çalışmaya Amerikan Anestezist Derneği (ASA) I-II ile PCNL uygulanan 40 hasta dahil edildi. Uygulanan anestezi tekniği aynı olup remifentanil-fentanil ilaç kullanımına göre tüm hastalar 2 gruba ayrıldı. Her iki grupta anestezi indüksiyonu bolus dozda propofol 2mg/kg ile idame sevofluran (MAC 2) ile sağlandı. Kas gevşemesi 0,6 mg/kg rokuronyum ile elde edildi. Grup 1'e anestezi indüksiyonu sırasında tek doz halinde 1 µgr/kg remifentanil, Grup 2'ye anestezi indüksiyonu sırasında tek doz olarak fentanil 2µg/kg verildi. Hemodinamik stabiliteyi sağlamak amaçlı Grup 1'de remifentanil infüzyon şeklinde (0.05 µg/kg/dk.), grup 2'de ise 45 dk. da bir fentanil 0,5 µg/kg iv puşe verildi. İntraoperatif hemodinamik parametreler ve iyileşme verileri kaydedildi. Aldrete Skoru, Ramsay Sedasyon Skalasında 15, 60, 360. dakikalardaki değerler ameliyat sonrası kaydedildi. Ağrı değerlendirmesi için görsel analog skala (VAS0-10) kullanıldı.

Bulgular: İntraoperatif hemodinamik ölçümler Grup 1'de daha stabildi. Nitro-gliserin ihtiyacı Grup 2'de anlamlı olarak arttı (p <0,05). Aldrete skorları, Ramsay sedasyon ölçekleri ve VAS gruplar arasında anlamlı farklılık göstermedi. Derlenme Grup 1'de Grup 2'den anlamlı olarak erkendi (p<0,05).

Sonuç: PCNL sırasında fentanile kıyasla Remifentanil ile stabil hemodinamik durum ve daha güvenli iyileşme sağlanabilir.

Anahtar Kelimeler: *fentanil, perkütan nefrolitotomi, remifentanil, görsel analog skor*

This study was approved by the Ethics Committee of Ankara Türkiye Yüksek İhtisas Training and Research Hospital (Approval Number: 51. Date: November 27, 2010). All research was performed in accordance with relevant guidelines/regulations, and informed consent was obtained from all participants.

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ABSTRACT

Objective: To compare the effects of fentanyl or remifentanil on intraoperative hemodynamic effects and postoperative recovery in patients undergoing percutaneous nephrolithotomy (PCNL).

Material and Methods: Randomized, and prospective study was conducted. Forty patients who underwent PCNL with American Society of Anaesthesiologist (ASA) I-II enrolled into the study. All patients were divided into 2 groups according to administered anaesthesiology technique and drugs, which are remifentanil and fentanyl. Induction of anaesthesia was same in both groups. Induction of anesthesia was obtained with a bolus dose of propofol (1-2 mg/kg), maintenance was achieved with sevoflurane (MAC2). Muscle relaxation was achieved with rocuronium. Group 1 was consisted of patients who were administered remifentanil and they received 1 μgr/kg of remifentanil as a single dose during the induction of anaesthesia Group 2 was received fentanyl 2 μg/kg as a single dose during the induction of anaesthesia. Group 1 received remifentanil 0.05 μgr/kg per minute as an infusion throughout the procedure for providing intraoperative hemodynamic stability, in group 2 fentanyl was given at a dose of 0.5 μg/kg iv bolus every 45 minutes. Intraoperative hemodynamic parameters and recovery data were recorded. Aldrete score, Ramsay sedation scale 15, 60, 360 minutes were noted after surgery. Visual analogue scale (VAS0-10)was used for pain evaluation.

Results: Intraoperative hemodynamic measurements were more stable in Group 1. The need for nitro-glycerine was significantly increased in Group 2 ($p<0.05$). The Aldrete scores, Ramsay sedation scales and VAS did not differ significantly between the groups. Immediate recovery was significiantly earlier in Group 1 than Group 2 ($p<0.05$).

Conclusion: Stable hemodynamic status and safer recovery can be provided with remifentanil compared to fentanyl during PCNL.

Keywords: *fentanyl, percutaneous nephrolithotomy, remifentanil, visual analog score*

INTRODUCTION

Opioids are used to provide analgesia and hemodynamic stability (1). Also, they can reduce the need for intravenous and inhalation anesthetic agents. However, continuous infusion of opioids may be restrictive because of their long half-lives (t1/2), which can accumulate and be stored in the body. All these can cause depression in respiratory functions (1).

Remifentanil is a specific mu (μ) -opioid peptide (MOP) receptor agonist and is different from other opioids. It has an ester bond in its ultrastructure. Remifentanil's analgesic efficacy is comparable to fentanyl (2–4). It is fast-acting waking up feature makes it easy to use. It is quick elimination and recovery; remifentanil is often the opioid of choice (2–6).

Percutaneous nephrolithotomy (PCNL) is one of the endoscopic surgery treatment options for removing nephroliths larger than 2cm diameter and is frequently preferred in many centers (7, 8). The benefits of PCNL include low morbidity rates, short recovery periods, and reduced intraoperative bleeding (9,10). The intraoperative hemodynamic stability of patients undergoing PCNL is important and is related to postoperative success (11). Studies on anesthetic drugs that affect hemodynamic status in PCNL are weak.

This study aimed to evaluate the effects of two different opioids during anesthesia management and postoperative recovery after PCNL. We hypothesize that remifentanil can have the advantages mentioned above during PCNL with its specific opioid receptor agonist mechanism.

MATERIAL AND METHODS

This study is randomized and prospective. All patients understood the aim of the study, and signed consent forms were obtained. Our institutional review board and the ethical committee approved the study. Patients with ASA I-II that underwent PCNL were enrolled in the study. Exclusion criteria were chronic use of opioids, hypersensitivity to opioids and/or propofol/lipid emulsions, serious cardiorespiratory, metabolic, renal, hepatic, or neuropsychiatric disease, and operation time shorter than one hour or longer than two hours. All patients were divided into 2 groups as group 1 consisted of patients who received remifentanil, and group 2 consisted of patients who received fentanyl. Patients were randomly assigned to receive either remifentanil or fentanyl via the sealed assignment method.

Intravenous access was gained via an 18-20 G catheter placed antecubital or on the dorsal hand followed by isotonic sodium chloride infusion at a rate of 5-10 ml/kg/hr. Preoxygenation was accomplished by administering 100% pure oxygen with a face mask for 10 minutes.

In group 1: intravenous 1 mg/kg lidocaine, 2 mg/kg propofol, 0.6 mg/kg rocuronium and a 1µg/kg remifentanil bolus followed by an infusion at a dose of 0.05µg/kg per minute. Intraoperative hemodynamic stability was accomplished when necessary, adjusted the infusion rate.

In group 2: intravenous 1 mg/kg lidocaine, 2µg /kg fentanyl, 2 mg/kg propofol, and 0.6 mg/kg rocuronium during induction anesthesia and repeated at a dose of 0.5µg/kg every 45 minutes. Intraoperative hemodynamic stability was accomplished, when necessary, with repeated doses of fentanyl bolus intravenous injections at a dose of 0.5 µg/kg.

Following intubation, all patients adjusted ventilation settings to determine the tidal volume between 8-10 ml/kg and respiratory carbon dioxide concentration ($ETCO_2$) pressure 35-40 mmHg. Both groups' anesthesia was continued with 2% sevoflurane (MAC 2), 50% pure O2, and 50% air. 0.15 mg/kg of rocuronium was given to maintain muscle relaxation. Negative hemodynamic responses were defined as; hypertension (mean arterial pressure exceeding the preoperative value by 20%), hypotension (a decrease in the mean preoperative arterial pressure by at least 20%), tachycardia (an increase of heart rate by at least 20%), bradycardia (heart rate lower than 45 beats/minute).

Tachycardia and hypertension were initially treated with repeated opioid doses; however, if the condition was not corrected, 0.1 mg intravenous nitro-glycerine was administered. Hypotension was initially treated with intravenous fluid replacement and a decrease in the infusion rate of remifentanil in Group 1. In cases of bradycardia, the opioid infusion rate was decreased, and 0.01 mg/kg atropine was administered. The subjects' systolic arterial pressure (SAP), diastolic arterial pressure (DAP), mean arterial pressure (MAP), heart rate (HR), peripheral oxygen saturation (SpO_2), end $ETCO_2$, and additional need for opioids were recorded for both groups. These values were further classified according to the period in which they were recorded, as follows;

B1: Two minutes prior induction anesthesia, B2: During induction, B3: During intubation, B4: When percutaneous dilation was initiated, B5: Five minutes after percutaneous dilation, B10: Ten minutes after percutaneous dilation, B15: Fifteen minutes after percutaneous dilation, B30: Thirty minutes after percutaneous dilation, B45: Forty-five minutes after percutaneous dilation, B60: One hour after percutaneous dilation;

Bend: Values recorded when surgery was finalized, Bex: During extubating, Bspon: Values recorded when spontaneous respiration returned. Sevoflurane was reduced, and 75 mg of naproxen sodium was administered intramuscularly for postoperative analgesia at the beginning of the skin closure. Sevoflurane was stopped with remifentanil infusion at the last skin suture. At the end of the procedure, the remaining neuromuscular block was reversed using a mixture of atropine (1 mg) and neostigmine (2.5 mg). Patients' lungs were ventilated with 100% oxygen. Time to spontaneous ventilation, eye-opening, and extubating was recorded. Total opioid consumption was also recorded. After extubating, the patients were transferred to the post-anesthesia care unit, where hemodynamic monitoring was continued. At this point, all of the patients' Ramsey sedation scale and Modified Aldrete scores were evaluated. The pain was scored according to the Visual Analogue Score (VAS). Patients yielding a VAS score ≥4 received 50 mg pethidine i.m. Postoperative Aldrete scores, Ramsey scales, and VAS values were recorded at 15 minutes, 60 minutes, and 6 hours.

Statistical Analysis

We used Statistical Package for the Social Sciences (SPSS V.22 for Mac) for analyses. All numeric data collected from both groups were compared using the Mann-Whitney U tests, whereas the necessity for nitro-glycerine and atropine doses was compared using the Chi-square tests. The "compare–mean" test was applied to all mean measurements. The significant p was accepted as $p<0.05$.

RESULTS

In total 40 patients (Group 1, n=20; Group 2, n=20) were completed the study. The demographics were comparable between groups; however, duration of anesthesia, duration of surgery, and the total dosage of anesthetic agents administered were significantly different ($p<0.001$, $p=0.005$, and $p=0.01$, respectively) (Table 1).

Table 1. Demographic and operative data are shown.

Parameters	Group 1 (n=20)	Group 2 (n=20)	P value
Age (years)	47.1±14.1	50.95±10.4	*p=0.071*
Gender (Male/Female)	13/7	12/8	*p=0.082*
Height (cm)	168.75±9	169.5±8.1	*P=0.0854*
Weight (kg)	74.95±13.4	80.35±13.8	*p=0.063*
ASA(I/II) physical status	11/9	10/10	*p=0.078*
Anesthetic time (min.)	109.9±20.6	149.25±45.3	*p<0.001**
Surgical time (min.)	90.5±21.4	118.45±40.9	*p=0.005**
Total opioid dosage (µg)	231±77.9	183.75±42	*p=0.015**

ASA; *American Society of Anesthesiologist; *Statistically significant P value*
(*): *p<0,007* ***(#):*** *p<0,024*
(*): *p<0,009* ***(#):*** *p<0,012*
(*): *p<0,05*

When groups were compared according to SAP, significant difference was seen in that SAP measurements recorded during B3 and B30 were higher in group 2. When groups were compared with respect to diastolic arterial pressure (DAP) measurements, values noted at B3 and Bex were statistically higher in group 2 in comparison to group 1. The HR values and SpO_2 levels were similar between groups (Table2).

In group 1, nitro-glycerine was used in 3/20 patients and atropine in 1/20 patients. In group 2, intraoperative nitro-glycerine administration was required in 9 out of 20 patients, while atropine was used in 3 patients. The need for nitro-glycerine was significantly increased in group 2 ($p<0.05$) (Table 3).

The groups differed with respect to extubating times, and time lapse to eye- opening, such that these periods of time were significantly longer in group 2 when compared to group 1 (Table 4).

The Aldrete scale, Ramsey sedation scores and VAS values found to be similar between groups. Similarly, the need for additional postoperative analgesia shows no significant difference between groups.

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Table 2. Hemodynamic data are shown systolic (sap) diastolic arterial pressures (dap) heart rates (hr) and SPO_2 levels in two groups.

	B1	B2	B3	B4	B5	B10	B15	B30	B45	B60	Bson	Beks	Bspon
Group1(R) sap	159.2±28	117.3±22	128.3±33	124.4±23	117.2±18	116.5	118.9±24	112.6±12	113.6±13	114.8±16	112,4±16	142.10	137.2±19
Group2(F) sap	148.6±24	117.3±16	153.9±38 (*)	130.1±28	127.4±21	119.3±18	115.9±14	120.6±18 (#)	126.5±27	118.2±23	123.6±1	153.0± 24	137.6±16
Group1 dap	89,7± 15	69.5± 14	79.2± 18	77.8±16	74.2± 13	75.7±19	74.3± 14	71.9±11	73.7±8	71.1± 10	69.7± 11	82.3± 11	81.6± 12
Group2 dap	87.1± 12	74.2± 12	95.7± 22(*)	78.8± 13	78.8± 11	74.7± 10	73.3± 9	74.6± 12	79.0±8	73.4± 15	75.7± 9	91.9± 10(#)	81.0± 7
Group1 hr	77.9± 15	76.2± 11	89.6± 16	72.8± 15	69.3± 14	67.5± 12	67.1± 11	68.3± 13	71.1±16	67.4± 13	71.2± 12	78.8± 13	76.2± 12
Group2 hr	89.2± 17	77.8± 12	82.8±13	70.9± 16	67.9± 15	69.1± 15	65.2± 10	65.7± 12	64.9±8	66.1± 11	70.2± 12	80.1± 11	79.4± 14
Group1 spo2	97.0± 2	98.7± 1	99.0± 1	99.1± 1	98.6± 2	98.9± 1	99.1± 1	98.9± 1	99.1±1	99.2± 1	99.3± 1	97.0± 1	99.35
Group2 spo2	96.8± 2	98.3± 1	98.8± 1	98.8± 1	98.3± 1	98.3± 1	98.9± 1	98.4± 1	99.1±1	99.5± 1	98.7± 1	96.8± 1	99.4± 1

(*): p<0,007 (#): p<0,024

Table 3: Patients receiving intraoperatively

	Group 1	Group 2
Nitro -glycerine	3(0.15%)	9*(0.45%)
Atropin	1(0.05%)	3(0.15%)

(*): p=0,015

Table 4: Recovery times (minute) after atropine-neostigmine administration are summarized.

Parameter	Group 1	Group 2	*P value*
Time to extubating (min.)	4.28±1.5	6.22±1.64	*p=0.0001**
Time to eye opening (min.)	4.90±1.78	7.10±1.72	*p=0.0001**

**Statistically significant P value*

DISCUSSION

In the present study, we compared the hemodynamic and recovery effects of chancing anesthetics after PCNL. We found that remifentanil was superior to fentanyl in recovery and hemodynamic parameters after PCNL. This result can contribute to minimally invasive specialties of PCNL.

An inhaled anesthetic should be combined with an opioid for successful surgical procedures, hemodynamic stability, and a good recovery period (12). Opioids are often used to suppress the hemodynamic response to painful stimulation, provide intraoperative analgesia, decrease postoperative pain and facilitate endotracheal intubation (13,14). Fentanyl is a synthetic opiate, and remifentanil is a μ-opioid receptor agonist with potency similar to fentanyl and a systemic half-life of approximately 9 to 11 minutes, which allows rapid emergence from anesthesia even after prolonged infusions (6,15, 16).

We found significantly different SAP settings as B3 and B30 were higher in group 2 than group 1. Additionally, B3 and Bex were statistically higher in group 2 than group 1. Intraoperative requirement for nitro-glycerine was much less frequent in group 1. It shows that intraoperative is more stable hemodynamic in group 1 than group 2. Jellish et al. compared the effects of remifentanil and fentanyl on hemodynamic stability during carotid surgery, and no significant difference was observed between opioids (17). Balakrishnan et al. compared remifentanil to fentanyl in patients undergoing intracranial surgery (18). We observed similar hemodynamic profiles for both drugs. That may relate to used anesthetic drugs isoflurane, nitrous oxide, and opioids. Kostopanagiotou et al. compared the effects of fentanyl and remifentanil in patients undergoing carotid surgery; intraoperative hypertension and the requirement for nitro-glycerine were significantly higher in the fentanyl group than remifentanil group (19).

Tversky et al. confirmed the better hemodynamic control with remifentanil compared with fentanyl in a large cohort study of 2438 patients (20). Our study's findings were in the same line as the studies above. However, we evaluated the effects of drug sets after PCNL. According to our best knowledge, this is the first study on this issue in published literature.

In immediate recovery, extubating and spontaneous eye-opening was shorter in group 1 than group 2. Wilhelm et al. found shorter extubating time in the remifentanil group than fentanyl (21). Motamed et al. concluded similar results in thyroid surgeries (22). Balakrishnan et al. Found the extubating time and verbal response shorter in the remifentanil compared to the fentanyl group (18). We found a significantly shorter duration of anaesthesia and operative time in group 1 with a significantly lower total dosage of anesthetic agents. We strongly think that immediate recovery with remifentanil can be related to the time to systemic half-time of remifentanil.

Postoperative pain is a common and acute clinical finding that begins with surgical trauma, peaks for approximately 24 hours, and ends with the tissue repair process. Once it begins, it is fairly difficult to manipulate. Following major abdominal surgical procedures, moderate to severe pain may be endured. That may specifically concern patients receiving a remifentanil infusion, which can be explained by the short

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life of remifentanil and no residual analgesic effect (23). Vinik et al. hypothesized that tolerance might be developed remifentanil as with other analgesics (24). It is necessary to give long-acting analgesics 20 to 30 minutes before the group using remifentanil as an anesthetic (25). Our study incorporated the use of 75 mg intramuscular naproxen sodium. For evaluation of postoperative pain, we used the VAS. VAS values at 15, 60, and 360 minutes were similar for both groups. We found a similar need for additional postoperative analgesia in both groups. Motamed et al. used 1gr paracetamol, and they found that analgesic requirement was higher in the remifentanil group (22).Kostopanagiotou et al. used 100 mg ketoprofen prior to induction anaesthesia and nano pin infiltration before waking up from anaesthesia even after prolonged infusions, skin closure postoperative VAS scores were similar in both groups (19). Ketoprofen and nano pin infiltration may explain differences in postoperative pain. We think that the suppressive effect of naproxen sodium was suitable for reducing postoperative pain in patients that received remifentanil.

Our study had some limitations. At first, this study was a randomized, double-blind study. We could not interfere with operative time in both groups. The second one is the limited number of participants in groups. After this study, a power analysis was performed, and eye-opening and extubating times were significant (0.98).

Surgery is teamwork that surgeons and anesthesiologists play the main role during PCNL. In the present study, we concentrate on the effects of chancing anesthetics on hemodynamic and recovery after PCNL, a minimally invasive treatment option of nephrolithiasis larger than 2 cm diameters. In the light of our findings, anaesthesiologists can contribute minimally invasive effects of PCNL by administering remifentanil. Thus, more stable hemodynamic and quick recovery can be provided after PCNL.

CONCLUSION

Remifentanil ensured more stable intraoperative hemodynamic readings and a safer recovery period than fentanyl administered patients after PCNL. When the anaesthesiologists infuse at appropriate doses of remifentanil, this seems advantageous over fentanyl with respect to more stable perioperative support and postoperative recovery inters of PCNL procedures.

Conflict of Interest: The authors declare to have no conflicts of interest.

Financial Disclosure: The authors declared that this study had received no financial support.

Ethical Approval: The study was approved by the Ethics Committee of Ankara Türkiye Yüksek İstisas Training and Research Hospital (No: 51, Date: November 27, 2010). The study protocol conformed to the ethical guidelines of the Helsinki Declaration.

Author Contributions: Conception and design; Höbek Aydın Y; Öztürk Kazancı D, Data acquisition; Höbek Aydın Y; Öztürk Kazancı D, Data analysis and interpretation; Höbek Aydın Y; Öztürk Kazancı D, Drafting the manuscript; Höbek Aydın Y; Öztürk Kazancı D, Critical revision of the manuscript for scientific and factual content; Höbek Aydın Y; Öztürk Kazancı D, Statistical analysis; Höbek Aydın Y; Öztürk Kazancı D, Supervision; Höbek Aydın Y; Öztürk Kazancı D.

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