The Effect of Opioid Infusion on Stress Response in Percutaneous Nephrolithotomy

Perkütan Nefrolitotomide Opioid İnfüzyonunun Stres Yanıt Üzerine Etkisi

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ABSTRACT Objective: We aimed to investigate the effect of opioid infusion on stress response in percutaneous nephrolithotomy (PCNL). **Material and Methods:** Forty adult patients were randomly divided into two groups. Anesthesia induction was performed with propofol 2 mg kg^{-1}, fentanyl 1 μg kg^{-1} and atracurium besilate 0.5 mg kg^{-1}. Anesthesia maintenance was done with sevoflurane 1.8-2% in O_2/air and 2 μg kg^{-1} hr-1fentanyl infusion in Group O (n= 20). Group N (n= 20) received only sevoflurane 1.8-2% in O_2/ N_2O. Hemodynamic values were measured before induction, after intubation and uretheral catheter placement, during prone position and percutaneous dilatation, following irrigation and extubation in recovery room. Access numbers, durations of operation, percutaneous dilatation and irrigation were also recorded. The levels of plasma epinephrine, norepinephrine, blood glucose and blood gas values were measured. Preoperative and postoperative levels of sodium, potassium, blood urea nitrogen, creatinine, blood glucose, hemoglobine, hematocrite, aldosterone, cortisol, adrenocorticotropic hormone and growth hormone were also recorded. **Results:** The epinephrine and norepinephrine levels of Group O were lower than those of Group N ($p< 0.05$). The postoperative blood glucose, aldosterone and adrenocorticotropic hormone levels were higher than preoperative levels in both groups ($p< 0.05$).The intraoperative epinephrine levels of Group N were higher than the preoperative level. The intraoperative blood glucose levels were higher than the preinduction levels in both groups ($p< 0.05$). All the epinephrine levels obtained after urinary catheter placement were lower than the control level in Group O ($p< 0.05$). **Conclusion:** PCNL causes an evident stress response as a low morbidity procedure under sevoflurane anesthesia and fentanyl manages to attenuate this response.

Key Words: Nephrostomy, percutaneous; stress, physiological; analgesics, opioid; 3-methylfentanyl; fentanyl

ÖZET Amaç: Perkütan nefrolitotomide (PCNL) opioid infüzyonunun stres yanıt üzerine etkisini araştırmayı amaçladık. **Gereç ve Yöntemler:** Kırk erişkin hasta randomize olarak iki gruba ayrıldı. Anestezi indüksiyonu propofol 2 mg kg^{-1}, fentanil 1 μg kg^{-1} ve atrakuryum besilat 0,5 mg kg^{-1} ile sağlandı. Anestezi idamesi Grup O'da (n= 20) O_2/Hava karışımı içinde %1,8-2 sevofluran ve 2 μg kg^{-1} s^{-1} fentanil infüzyonu ile yapıldı. Grup N (n= 20) sadece O_2/N_2O karışımı içinde %1,8- 2 sevofluran aldı. Hemodinamik değerler indüksiyondan önce, entübasyon ve uretral kateter yerleştirilmesinden sonra, pron pozisyon ve perkütan dilatasyon sırasında, irrigasyon ve ekstübasyonu takiben ayılma odasında ölçüldü. Girişim sayıları ile operasyon, perkütan dilatasyon ve irrigasyon süreleri de kaydedildi. Plazma epinefrin, norepinefrin, kan glukozu düzeyleri ve kan gazı değerleri ölçüldü. Sodyum, potasyum, kan üre nitrojeni, kreatinin, kan glukozu, hemoglobin, hematokrit, aldosteron, kortizol, adrenokortikotropik hormon ve büyüme hormonunun preoperatif and postoperatif düzeyleri de kaydedildi. **Bulgular:** Grup O'nun epinefrin and norepinefrin düzeyleri Grup N'nin değerlerine göre daha düşüktü ($p< 0,05$). Her iki grubun postoperatif kan glukozu, aldosteron ve adrenokortikotropik hormon düzeyleri preoperatif düzeylerinden daha yüksekti ($p< 0,05$). Grup N'de intraoperatif epinefrin düzeyleri preindüksiyon düzeyine göre yüksekti ($p< 0,05$). Grup O'da üriner kateter konduktan sonra alınan epinefrin düzeylerinin tümü kontrol değerinin altındaydı ($p< 0,05$). Her iki grubun intraoperatif kan glukozu düzeyleri preindüksiyon değerlerine göre yüksekti ($p< 0,05$). **Sonuç:** PCNL'nin sevofluran anestezisi altında belirgin bir stres yanıta neden olduğu ve fentanil infüzyonunun bu yanıtı azaltabildiği kanısındayız.

Anahtar Kelimeler: Nefrostomi, perkütan; stres, fizyolojik; analjezikler, opioid; 3-metilfentanil; fentanil

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Percutaneous nephrolithotomy (PCNL) is a widely accepted endoscopic procedure as an alternative to open surgery in the treatment of kidney stones. PCNL has advantages of lower morbidity rate, short postoperative recovery time and less blood loss especially in high risk patients.[1,2] Endoscopic procedures are thought to be advantegous due to reduced injury and lower stress response. However, a significant stress response is detected in laparoscopic cholecystectomy due to peritoneal incision independent of size and distention of the peritoneum with CO_2.[3,4] Although there is no CO_2 insuflation in PCNL procedures, invasive interventions and continuous irrigation of the kidney lead us to question the probable stress response in these procedures.

Surgical stress causes an increase in secretion of pituitary hormones and activation of the sympathetic nervous system.[5] This endocrine-metabolic response may be responsable for intraoperative and postoperative morbidity, such as cardiocirculatory effects (arrhythmias, myocardial ischemia), respiratory alterations, infections and thromboembolic complications.[6] Opioids in therapeutic or large doses are known to attenuate surgical stress by blocking autonomic nervous system and somatic responses to noxious surgical stimuli.[5,7] For this reason, we aimed to examine the effect of fentanyl infusion on stress response due to the endoscopic procedure in PCNL.

MATERIALS AND METHODS

This study was performed at Zonguldak Karaelmas University Research Hospital, Turkey. After obtaining approval of the Hospital Ethics Committee (11.09.2006, no: 2006/07/7) and patients' written informed consents, forty adult patients, classified as ASA physical status I-II, receiving general anaesthesia for PCNL were included in the study. None of the patients was receiving corticosteroids, catecholamines, or nonsteroidal anti-inflammatory agents. We excluded the patients with a history of cardiovascular or nervous system diseases, diabetes, endocrine disorders, drug or alcohol abuse and obesity.

After premedication with im midazolam 0.05 mg kg^{-1} and standard monitorisation, Ringer's Lactate solution was used for fluid infusion at a constant rate of 5-10 mg $kg^{-1}hr^{-1}$. All patients received 1 mg kg^{-1} lidocaine, 1 μg kg^{-1} fentanyl, 2 mg kg^{-1} propofol and 0.5 mg kg^{-1} atracurium besilate for anesthesia induction. The patients were randomly divided into two groups. After intubation, opioid group (Group O, n= 20) received 1 minimum alveolar concentration (MAC) of sevoflurane (end-tidal concentration 1.8-2%) in a mixture of O_2/air and 2 μg kg^{-1} hr^{-1}fentanyl infusion and control group (Group N, n= 20) received the same sevoflurane dose in a mixture of O_2/N_2O to obtain FiO_2= 0.50. The inspired and end-tidal concentrations of all the gases were measured continuously. All the patients were ventilated mechanically to maintain an end-tidal CO_2 ($EtCO_2$) value between 30-35 mmHg. The neuromuscular block was maintained with 0.015 mg kg^{-1} atracurium besilate as required. An increase in the mean arterial pressure more than 30% from baseline values, heart rate measured more than 90 bpm and persistence of these increments for more than one minute was considered as light anaesthesia. For this reason, we adjusted the sevoflurane concentrations in both groups to maintain the hemodynamic values between 70% and 100% of preinduction levels as a guide of the adequate surgical anaesthesia.

Following the placement of ureteral catheter 6F, the patients were turned to prone position with appropriate padding. Percutaneous access to renal collecting system was established by the guidance of fluoroscopy (Philips BV 25 Gold, Turkish Phillips Medical Systems) and a percutaneous introducer needle. After dilatation with Amplatz semirigid dilators up to 30 F and working sheat placement, rigid nephroscopy, fragmentation and extraction of the stones were done and additional access sites were created when necessary. The procedure was terminated with the placement of 18-20 F nephrostomy tube. Normal saline was used as irrigant solution.

The measurement times for systolic (SAP) and diastolic (DAP) arterial pressures, heart rate (HR), SpO_2 and $EtCO_2$ values were as follows;

T1: Two minutes before induction (Control value),

T2: One minute after intubation,

T3: One minute after the placement of uretheral catheter,

T4, T5: Five and ten minutes after prone position,

T6, T7, T8, T9: One, five, ten and fifteen minutes of percutaneous dilatation

T10: Immediately after the end of percutaneous dilatation,

T11, T12, T13, T14: One, five, ten and fifteen minutes of irrigation,

T15: Immediately after the end of irrigation,

T16, T17: One and five minutes after extubation,

T18: Fifteen minutes after recovery room entrance.

Operation times, access numbers, percutaneous dilatation times and irrigation times were also recorded. After cannulation of radial arter, arterial blood samples were collected for the measurements of plasma epineprine, norepinephrine, blood glucose levels and blood gas analysis. The sodium (Na^+), potassium (K^+) , hemoglobine (Hb) and hematocrite (Hct) levels were obtained from blood gas measurements. The arterial blood collection times were T2, T3, T4, T10 and T18. In addition, venous blood was collected in ward for measurement of preoperative and postoperative levels of Na^+, K^+, blood urea nitrogen (BUN), creatinine (Cre), blood glucose, Hb, Hct, aldosterone, cortisol, adrenocorticotropic hormone (ACTH) and growth hormone (GH). Blood glucose, BUN and Cre were measured with spectrophotometric method (Cobas Modular P, Roche, Tokio, Japan). Epinephrine, norepinephrine (LDN, Germany) and aldosterone were measured with enzyme immunoassay method (IBL, US, LP-400 ELİSA, Italy). Cortisol was measured with enzyme competition method (Modular E170, Roche, Tokio, Japan). After the skin closure, the patients were turned to supine position, extubated and 1 mg kg^{-1} iv tramadol was injected for postoperative analgesia. The patients with visual analogue scale scores over 3 received im 1 mg kg^{-1} meperidine.

Statistical analysis was performed by using SPSS for Windows-11.0 program. Data were expressed as mean ± SD. Kolmogorov- Smirnov, Student's t, Mann-Whitney U, Wilcoxon and Chi Square tests were used for statistical analysis. $p< 0.05$ was accepted as statistically significant.

RESULTS

Group N and Group O were similar when compared according to demographic data, ASA status, access number, percutaneous dilatation, irrigation and operation times (Table 1).

There was no difference between the study groups according to arterial blood pressure values in all the measurement times. When we compared the systolic arterial blood pressure values of Group N, we found out that all the values were lower than control values (T1), except the values after intubation and extubation ($p< 0.05$, Figure 1). The lowest systolic arterial blood pressure value of Group N was measured 5 minutes following prone position. In Group O, only systolic arterial blood pressure values after extubation were significantly higher than control values ($p< 0.05$, Figure 1). The lowest arterial pressures of Group O were measured after ureteral catheter placement (Figure 1). In Group O, all of the diastolic arterial blood pressure values were lower than the preinduction value, except the values measured after intubation and extubation ($p< 0.05$, Figure 2). The only differences between the study groups according to heart rate values were measured after extubation ($p< 0.05$, Figure 3).

TABLE 1: Demographic data.

Parameters	Group N (n= 20)	Group O (n= 20)	p
Age (year)	42.20 ± 12.70	49.20 ± 8.95	0.064
Weight (kg)	75.27 ± 12.39	77.87 ± 9.75	0.849
ASA (I/II)	11/9	13/7	0.519
Sex (W/M)	10/10	13/7	0.337
Access number (First /Second)	17/3	19/1	0.292
Percutaneous dilatation time (min)	12.50 ± 4.72	14.00 ± 2.05	0.075
Irrigation time (min)	64.00 ± 32.01	49.75 ± 24.86	0.101
Operation time (min)	164.50 ± 47.37	150.75 ± 44.70	0.351

Group N: Patients given N_2O Group O: Patients given fentanyl.
(mean ± SD)

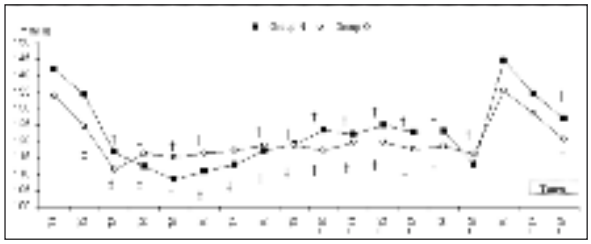

FIGURE 1: Systolic arterial pressure changes in time. Two minutes before induction (T1), one minute after intubation (T2), one minute after the placement of uretheral catheter (T3), five and ten minutes after prone position (T4, T5), one, five, ten and fifteen minutes of percutaneous dilatation (T6, T7, T8, T9), immediately after the end of percutaneous dilatation (T10), one, five, ten and fifteen minutes of irrigation (T11, T12, T13, T14), immediately after the end of irrigation (T15), one and five minutes after extubation (T16, T17) and fifteen minutes after recovery room entrance (T18).

† p< 0,05: T1 vs. the other measurement times (Group N).

‡ p< 0,05: T1 vs. the other mesurement times (Group O).

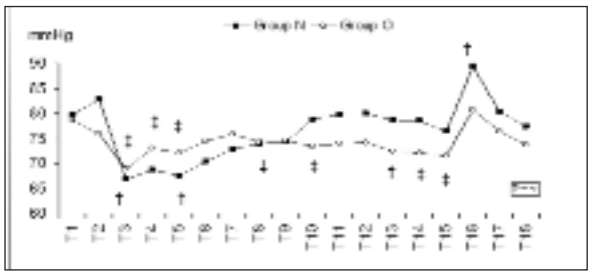

FIGURE 2: Diastolic arterial pressure changes in time. Two minutes before induction (T1), one minute after intubation (T2), one minute after the placement of uretheral catheter (T3), five and ten minutes after prone position (T4, T5), one, five, ten and fifteen minutes of percutaneous dilatation (T6, T7, T8, T9), immediately after the end of percutaneous dilatation (T10), one, five, ten and fifteen minutes of irrigation (T11, T12, T13, T14), immediately after the end of irrigation (T15), one and five minutes after extubation (T16, T17) and fifteen minutes after recovery room entrance (T18).

† p< 0,05: T1 vs. the other measurement times (Group N).

‡ p< 0,05: T1 vs. the other mesurement times (Group O).

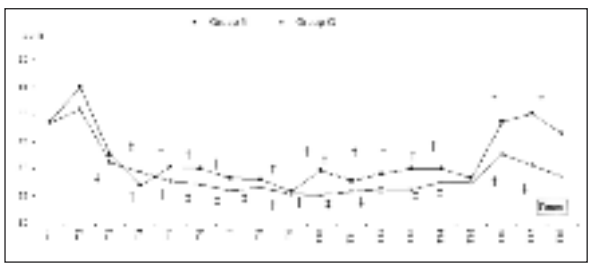

FIGURE 3: Heart rate changes in time. Two minutes before induction (T1), one minute after intubation (T2), one minute after the placement of uretheral catheter (T3), five and ten minutes after prone position (T4, T5), one, five, ten and fifteen minutes of percutaneous dilatation (T6, T7, T8, T9), immediately after the end of percutaneous dilatation (T10), one, five, ten and fifteen minutes of irrigation (T11, T12, T13, T14), immediately after the end of irrigation (T15), one and five minutes after extubation (T16, T17) and fifteen minutes after recovery room entrance (T18).

*p< 0.05: Group N vs Group O,

† p< 0.05: T1 vs. the other measurement times (Group N),

‡ p< 0.05: T1 vs. the other mesurement times (Group O).

The $EtCO_2$ and SpO_2 values of the groups were similar and remained in normal ranges at all the measurement times. The study groups did not differ according to preoperative and postoperative levels of Na^+, K^+, BUN, Cre, blood glucose, Hb, Hct, aldosteron, cortisol, GH and ACTH levels except aldosterone levels (Table 2). The postoperative aldosteron level of Group O at recovery room was lower than that of Group N ($p< 0.05$).

Although the levels of epinephrine and norepinephrine after intubation were similar in both groups, the levels of epinephrine and norepinephrine in Group O were lower than those of Group N in all the measurement times ($p< 0.05$, Figure 4, Figure 5).

There were no differences between the study groups according to blood gas analysis, electrolytes, Hb and Hct (Table 2).

The postoperative blood glucose, aldosterone and ACTH levels were higher than preoperative levels in Group N and Group O ($p< 0.05$, Table 2). The postoperative Hb and Hct levels were lower than preoperative levels in both groups ($p< 0.05$, Table 2). All the epinephrine and blood glucose levels were higher following intubation in Group N ($p< 0.05$, Table 3). The T3 and T4 levels of epinephrine were lower than the after intubation levels in Group O ($p< 0.05$, Table 4). All the blood glucose levels were higher after intubation in Group O ($p< 0.05$, Table 4). There were no differences in the blood gas results of both groups, except SaO_2 and PaO_2 which were increased after ureteral catheter placement ($p< 0.05$), but were not affected by prone position (Table 3, 4).

DISCUSSION

In this study, the increase in levels of epinephrine, ACTH, aldosterone and blood glucose during the procedure demonstrates that PCNL causes significant stress response as an endoscopic procedure. Surgical stress produces a neuroendocrine response activated by afferent neuronal impulses from the site of injury and the stimulation of pituitary-adrenal axis causes hyperglisemia and an elevation in the levels of catecholamines and stress hormones

TABLE 2: The comparison of the study groups according to preoperative and postoperative levels of blood glucose, stress hormones, hemoglobine and hematocrite.

Groups	Group N		Group O	
Parameters	Preoperative	Postoperative	Preoperative	Postoperative
Hb (gr dl^{-1})	13,52 ± 1,64	11,37 ± 1,71*	13,93 ± 1,44	11,15 ± 1,27*
Htc (%)	39,89 ± 5,05	33,30 ± 5,48*	41,08 ± 4,26	31,96 ± 3,34*
Aldosteron (pg ml^{-1})	116,71 ± 44,07	476,61 ± 167,84*	120,27± 32,77	209,09 ± 61,02* ƒ
Cortisol (µg dl^{-1})	20,26 ± 11,17	22,16 ± 11,31	17,93±10,31	21,36 ± 9,88
GH (mIU ml^{-1})	1,50 ± 1,87	1,85 ± 2,07	2,21 ± 4,52	2,66 ± 4,70
ACTH (pg ml^{-1})	36,80 ± 64,48	167,30 ± 210,69*		160,81 ± 223,96*
	(5-297)	(9,89-700)	23,57 ± 17,23	(8,16-874)
BG (mg dl^{-1})	94,70 ± 15,08	106,80 ± 12,97*	93,40 ± 15,16	103,50 ± 14,59*

Hb: hemoglobine, Hct: Hematocrite, GH: Growth hormone, ACTH: Adrenocorticotropic hormone, BG: Blood glucose.

Group N: Patients given N2O Group O: Patients given fentanyl.

(mean± SD).

*p<0.05: Preoperative vs. Postoperative, ❦p>0.05: Group O vs. Group N.

(ACTH, GH, cortisol, aldosterone).[5] Since hormones are important mediators of the body's response to surgical stress, the surgery and anesthesia induced hormonal changes and adrenergic response reflect the degree of surgical stress.[6,8] During laparoscopic procedures, peritoneal incision can be the major stimulus for ACTH and cortisol secretion and distention of the peritoneum with CO_2 may increase the catecholamine levels.[3,4] The only study evaluating hormonal changes during PCNL procedures belongs to Atıcı et al.[9] In their study, twenty-one PCNL cases were examined under sevoflurane anesthesia and renin, aldosterone and ACTH levels were found to increase at the end of the procedure as similar to our study.[9] Atıcı et al[9] related renin and aldosterone increases to a hormonal response to hyponatremia and traumatic interventions to kidney associated with ACTH secretions. The continuous irrigation, the height of irrigation fluid bag, the diameter of nephroscope and the working sheat may also influence the pressure changes within the kidney and peritone which can result in several hormonal responses.

Several factors as magnitude of surgery, type of procedure and type of anaesthesia may affect the stress response to surgery. Marana et al[10] compared the effects of sevoflurane and isoflurane anesthesia combined with fentanyl on the release of stress hormones in patients undergoing laparoscopic pelvic surgery. They reported that the use of sevoflurane anaesthesia decreased ACTH, cortisol and GH release, but enhanced prolactine release when

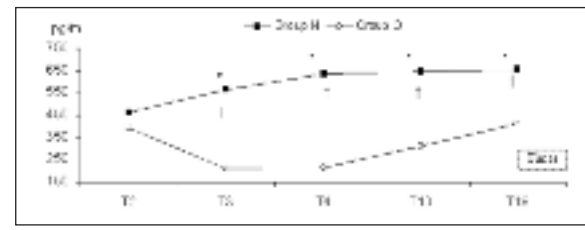

FIGURE 4: The comparison of the changes in epinephrine values. One minute after intubation (T2), one minute after the placement of uretheral catheter (T3), five minutes after prone position (T4), immediately after the end of percutaneous dilatation (T10) and fifteen minutes after recovery room entrance (T18).

* p< 0.05: Group N vs Group O

† p< 0.05: T2 vs. the other measurement times (Group D).

‡ p< 0.05: T2 vs. the other measurement times (Group O).

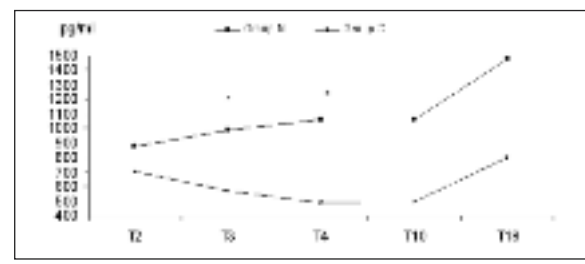

FIGURE 5: The comparison of the changes in norepinephrine values. One minute after intubation (T2), one minute after the placement of uretheral catheter (T3), five minutes after prone position (T4), immediately after the end of percutaneous dilatation (T10) and fifteen minutes after recovery room entrance (T18).

* p< 0.05: Group N vs. Group O.

TABLE 3: The results obtained at intraoperative blood collection times in Group N.

	T2	T3	T4	T10	T18
E (pg ml^{-1})	467,6 ± 164,07	564,90 ± 213,11*	639,99 ± 216,90*	647,30 ± 309,13*	658,38 ± 328,58*
NE (pg ml^{-1})	872,13 ± 451,22	990,74 ± 515,04	1062,04 ± 694,24	1063,14 ± 917,43	1476,76 ± 1450,80
BG (mg dl^{-1})	92,50 ± 11,61	97,65 ± 10,81*	99,70 ± 6,89*	108,05 ± 8,66*	116,30 ± 7,61*
Htc (%)	40,25 ± 3,33	37,65 ± 4,24	37,70 ± 3,16	37,35 ± 3,99	37,10 ± 5,49*
Hb (gr dl^{-1})	13,39 ± 1,12	12,61 ± 1,34	12,42 ± 1,48	12,42 ± 1,32	12,22 ± 1,76*
SaO_2	97,64 ± 1,37	98,85 ± 0,55*	98,94 ± 0,57*	98,99 ± 0,60*	98,63 ± 0,72*
PaO_2	127,51 ± 54,91	223,84 ± 54,74*	230,26 ± 59,85*	226,65 ± 51,22*	207,21 ± 59,82*

Group N: Patients given N2O Group O: Patients given fentanyl, (mean± SD)

E: Epinephrine, NE: Norepinephrine, BG: Blood sugar, Hct: Hematocrite, Hb: Hemoglobine, SaO2: Blood oxygen saturation, PaO2 : Partial oxygen pressure, T2: One minute after intubation, T3: One minute after the placement of uretheral catheter, T4: Five minutes after prone position, T10: Immediately after the end of percutaneous dilatation, T18: Fifteen minutes after recovery room entrance.

*p<0.05: T2 vs T3, T4, T10, T18.

TABLE 4: The results obtained at intraoperative blood collection times in Group O.

Parameters	T2	T3	T4	T10	T18
E (pg ml^{-1})	393,78 ± 215,48	209,11 ± 55,82*	213,71 ± 87,71*	313,82 ± 265,53	414,73 ± 349,04
NE (pg ml^{-1})	702,42 ± 732,90	568,37 ± 332,19	486,08 ± 327,56	498,27 ± 250,90	802,46 ± 796,42
BG (mg dl^{-1})	89,35 ± 11,08	93,85 ± 9,18*	98,65 ± 9,24*	105,45 ± 10,24*	111,90 ± 8,63*
Htc (%)	39,15 ± 5,00	37,15 ± 5,12	37,75 ± 5,18	36,95 ± 3,76	35,50 ± 3,47*
Hb (gr dl^{-1})	13,04 ± 1,65	12,35 ± 1,69	12,57 ± 1,76	12,32 ± 1,30	11,88 ± 1,11*
SaO_2	97,91 ± 1,21	99,18 ± 0,72*	99,72 ± 0,73*	99,20 ± 0,73*	99,03 ± 0,70*
PaO_2	126,09 ± 63,93	234,29 ± 44,36*	255,21 ± 48,27*	254,77 ± 59,80*	240,86 ± 76,58*

Group N: Patients given N2O Group O: Patients given fentanyl, (mean± SD)

E: Epinephrine, NE: Norepinephrine, BG: Blood sugar, Hct: Hematocrite, Hb: Hemoglobine, SaO2: Blood oxygen saturation, PaO2 : Partial oxygen pressure, T2: One minute after intubation, T3: One minute after the placement of uretheral catheter, T4: Five minutes after prone position, T10: Immediately after the end of percutaneous dilatation, T18: Fifteen minutes after recovery room entrance.

*p<0.05: T2 vs T3, T4, T10, T18.

compared with isoflurane.[10] There are also studies revealing that sevoflurane anesthesia does not affect the metabolic endocrine changes induced by surgical tissue trauma.[11,12] Nishiyama et al[13] revealed that sevoflurane-nitrous oxide anesthesia had caused less stress hormone changes than those of isoflurane- nitrous oxide anesthesia. Nitrous oxide is known to stimulate catecholamines, but directly depresses myocardial contractility with the net effect of unchanged or slightly elevated hemodynamic values.[14] Nitrous oxide also may have an additional role in the rise of catecholamine levels in our study. In light of our results, we can postulate that PCNL causes an evident stress response in spite of sevoflurane anesthesia and fentanyl infusion manages to attenuate this response. Opioids are well known to suppress hypothalamic and pituatary hormone secretion in high doses.[5,7] Aono et al[4] reported that 4 μg kg^{-1} fentanyl administered intravenously after endotracheal intubation partially attenuated an increase in norepinephrine but not epinephrine in laparoscopic cholecystectomy. In our study, fentanyl infusion of 2 μg kg^{-1} hr^{-1} was successful in decreasing the levels of epinephrine, norepinephrine and aldosterone and controlling the increase in heart rate during dilatation and irrigation period.

The hemodynamic parameters in our study were rather stable. This stability may have several reasons. First reason may be our purposely care to maintain the hemodynamic values between 70% and 100% of preinduction levels by changing sevoflurane concentrations in order to prevent the additional effect of light anesthesia on the

stress response. Aono et al[4] concluded that general anesthesia with sevoflurane and N_2O could not suppress stress responses of both the hypothalamus-pituitary-adrenocortical axis (increase in plasma cortisol) and sympathoadrenal system (increases in plasma epinephrine and norepinephrine), even though blood pressure and heart rate were maintained in normal limits during laparoscopic cholecystectomy. This discordance may be the other reason. Atıcı et al[9] found out that the mean diastolic arterial blood pressures were increased during the PCNL procedure in their study. They also observed hyponatremia in different grades and pulmonary edema in two patients, which were related to renal tubular dysfunction due to mechanic irritations to kidney.[9] The absence of hyponatremia, postoperative pulmonary edema and hypervolemia in our study may be the other reason for comparatively low arterial blood pressures.

Prone position is another important factor in PCNL procedures due to its cardiac effects. It is revealed that there have been a significant decrease in stroke volume and cardiac index which results in decrease of mean arterial, right atrial, or pulmonary artery occlusion pressures despite the careful use of measures to prevent venous pooling and abdominal compression.[15,16] In addition, Pump et al[17] mentioned about an increase in plasma levels of epinephrine and norepinephrine during prone position. Backlund et al[18] reported that an increase in intraoperative norepineprine levels was in correlation with postoperative myocardial ischemia especially in elderly. For this reason, the placement of invasive monitors to determine unrecognizable deterioration of cardiac function in the prone position is highly recommended in patients whose cardiac status are precarious before induction.[15,19] In our study, the lowest values of arterial pressures were measured at prone position in Group N, but this finding was not significant as we could not determine the same results in Group O.We could obtain more accurate hemodynamic results in our study with central venous pressure measurements, but invasive cannulation would be inappropriate for ASA risk classification I-II patients who were planned for endoscopic surgery.

There are several studies reporting an improvement in oxygenation in prone position which is related to the decreases in pulmonary shunt fraction and alveolar dead space.[20,21] However, in our study, we did not notice a change in PaO_2 and $PaCO_2$ values during prone position as similar to Atıcı et al's study.[9]

Although Sacha et al[22] reported a hemorrhage rate of 0.3%, massive hemorrhage can be seen in PCNL due to injury in veins and arteries.[23] In our study, the postoperative reduction in Hct values of Group N and Group O were 20% and 16.5%, respectively. In Atıcı's study, the Hct level lowered from 41.6% to 35% and no correlation was found between Hct value and the amount of irrigation fluid, the number of interventions and, the volume of the stones.[9] For this reason, we recommend monitorisation of Hct levels during the procedure.

In conclusion, in the clinical setting of PCNL which is accepted as a low morbidity endoscopic procedure, significant stress hormone release may be determined and the use of fentanyl infusion attenuates the increase in plasma cathecolamines and aldosteron levels. As decreasing the stress response to surgery and trauma is very vital, care must be given to prevent surgical stress especially in high risk and elderly patients planned for PCNL procedures.

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