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Original Research / Özgün Araştırma

The Effect of Sedative Agents on Stress Hormones and High-Sensitive Troponin in Patients Catheterized by Permanent-tunnel Port Catheter

Kalıcı Tünelli Port Kateter Takılan Hastalarda Sedatif Ajanların Stress Hormonları ve High Sensitif Troponin Üzerine Etkileri

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ABSTRACT

Objective: To evaluate the effects of sedation and analgesia combinations on pain scales, anxiety, adrenocorticotropic hormone (ACTH), cortisol, and high-sensitive troponin in patients with a central venous catheter.

Methods: The present study was prospectively conducted in 90 patients who had been indicated for port catheterization in hematology and oncology in the emergency medicine department of Gaziantep University Medical Faculty between March 1st and September 1st, 2015. The patients were divided into three groups of 30 each. Pain levels were assessed using the Visual Analog Scale, anxiety levels using the Beck Anxiety Scale, and blood samples were collected before (0 min) and after (30 min) the procedure in order to obtain ACTH, cortisol, and high-sensitive troponin values.

Results: No statistically significant differences were observed between the groups with regard to gender and age (p=0.836 and p=0.182, respectively). Anxiety significantly decreased in all three groups. A significant decrease in level of pain was found in patients administering midazolam-fentanyl and those who received propofol; a significant decrease in systolic and diastolic blood pressure was also observed in these two groups. In all three groups, no significant cortisol change was found; however, significant high-sensitive troponin values were observed. There was no significant difference between the groups.

Conclusion: Sedative agents can be used efficiently, safely, and easily in minor surgical procedures, such as central venous catheterization. We also recommend the use of analgesic drugs, in addition to anxiolytic and sedative agents, during invasive procedures conducted in the emergency room.

Keywords: Port catheter, sedation, anxiety, troponin

ÖZ

Amaç: Santral venöz kateter takılan hastalarda sedasyon ve analjezinin ağrı sakalaları, anksiyete; adrenokortikotropik hormon (ACTH), kortizol ve High-sensitif troponin üzerine etkilerini araştırmak.

Yöntemler: Bu çalışma hematoloji ve onkoloji servisinde yatan ve acil serviste port kateterizasyon işlemi uygulanan 90 hastada yapılan prospektif bir çalışmadır. Çalışma 1 Mart- 1 Eylül 2015 tarihleri arasında Gaziantep Üniversitesi Tıp Fakültesi Acil Tıp Anabilim Dalı'nda yapıldı. Hastalar 30 kişilik gruplar halinde 3 gruba ayrıldı. Ağrı seviyeleri Visüel Anolog Skala (VAS), anksiyete seviyeleri Beck Anksiyete Skalası kullanılarak ölçüldü. İşleme başlandığı anda, işlem bittikten sonraki 30. dakikada kan alındı. ACTH, kortizol ve high sinsitif troponin seviyelerine bakıldı.

Bulgular: Gruplar arasındaki yaş ve cinsiyet farkı istatistiksel olarak anlamsızdı (p=0,836 ve p=0,182). Anksiyete her üç grupta da belirgin azalmıştı. Midazolam-fentanil grubunda ve propofol alan hastalarda ağrıda belirgin azalma oldu. Bu hastalardan aynı zamanda her iki grupta da sistolik ve diastolik kan basınçlarında belirgin azalma oldu. Her 3 grupta da high sensitive troponin düzeylerinde belirgin değişiklik olurken kortizol seviyelerinde belirgin bir değişiklik olmadı. Gruplar arası farklılıklar anlamlı değildi.

Sonuç: Özellikle santral venöz kateterizasyon olmak üzere küçük cerrahi girişimlerde sedatif ilaçların kullanımı etkili ve güvenlidir. Acil serviste yapılan invaziv işlemler sırasında anksiyolitik ve sedative ilaçların yanında analjezik ilaçların da kullanımını öneriyoruz.

Anahtar kelimeler: Port kateter, sedasyon, anksiyete, troponin

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INTRODUCTION

Port catheter is an artificial vessel with one end attached to the main vein and the other placed under the skin in the upper chest, allowing drug application. These are generally preferred in patients requiring long-course, repeated chemotherapy treatment (1).

The underlying causes of changes in serum cortisol levels were observed as unusual adrenocorticotropic hormone (ACTH) levels, clinical depression, and physiological stress sources (hypoglycemia, disease, fever, trauma, surgery, fear, pain, extreme cold or hot, and physical strain) (2).

High-sensitivity troponin testing allows for the determination of concentration levels, which cannot be detected earlier using conventional cardiac troponin tests and also allows for precise measurement and diagnosis and/or elimination of myocardial infarction without elevation of ST during admission to the hospital (3).

The present study aimed to evaluate the effect of sedative agents on stress hormones (ACTH and cortisol), high-sensitivity troponin, pain, and anxiety of patients admitted to the emergency service with requirement of port catheterization that was guided by bedside ultrasound imaging and classified according to the American society of Anesthesiologists (ASA) Physical Classification System. Simultaneously, it aims to increase patient satisfaction and the frequency of application of bedside ultrasound imaging in emergency departments.

METHODS

This prospective cohort study was conducted at the Gaziantep University Şahinbey Research and Practice Hospital Emergency Service. Approval was obtained from the Gaziantep University Faculty of Medicine Ethics Committee (ethics committee decision no: 09.03.2015/84, date: 03.09.2015). The study protocol was conducted in accordance with the Declaration of Helsinki, and was prospectively conducted at the Gaziantep University Şahinbey Research and Practice Hospital Emergency Service between March and August 2015. The patients were taken to an emergency room for port catheterization, which had been prepared earlier for the procedure. A "Patients Consent Form" was obtained from all patients.

Population and Samples

Patients who were referred to the emergency department by the hem atology and oncology departments for port catheterization were divided into three groups based on the three different sedation options planned. A total of 90 patients were included in the study. The following inclusion and exclusion criteria were followed when enrolling patients in the study:

Inclusion Criteria

- Men and women aged >18 years,
- Patients who volunteered to participate in the study,
- Those who speak Turkish or to whom the procedure can be explained to,
- Those who have stable vital findings,
- Patients to whom the port catheter was applied for the first time.

Exclusion Criteria

- Patients who did not volunteer to participate in the study,
- Male and female patients aged <18 years,
- Patients who are pregnant,
- Patients who do not speak Turkish or to whom the procedure cannot be explained to,
- Patients with unstable vital findings,
- Patients with pituitary or adrenal gland tumors affecting blood ACTH and cortisol levels,
- Patients who used drugs that affected ACTH and cortisol levels,
- Patients who previously had port catheterization,
- Patients with hormonal dysfunction,
- Patients who had been using steroids, anxiolytics, and sedative drugs,
- Patients with severe anxiety disorder, active psychosis, or dementia,
- Patients with uncontrollable hypertension,
- Patients with substance abuse,
- Patients with complications during the procedure,
- Patients with coronary artery disease,
- Patients with cerebrovascular disease,
- Patients with chronic renal failure.

The patients' ASA physical classification system values were assessed. Application of sedation analgesia to non-emergency cases in the emergency service was limited to ASA 1-2 patients.

Beck Anxiety Scale and Visual Analog Scale (VAS) were applied to the patients before and after the procedure.

The vital signs (blood pressure, pulse rate, and respiration rate) of the patients were followed and recorded (Nihon Kohden Corporation, model BSM-2351 K, 2008, Japan). ACTH, cortisol, and high-sensitive troponin levels were measured in the blood samples collected before the procedure, whereas ACTH and cortisol levels at the 30th minute and high-sensitive troponin I level at the third hour were obtained and measured in the routine biochemistry laboratory.

Blood samples were collected in biochemical tubes each time for ACTH, cortisol, and highly sensitive troponin levels. Samples collected from each patient were separated into serum by centrifugation for 10 min at 4000 rpm for comparison of ACTH, cortisol, and highly sensitive troponin levels. Serum specimens were placed in separate Eppendorf tubes, and stored at -80°C in a deep freezer at Gaziantep University Faculty of Medicine Basic Science Laboratory until use (Biotek ELx800 model, ELISA reader, USA). Patients were examined for vital signs, and the findings were recorded in the follow-up table generated by the researcher at the time of initial application, at the beginning of the procedure, and at the end of the procedure. The anxiety status of patients was assessed using the Beck Anxiety Scale when patients were first taken into the room and after the completion of the procedures. VAS was used to determine the level of pain felt by patients after the procedure was over.

The Social Sciences 18 program (IBM Ltd.; Rm 1804, 18/F, Westlands Center, Quarry Bay, Hong Kong) was used for statistical analysis. Distribution of continuous variables (ASA value, anxi-

ety value, VAS value, respiratory rate, pulse rate, diastolic blood pressure, systolic blood pressure, cortisol, and ACTH hormone level) was analyzed using Analysis of Variance tests. Independent t-test was used for comparison of independent groups showing normal distribution. Paired t-test was used for comparison of dependent variables showing normal distribution. All data were expressed as mean±standard deviation, and $p<0.05$ was considered statistically significant.

Table 1. Comparison of pain and anxiety levels of patients in the treatment and control groups

Parameter	Group 1 (n=30)	Group 2 (n=30)	Group 3 (n=30)	p*
VASPRE	0.66±1.64	1.03±1.58	1.06±2.1	0.635
VASPOST	1.20±1.9[a,b]	0.16±0.37	0.010	**0.001**
px	0.122	**0.009**	**0.010**	
ANXPRE	7.43±5.89	7.43±4.84	6.50±4.07	0.706
ANXPOST	2.93±2.82[c]	1.43±4.84	1.60±2.02	0.023
px	**0.001**	**0.001**	**0.001**	
ASA	1.48±0.58	1.40±0.62	1.60±0.89	0.586

VASPRE: VAS before procedure; VASPOST: VAS after procedure; ANXPRE: anxiety value before procedure; ANXPOST: anxiety value after procedure; ASA: ASA values of patients

Group 1: Treated with midazolam and ketamine; Group 2: Treated with midazolam and fentanyl; Group 3: Treated with propofol. p*: ANOVA test, px: paired-sample t-test

ap=0.002, bp=0.000, cp=0.032

a, c: Group 1 and Group 2; b: Group 1 and Group 3

Table 2. Comparison of Systolic (SBP) and Diastolic Blood Pressure Values (DBP) of patients in all the three groups

Parameter	Group 1 (n=30)	Group 2 (n=30)	Group 3 (n=30)	p*
SBP1	121.36±15.96[a]	132.10±16.33	124.33±18.17	**0.044**
SBP2	125.23±18.01[b]	128.23±15.00[d]	111.76±16.77	**0.001**
SBP3	121.53±17.22	125.03±14.41[e]	112.03±15.28	**0.006**
px	0.958	**0.003**	**0.001**	
DBP1	73.10±12.30	78.56±12.92	71.76±9.66	0.064
DBP2	73.76±10.69c	72.13±12.12[f]	64.06±8.84	**0.001**
DBP3	69.60±10.94	67.36±9.58	64.96±11.17	0.243
px	0.080	**0.001**	**0.001**	

SBP1: systolic blood pressure before procedure; SBP2: systolic blood pressure during procedure; SBP3: systolic blood pressure after procedure; DBP1: diastolic blood pressure before procedure; DBP2: diastolic blood pressure during procedure; DBP3: diastolic blood pressure after procedure

Group 1: treated with midazolam and ketamine; Group 2: treated with midazolam and fentanyl; Group 3: treated with propofol

p*: ANOVA test, px: paired-sample t-test

ap=0.041, b,ep=0.005, cp=0.002, dp=0.001, fp=0.012

a: Group 1 and Group 2; b, c: Group 1 and Group 3; d, e, f: Group 2 and Group 3

RESULTS

Characteristics of gender and age of the individuals in the three sedation groups were similar to each other. No statistically significant difference in gender distribution was observed in the study. Further, no statistically significant difference in terms of age was observed in the present study.

The mean VAS before procedure (VASPRE) before treatment in the midazolam and fentanyl group was 1.03±1.58, whereas the mean VAS after procedure (VASPOST) after treatment was 0.16±0.37; this decrease in pain was found to be statistically significant (p=0.009). The mean VASPRE before treatment in the propofol group was 1.06±2.1, whereas the mean VASPOST after treatment was 0.010; this decrease in pain was found to be statistically significant (p=0.010) (Table 1, Figure 1).

The mean diastolic blood pressure 2 (DBP2) in the midazolam and ketamine group was 73.76±10.69 mm Hg, whereas the mean DBP2 in the midazolam and fentanyl group was 73.13±12.12 mm Hg. The mean DBP2 in the propofol group was 64.06±8.84 mm Hg. A statistically significant difference was observed between the DBP2 values of the midazolam with fentanyl and propofol groups (p=0.012) (Table 2, Figure 2).

Figure 1. Values of anxiety levels of patients before procedure (ANXPRE) and after procedure (ANXPOST)

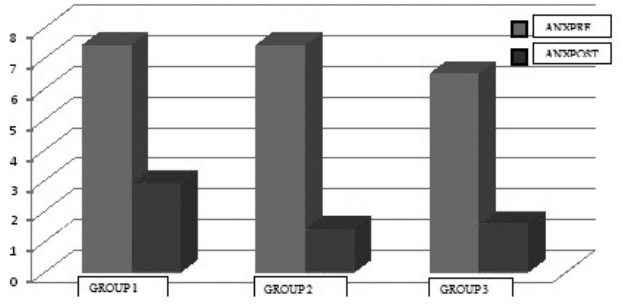


Figure 2. Comparison of systolic blood pressure (SBP) values and diastolic blood pressure (DBP) values of patients in all the three groups

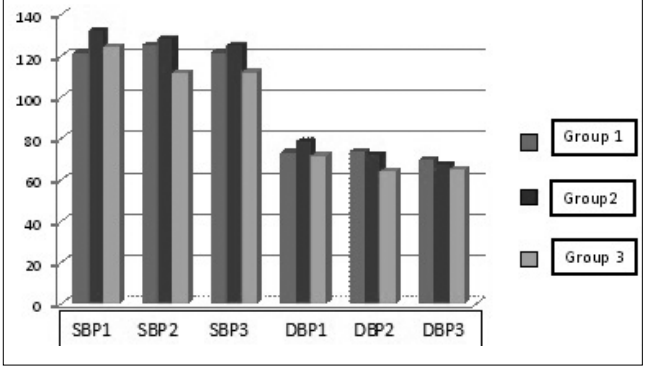


Table 3. Comparison of Pulse (PLS) and Respiratory Rate (RR) values of patients in all the three groups

Parameter	Group 1 (n=30)	Group 2 (n=30)	Group 3 (n=30)	p*
PLS1	95.40±19.58	94.86±16.42[d]	91.00±18.55	0.596
PLS2	100.93±19.59[a]	94.30±15.51	89.03±18.04	**0.039**
PLS3	101.26±19.89	100.30±14.65	91.40±16.85	0.056
px	**0.029**	**0.003**	0.816	
RR1	18.83±6.29	17.96±6.02	17.70±4.96	0.731
RR2	20.06±8.08[b]	15.80±5.52	18.73±6.15	**0.045**
RR3	19.13±7.05	19.30±8.00	18.20±5.68	0.806
px	0.710	0.453	0.629	

PLS1: pulse before procedure; PLS2: pulse during procedure; PLS3: pulse after procedure

RR1: respiratory rate before procedure; RR2: respiratory rate during procedure; RR3: respiratory rate after procedure

Group 1: treated with midazolam and ketamine; Group 2: treated with midazolam and fentanyl; Group 3: treated with propofol

p*: ANOVA test, px: paired-sample test

ap=0.039, bp:=0.045

a: Group 1 and Group 3; b: Group 1 and Group 2

Table 4. Comparison of Oxygen Saturation Percentages (SPO2) of patients in the all three groups

Parameter	Group 1 (n=30)	Group 2 (n=30)	Group 3 (n=30)	p*
SPO2-1	97±1.77[a]	96.66±2.13d	98.40±1.61	**0.002**
SPO2-2	95.63±3.37[b]	96.53±2.58	97.73±2.40	**0.018**
SPO2-3	95.56±1.97[c]	96.66±2.55	98.00±2.33	**0.001**
px pre-post	**0.001**	1.000	0.173	

SPO2-1: oxygen saturation before procedure; SPO2-2: oxygen saturation during procedure; SPO2-3: oxygen saturation after procedure.

Group 1: treated with midazolam and ketamine; Group 2: treated with midazolam and fentanyl; Group 3: treated with propofol.

p*: ANOVA test, px: paired-sample test.

ap: 0.044 SPO2 Group 1 and Group 3; bp: 0.014 SPO2 Group 1 and Group 3; cp: 0.000 SPO2 Group 1 and Group 3; dp: 0.001 SPO2 Group 2 and Group 3.

Table 5. Comparison of puncture numbers of patients in all the three groups

	Number of punctures				
	1	2	3	4	Total
Group 1 (n=30)	16 (53.3%)	11 (36.6%)	2 (6.6%)	1 (3.3%)	30
Group 2 (n=30)	20 (66.6%)	7 (23.3%)	2 (6.6%)	1 (3.3%)	30
Group 3 (n=30)	18 (60%)	7 (23.3%)	5 (16.6%)	0	30
Total	54 (60%)	25 (27.7%)	9 (10%)	2 (2.2%)	90
p*	0.786				

Group 1: treated with midazolam and ketamine; Group 2: treated with midazolam and fentanyl; Group 3: treated with propofol

The mean respiratory rate 2 (RR2) in the midazolam and ketamine group was 20.06±8.08/min, whereas the mean RR2 in the midazolam and fentanyl group was 15.80±5.52/min. The mean RR2 in the propofol group was 18.73±6.15/min. A statistically significant difference was observed between the mean RR2 values of the midazolam with ketamine and propofol groups (p=0.045; Table 3).

The mean oxygen saturation (SPO) before procedure 2-3 in the midazolam and ketamine group was 95.56%±1.97%, whereas the mean SPO2-3 in the midazolam and fentanyl group was 96.66%±2.55%. The mean SPO2-3 in the propofol group was 98.00%±2.23. A statistically significant difference was observed between the mean SPO2-3 values in the midazolam with ketamine and propofol groups (p=0.001; Table 4).

Access to the vein was obtained through 1 puncture in 18 individuals (60%), 2 in 7 (23.3%), and 3 in 5 (16.6%) of the propofol group. No statistically significant difference was observed in terms of the number of punctures in the individuals in our study (p>0.05; Table 5).

In terms of diagnosis, 8 (26.6%) individuals in the midazolam and ketamine group had a hematologic diagnosis, whereas 22 (73.3%) had an oncologic diagnosis. Twelve (40%) individuals in the midazolam and fentanyl group had a hematologic diagnosis, whereas 18 (60%) had an oncologic diagnosis. Twelve (40%) individuals in the propofol group had a hematologic diagnosis, whereas 18 (60%) had an oncologic diagnosis. Oncologic diagnosis was the most common among patients.

The mean ACTH pre measured in blood samples when the patient was first received in the room and was prepared for port

Table 6. Comparison of ACTH, cortisol, and high-sensitive troponin values of patients in all the three groups

Parameter	Group 1 (n=30)	Group 2 (n=30)	Group 3 (n=30)	p*
ACTH Pre	13.83±7.84	17.21±12.66	13.27±10.29	0.293
ACTH Post	29.44±27.83a	17.95±7.31	19.52±7.40	0.023
p[x]	**0.007**	0.733	**0.001**	
Cort Pre	155.90±105.10	176.89±99.25	165.05±162.70	0.811
Cort Post	179.15±115.22	196±36	174.56±185.22	0.839
p[x]	0.117	0.286	0.526	
Trp Pre	1.22±0.34	1.18±0.45b	1.48±0.54	**0.026**
Trp Post	1.71±1.03	1.48±0.53	1.80±0.54	0.239
p[x]	**0.013**	**0.001**	**0.003**	

ACTH Pre: ACTH before procedure; ACTH Post: ACTH after procedure; Cort Pre: cortisol before procedure; Cort Post: cortisol after procedure; Trp Pre: troponin before procedure; Trp Post: troponin after procedure

Group 1: treated with midazolam and ketamine; Group 2: treated with midazolam and fentanyl; Group 3: treated with propofol

p*: ANOVA test; px: paired-sample test

[a]p: 0.030; [b]p: 0.034. a: Group 1 and Group 2, b: Group 2 and Group 3

catheterization procedure was 13.83±7.84 pg/mL, and the mean ACTH post-measured in blood samples after the procedure was 29.44±27.83 pg/ml in the midazolam and ketamine group. An increase in the ACTH levels of individuals in the midazolam and ketamine group was observed; this increase was found to be statistically significant (p-0.007; Figure 3).

The mean first cortisol before procedure (Cort Pre) result obtained from the blood samples in the midazolam and ketamine group was 179.15±115.22 µg/dL, whereas the mean cortisol after procedure (Cort Post) result in the midazolam and fentanyl group was 176.89±99.25 µg/dL. The mean Cort Post result in the propofol group was 165.05±162.70 µg/dL. No statistically significant difference was found between the Cort Pre results of all the three groups (p=0.811; Table 6).

The mean first Cort Pre result obtained from the blood samples in the midazolam and ketamine group was 179.15±115.22 µg/dL, whereas the mean Cort Post result in the midazolam and fentanyl group was 196±36 µg/dL. The mean Cort Post result in the propofol group was 174.56±185.22 µg/dL. No statistically significant difference was found between the Cort Pre results of all three groups (p=0.839; Figure 4).

Figure 3. Comparison of ACTH before procedure (ACTH Pre) and after procedure (ACTH Post) values of patients in all the three groups

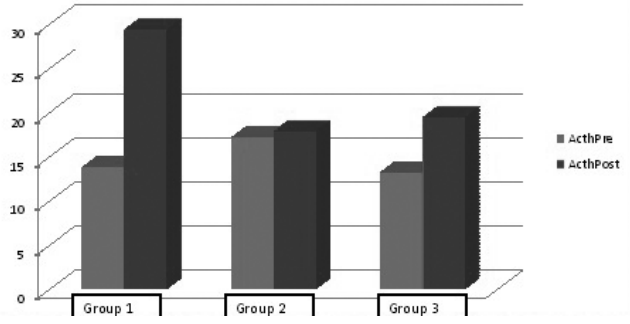
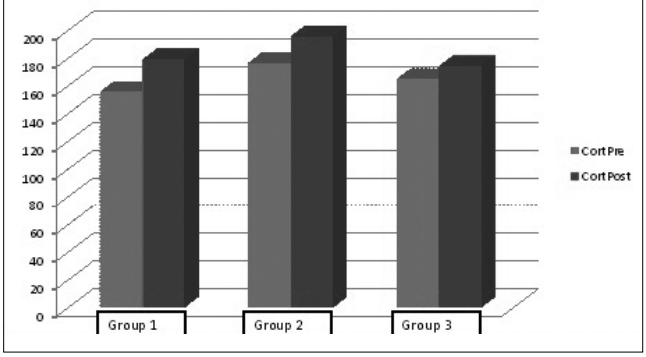


Figure 4. Comparison of cortisol before procedure (Cort Pre) and after procedure (Cort Post) values of patients in all thethree groups



The mean troponin before procedure (Trp Pre) in the midazolam and ketamine group was 1.22±0.37 ng/mL, whereas the mean Trp Pre in the midazolam and fentanyl group was 1.18±0.45 ng/mL. The mean Trp Pre in the propofol group was 1.48±0.54 ng/mL. A statistically significant difference was observed between the mean Trp Pre in the midazolam with fentanyl and propofol groups (p=0.026; Table 6).

DISCUSSION

The present study showed that sedative agents have statistically significant beneficial effects in reducing anxiety in port catheterized patients. Patients who are hospitalized or who are to be invasively treated often have anxiety. This resulting anxiety can affect the body's physiological response and pain perception (4). The body's physiological response to anxiety is a response of stress, which activates the hypothalamo-hypophyse-adrenal axis and sympathetic nervous system, resulting in stress hormone secretion (5). Anxiety is a problem that increases an individual's heart rate, blood pressure, body temperature, and respiratory rate. It decreases the pain threshold and increases postoperative analgesic requirements and the possibility of developing complications (6).

In a multicenter study assessing the effects of propofol and remifentanil with intravenous anesthesia in elective cases of 161 patients, Hogue et al. (7) reported that in addition to propofol, another opioid remifentanil infusion was added to the study and that they were able to quickly and efficiently control intraoperative stress.

In our study, the Beck Anxiety Scale was used to measure the anxiety level in patients. The results showed that midazolam with ketamine, midazolam with fentanyl, and propofol significantly reduced anxiety.

In a prospective study performed on 62 patients (31 in the ketamine/propofol group and 31 in the midazolam/fentanyl group) by Nejati et al. (8), the pain sensation in the ketamine/propofol group measured using VAS was significantly lower than that in the midazolam/fentanyl group.

In our study, VAS was also used to measure the level of pain. In conclusion, pain reduction in patients in the midazolam and ketamine group was not significant; however, pain reduction in the midazolam with fentanyl and propofol groups was significant.

Palpitation, elevation of blood pressure, and increase in respiratory rate are the physiological indicators of anxiety. Anxiety and stress can increase the number of pulsations, respiratory rate, and blood pressure by stimulating the nervous system and producing large amounts of stress hormone (5).

In a study conducted by Motov et al. (9) on 90 patients, 45 of which were in the ketamine group and 45 others in the morphine group, patients were treated with mean values of 21.8 mg ketamine or 7.7 mg morphine. No significant difference was observed between the two groups in terms of sociodemographic characteristics, basal vital findings, basal pain values, and com-

plaints. Significant reduction in pain scale value was observed in all patients at 15 and 30 minutes.

A study performed by Kramer et al. (10) aimed to compare propofol-ketamine and propofol-remifentanil infusions for sedation during the third molar tooth extraction; the intraoperative mean arterial pressure values decreased in both the groups compared with the pre-intervention values; however, this decrease was significantly different between both the groups.

In a study conducted by Funk et al. (11) on 120 pediatric patients using a combination of midazolam and ketamine, only midazolam, and only ketamine, no significant differences were observed between the vital parameters such as blood pressure, heart rate, and oxygen saturation at any stage of the study.

Chung et al. (12) reported that fentanyl was effective in suppressing tachycardia and hypertension in an attempt to measure hemodynamic response during anesthesia induction and intubation in elderly patients.

Arslan et al. (13) performed angiographic anesthesia for a case of nesidioblastosis with insulinoma and reported that an infusion of propofol and remifentanil did not impair hemodynamic stability in their study.

In the present study, midazolam and ketamine did not cause any significant changes in the systolic and diastolic blood pressure rates of patients. Patients treated with midazolam with fentanyl and propofol showed a significant decrease in the systolic and diastolic blood pressures in the results after procedure compared with those before procedure. In comparison with the measured systolic blood pressures during and after the treatment of midazolam with fentanyl and propofol in patients, a significant decrease in blood pressure was observed in patients treated with propofol. In comparison with the measured diastolic blood pressures of midazolam with fentanyl and propofol treated patients during the procedure, a significant decrease in blood pressure was observed in patients treated with propofol. No significant difference was observed between the diastolic blood pressures measured after the procedure.

In our study, the increase in pulse rates measured in follow-ups of patients who were treated with midazolam with ketamine and with fentanyl was statistically significant. The difference in the propofol group was not found to be statistically significant. Patients treated with midazolam and ketamine had a higher pulse rate during the procedure than the propofol group, and this difference was found to be statistically significant. No significant difference was observed between the respiratory rates measured before and after the procedure in the groups. In our study, the decrease in oxygen saturation in patient follow-ups in the midazolam with ketamine group was found to be statistically significant. No statistically significant difference was observed between the oxygen saturation of midazolam with fentanyl and propofol groups. The oxygen saturation rates of the patients in the midazolam and ketamine group were lower, and the difference was statistically significant compared with the oxygen saturation results of the midazolam with ketamine and propofol treated patient groups during and after the procedure.

Port catheters are most commonly placed percutaneously in the right internal jugular vein (14). In a study by Biffi et al. (15), 403 patients were administered intravenous chemotherapy, and the placement of the single port implant was randomly chosen either as percutaneous internal jugular vein, subclavian vein with coexistence of ultrasonography or cephalic vein in the deltopectoral groove with surgical cut-down. A total of 401 patients were evaluated, and internal jugular vein access was chosen in 132 patients, subclavian vein access in 136, and cephalic vein access in 133. In our study, USG was used, and the right internal jugular vein was the commonest access location (63%) for port catheterization.

The increased pain and anxiety experienced by the patients to be invasively treated increases the release of stress hormones by intraoperative stimulation of the afferents in the surgical area. ACTH, cortisol, epinephrine, and norepinephrine are frequently used as surgical stress markers. Cortisol is a corticosteroid hormone produced in the cortical region of the adrenal gland and is associated with the body's stress response. The reasons behind the change in serum cortisol levels include unusual ACTH levels, clinical depression, and physiological stress sources such as hypoglycemia, disease, fever, trauma, surgery, fear, pain, extreme cold or hot, and physical strain.

Several studies aimed to reduce the release of preoperative stress hormones. Gruber et al. (16) compared the different uses of fentanyl to the use of midazolam in addition to fentanyl to reduce the increase in stress hormones caused by surgery in children undergoing congenital heart surgery. It has been emphasized that congenital heart surgery has a significant stress response in children, and fentanyl treatment (with or without midazolam) could not prevent this stress response as reported in the study.

In a similar group of patients, Bell et al. (17) found that serum cortisol levels did not differ between groups when a combination of remifentanil compared with fentanyl-morphine; however, serum glucose levels were higher in the remifentanil group, and consequently, there was no difference between these two methods in the prevention of stress response to surgery.

Dönmez et al. (18) compared cortisol and ACTH levels using etomidate and ketamine in the pediatric cardiac surgery population. The cortisol level was increased in the ketamine group, whereas in the etomidate group, it was decreased after induction, remained low during bypass, and was close to the control value at the end of surgery. At all stages, cortisol levels were significantly lower in the etomidate group than in the ketamine group. In the etomidate group, ACTH slightly decreased after induction, started to rise with systolic blood prossure, and reached the highest value at the end of surgery. ACTH levels in the ketamine group also tended to increase from the beginning of the induction. Plasma ACTH concentrations were not significantly different between the two groups.

Adams et al. (19) measured plasma ACTH levels in patients treated with propofol and isoflurane and found that plasma cortisol, adrenaline, and noradrenaline levels were significantly lower in the propofol group than in the isoflurane group.

In a study performed by Gülbayrak et al. (20) to investigate the comparison of monitorization of neuromuscular blockage and the depth of inhalation anesthesia and propofol anesthesia and hemodynamic and neuroendocrine responses, plasma ACTH levels were postoperatively increased at 30 minutes and lowered at 24 hours compared with preoperative control values.

In a study investigating hormonal and hemodynamic changes in percutaneous nephrolithotomy cases, Atıcı et al. (21) reported that ACTH values were increased in the postoperative period compared with preoperative measurements.

In a comparative study comparing propofol and its application as an infusion, no significant difference was observed in the cortisol and glucose levels between both the groups; however, there was a significant decrease in insulin concentrations (22).

In our study, the increase in ACTH levels of patients treated with midazolam and ketamine, midazolam and fentanyl, and propofol was statistically significant. The ACTH level of the midazolam and ketamine group was higher than that of the midazolam and fentanyl group, and this difference was statistically significant. Stress-inducing conditions such as trauma, surgical intervention, shock, heavy infection, anxiety, and hypoglycemia can increase cortisol secretion up to 10 times through neural pathways in the brain.

In a study by Aono et al. (23) involving 52 patients from the ASA I-II group that underwent laparoscopic cholecystectomy, patients underwent general anesthesia, fentanyl-assisted general anesthesia, and epidural anesthesia combined with general anesthesia. They noted that the cortisol values increased immediately before surgery and half an hour after the start of the surgery in all the three groups.

In our study, the changes in cortisol levels after treatment with midazolam and ketamine, midazolam and fentanyl, and propofol were not statistically significant.

De Hert et al. (24) investigated the effects of propofol, desflurane, and sevoflurane on cardiopulmonary function in patients with coronary surgery and found that cardiac index values of patients significantly decreased under propofol anesthesia.

A study by Lowe et al. (25) investigated gene expression to recognize expression profiles and determine the metabolic pathways affected in ketamine-treated adult mice brains. Adult male mice were intraperitoneally injected with either ketamine (80 mg/kg) or distilled water (control group). The control group showed that 50 genes were differently expressed when compared with ketamine-treated mice brains, and the expression of troponin T1 gene was 2-4 times higher in concordance.

A study by Serinken et al. (26) aimed to determine the relationship between 1.5 mg/kg intravenous ketamine treatment for minor procedures and myocardial injury in children with a mean age of 2 years (quartile width, 1-4 years). High-sensitive troponin levels were measured before and 3 hours after the application of ketamine. A total of 30 patients were included in the study. Two patients had elevated troponin levels after 3 hours of ketamine application. The study concluded that ketamine may be associated with elevated troponin levels in children without causing permanent cardiac dysfunction in minor procedures.

In our study, the increase in high-sensitive troponin I levels after treatment with midazolam and ketamine, midazolam and fentanyl, and propofol was found to be statistically significant. No significant difference was observed between the groups because of high-sensitive troponin I levels after the procedure.

CONCLUSION

In conclusion, since sedative agents suppress sympathetic activity, application of sedative agents is an effective, safe, and easily applicable treatment method for minor surgical procedures in emergency service. We therefore recommend the application of simultaneous sedation for invasive procedures in the emergency service, so as to be more careful in terms of cardiac events because of the negative effects of simultaneous sedation to troponin values.

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REFERENCES

1. Camp-Sorrell D. Implantable ports: everything you always wanted to know. J Intraven Nurs 1992; 15: 262-73.
2. Carpenter A, Plum B. Cecil essentials of medicine, diabetic disorders. 4th edition. London: WB Saunders; 2000.p.533-45.
3. Reichlin T, Holchholzer W, Basetti S, Steuer S, Stetlzig C, Hartwiger S. Diagnosis of acute myocardial infarction using more sensitive troponin assays. N Engl J Med 2009; 361: 858-67.
4. Tan X, Yowler CJ, Super DM, Fratianne RB. The Efficacy of Music Therapy Protocols for Decreasing Pain, Anxiety, and Muscle Tension Levels During Burn Dressing Changes: A Prospective Randomized Crossover Trial J Burn Care Res 2010; 31: 590-7.
5. Pittman S, Kridli S. Music intervention and preoperative anxiety: an integrative review. Int Nurs Rev 2011; 58: 157-63.
6. İşkey M. Effects of Listening to Music Before and During Procedure of Angiography on Anxiety Levels and Vital Findings of Individuals, Post Graduate Thesis. Cumhuriyet University Institute of Medical Sciences. 2008.
7. Hogue CW, Bowdle TA, O'leary C, Duncalf D, Miguel R, Pitts M, et al. A multicenter evaluation of total intravenous anesthesia withremifentanil and propofol for elective inpatient surgery. Anesth Analg 1996; 83: 279-85.
8. Nejati A, Moharari RS, Ashraf H, Labaf A, Golshani K. Ketamine/propofol versus midazolam/fentanyl for procedural sedation and analgesia in the emergency department: a randomized, prospective, double-blind trial. Acad Emerg Med 2011; 18: 800-6.
9. Motov S, Rockoff B, Cohen V, Pushkar I, Likourezos A, McKay C, et al. Intravenous Subdissociative-Dose Ketamine Versus Morphine for Analgesia in the Emergency Department: A Randomized Controlled Trial. Ann Emerg Med 2015; 66: 222-9.
10. Kramer KJ, Ganzberg S, Prior S, Rashid RG. Comparison of propofol-remifentanil versus propofol ketamine deep sedation for third molar surgery. Anesth Prog 2012; 59: 107-17.
11. Funk W, Jakob W, Riedl T, Taeger K. Oral pre anaesthetic medication for children: double-blind randomize dstudy of a combination of midazolam and ketamine vs midazolam or ketamine alone. British Journal of Anaesthesia 2000; 8: 335-40.
12. Chung F, Evans D. Low-dosefentanyl: haemodynamic response during induction and intubation in geriatric patients. Can Anaesth Soc J 1985; 32:6 22-8.
13. Arslan M, Öztürk L, Güngör et al. A Case of Blastinoma with Insulinoma: Practice of Anesthesia in Angiography. Fırat Medical Journal 2005; 10: 86-8.
14. Holmes JH. Perspectives in ultrasonography: early diagnostic ultrasonography. Ultrasound Med 1983; 2: 33.
15. Biffi R, Pozzi S, Bonomo G, Della Vigna P, Monfardini L, Radice D, et al. Cost Effectiveness of different central venous approaches for port placement and use in adult oncology patients: evidence from a randomized three armtrial. Ann Surg Oncol. 2014; 21: 3725-31.
16. Gruber EM, Laussen PC, Casta A, Zimmerman AA, et al. Stres response in infants undergoing cardiac surgery: a randomized study of fentanyl bolus, fentanyl infusion and fentanyl-midazolam infusion. Anesth Analg 2001; 92: 882-90.
17. Bell G, Dickson U, Arana A, Robinson D, Marshall C, Morton N. Remifentanil vs fentanyl/morphine forpainandstres control during pediatric cardiac surgery. Paediatr Anaesth 2004; 14: 856-60.
18. Dönmez A, Kaya H, Haberal A, Kutsal A, Arslan G. The effect of etomidateinduction on plasmacortisollevels in childrenundergoingcardiacsurgery. J Cardiothorac Vasc Anesth 1998;12: 182-5.
19. Adams HA, Schmitz CS, Baltes-Gotz B. Endocrine stress reaction, hemodynamic sandrecovery in total intravenous and inhalation anesthesia propofol versus isoflurane. Anaesthesist 1994; 43: 730-7.
20. Gülbayrak H, Erhan ÖL, Önal A et al. Comparison of Monitorization of Neuromuscular Blockage and Depth of Anesthesia of Inhalation and Propofol Anesthesia and Hemodynamic and Neuroendocrine Responses, FU Medical Sciences Journal 2004; 18: 131-7.
21. Atıcı S, Zeren S, Arıbogan A. Hormonal and hemodynamic changes during percutaneous nephrolithotomy. Int Urol Nephrol 2001; 32: 311-4.
22. Venn RM, Bryant A, Hall GM, Grounds RM. Effects of dexmedetomidine on adrenocorticalfunction, andthecardiovascular, endocrineandinflammatoryresponses in post-operativepatientsneedingsedation in theintensivecareunit. Br J Anaesth 2001; 86: 650-6.
23. Aono H, Takeda A, Tave SD, Goto H. Stress responses in three different anesthetic tecniques for carbon dioxide laparoscopic cholecysecomy J ClinAnesth 1998;10: 546-50.
24. De Hert SG, Cromheecke S, ten Broecke PW, Mertens E, De Blier IG, Stockman BA, et al. Effects of propofol, desflurane, and sevoflurane on recovery of myocardial function after coronary surgery in elderly high-risk patients.Anesthesiology. 2003; 99: 314-23.
25. Lowe XR, Lu X, Marchetti F, Wyrobek AJ. The expression of troponin T1 gene is induced by ketamine in adult mouse brain. Brain Research 2007; 1174: 7-1.
26. Serinken M, Cenker E. Ketamine may be related to minor troponin elevation in children undergoing minor procedures in the EM. Am J Emerg Med 2015; 33: 904-6.

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