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Evaluation of the effect of analgesic nociceptive monitorization in cases of urological surgery undergoing general anesthesia and spinal anesthesia

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Abstract
Aim: In this study, it was aimed to identify and compare the effectiveness of spinal block and general anesthesia and to evaluate postoperative pain relations using the analgesic nociceptive index (ANI) monitoring in urologic surgery cases under general anesthesia and spinal anesthesia.
Material and Methods: Sixty patients were included in this study. The ANI palette was placed 2 cm below sternum xiphoid projection noninvasively, and ECG palette was placed to the V5 chest leads place, and ANI values after general anesthesia or spinal anesthesia and in set time intervals measurements were performed for each patient. In order to evaluate postoperative pain of patients, the visual analogue pain scale (VAS) and ANI values were recorded.
Results: Study groups were compared in terms of median ANI values at the intraoperative 0, 5, 10, 15, 20, 25, 30, 60, 90, and 120 Minutes, and there was no significant statistical difference between the two groups. Study groups were compared in terms of postoperative median ANI values. There was no significant statistical difference between the two groups. There was a low and negligible negative correlation between postoperative ANI values and postoperative VAS values. It was not statistically significant (P <0.05).
Discussion: When the study groups were compared, ANI values showed no significance in terms of intraoperative and postoperative measurements. The presence of a low and negligible negative correlation between postoperative ANI and VAS values measured in these groups is assumed to be insignificant.

Keywords
ANI, VAS, General Anesthesia, Spinal Anesthesia, Urologic Surgery

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Introduction

Postoperative pain is acute pain that begins with surgical trauma and gradually decreases with tissue healing [1]. In addition to the unpleasant feeling of postoperative pain, the stress, response, and hyper metabolism developed after surgery can impair the neuroendocrine system, respiratory system, cardiovascular and gastrointestinal system functions, and increase the rate of postoperative mortality and morbidity. Therefore, effective pain management is an important part of postoperative patient care [2].

Appropriate and adequate postoperative pain management is an important factor contributing to the acceleration of postoperative recovery and healing, shortening the hospital stay and reducing the management costs [3].

The Analgesic Nociceptive Index (ANI) calculates the parasympathetic reflex cycle strength. ANI is based on electrocardiography (ECG) data obtained using two electrodes placed on the patient's chest. The ANI index is indicated on a scale from 0 to 100. The displayed ANI value is the result of calculations made in an average of 64 seconds and progresses in 1-second windows. A patient experiencing pain responds to painful stimuli by activating his sympathetic tonus, so ANI values decrease with pain [4].

The Visual Analogue Scale (VAS) (0: The patient marked the severity of the pain on a 10 cm line, one end of which indicates no pain, and the other end represents unbearably severe pain) is a pain assessment scale [5].

The study aims to prevent misevaluation of pain perception as a result of anxiety during and after surgery in patients undergoing spinal anesthesia or general anesthesia, and to determine the effectiveness of spinal block under adequate sedation with adequate general anesthesia and spinal block without sedation before hemodynamic parameters, using analgesic nociceptive index monitoring, and thus, to detect the need for intraoperative sedation and anesthesia in the early period and to follow up postoperative pain with more objective criteria.

Material and Methods

The approval from the Clinical Trials Ethics Committee of Harran University Faculty of Medicine has been obtained (Approval No: 20.03.2015/3). The study is supported by Harran University Scientific Research Board with the date of 02/09/2015 and project no. 15100. Patients between the ages of 18-80, included in the I-II-III risk group of the American Society of Anesthesiologists (ASA), who were scheduled for elective endoscopic surgery between 01/10/2015 and 01/12/2015 in the operating room of Harran University Faculty of Medicine Research and Practice Hospital were included in the study. In any group, patients with liver and/or kidney failure, obese patients (BMI>30), trauma patients, cancer patients, ASA-IV patients, emergency surgery, cardiac arrhythmia, those with an implanted pacemaker, patients on beta blocker, those with a history of chronic pain, and those who did not want to participate in the study were considered as exclusion criteria. Sixty patients without exclusion criteria are included in the study. Study groups were divided into 3 groups with 20 patients in each group according to the type of anesthesia applied. Groups were determined by random matching. It is determined as Group1: general anesthesia, Group2: spinal anesthesia, Group3: spinal + sedation anesthesia. Patients to be included in the study were visited before surgery, and verbal and written consent was obtained one day before the operation. Age, comorbidities, previous surgeries, and drug use of the patients have been recorded.

In patients who were taken to the operating room without premedication, heart rate was monitored using ECG, non-invasive blood pressure, and peripheral oxygen saturation were monitored using pulse oximetry. General anesthesia has been prepared for possible complications. Peripheral vascular cannulation was performed on the dorsal side of the hand with a 20 G cannula, and an isotonic solution of 10 ml/kg/hour was given intravenously to finish in 30 minutes for pre-load. We performed fluid loading before anesthesia to prevent the negative effect of anesthesia-induced vasodilation on tissue perfusion by increasing intravascular volume.

All preparations (for induction of 0.1 mcg/kg remifentanil + 2 mg midazolam + 2 mg/kg propofol + for muscle relaxation with 0.6 mg/kg rocuronium) have been made for the group to be administered general anesthesia. Total intravenous anesthesia (TIVA) (propofol (4-6 mg/kg/h) + remifentanil (0.15 mcg/kg/min)) preparation has been made for the maintenance of general anesthesia.

The patients have been placed in a sitting position for spinal anesthesia. The lumbar region has been cleaned with an antiseptic solution and covered. After local anesthesia with 2 ml of 2% lidocaine was applied to all patients, 12.5 mg (the dose according to the desired level of the blockade) Bupivacaine hydrochloride (0.5% Heavy Marcaine, Dextrose monohydrate 80 mg/ml, Astra Zeneca, Turkey) was administered to the subarachnoid space after free CSF flow is observed by entering through the L3-4 space with a 25G Quincke spinal needle. At the end of the procedure, the patient was placed in a supine position and the head has been elevated. The sensorial block level of the patients is checked with the "Pinprick" test. After the block reached T4 level, the operation started. It has been done by recording ANI values and hemodynamic parameters to be obtained by placing an analgesic nociceptive index (ANI, MetroDoloris, Loos, France) palette 2 cm below the sternum xiphoid process in a non-invasive way in patients who will undergo urological surgery, and by placing the ECG palette in the region corresponding to the V5 chest derivation, in the forms prepared at the specified time intervals (0,5,10,15,20,25,30,60,90,120 minutes) during anesthesia application and after the anesthesia. In addition, visual analog pain scale (VAS: 0: no pain, 5: moderate pain, 10: excruciating pain) and postoperative ANI values have been recorded to evaluate postoperative pain of the patients (5,10,15,30,60 minutes) in the post-recovery unit.

Statistical Evaluation

The Chi-square test was used for categorical variables. One-way ANOVA (One-Way Analysis of Variance) test was used if the distribution is normal and the variances are homogeneous for continuous variables. Tukey's test was used as the Posthoc test to find out which groups the difference was associated with. Welch ANOVA test was used for continuous variables if the distribution was normal but the variances were not homogeneous. The Tamhane T2 test was used as the Posthoc

test to find out which groups the difference was associated with. If the distribution is not normal for continuous variables, the Kruskal-Wallis test was used and p<0.05 is accepted as significant. The groups were analyzed in pairs with the Mann-Whitney U test to find out which groups the difference was associated with, and the Bonferroni correction was used (p<0.05/3 is considered significant). Correlation coefficients and statistical significance were calculated with Spearman's test for the relationships between variables, at least one of which is not normally distributed. The results were evaluated at the 95% confidence interval, and the significance was at the p<0.05 level.

Results

The average age of the patients participating in the study was 47.5, with a minimum value of 18 and a maximum value of 80. When the study groups formed according to the type of anesthesia applied were compared in terms of average age, no statistically significant difference was found (p>0.05) (Table1).

The most common comorbidities detected in the participants are previous surgery with 23.33% followed by previous surgery + drug use with 20%. No concomitant disease was detected in 10% of the group.

The most common postoperative complication in the participants was hypertension with 3.33%, and the second most common complication was nausea-vomiting with 1.66%. The patients were given ondansetron 0.1 mg/kg (Ondaren 8 mg, Vem Medicine, Istanbul, Turkey) for the treatment of postoperative nausea, and antihypertensive medication was administered for hypertension. On the other hand, postoperative complications were not observed in 95% of the participants.

When the average ANI values of the study groups at intraoperative 0.5,10,15,20,25,30,60,90,120 minutes were compared, no statistically significant difference was found (p>0.05) (Table 2) (Figure 1).

When the study groups were compared in terms of mean ANI values at postoperative 5,10,15,30,60 minutes, no statistically significant difference was found (p>0.05) (Table 3).

There was a low or insignificant negative correlation between the postoperative ANI value and the postoperative 5,10,15,30,60-minute VAS value and it was not statistically significant (respectively r= -0.070 and p>0.05; r= -0.094 and p>0.05; r= -0.043 and p>0.05; r= 0.008 and p>0.05; r= -0.070 and p>0.05) (Figures 2, 3).

Table 1. Comparison of median age by study groups

	Group	n	Median	Min.	Max.	p
age	general anesthesia	20	41,5	24	80	0,234
	spinal anesthesia	20	45,5	18	77	
	Sedation	20	51,5	27	71	
	Total	60	47,5	18	80	

p<0.05 was considered statistically significant.

Table 2. Comparison of the medians of the intraoperative ANI value at 0.5,10,15,20,25,30,60,90,120 minutes according to study groups

Intraoperative Time-ANI values	Group	n	Median	Min.	Max.	P
0th min. ANI values	general anesthesia	20	75.0	23.0	81.0	>0.05
	spinal anesthesia	20	71.0	29.0	81.0	
	sedation	20	72.5	51.0	81.0	
	Total	60	73.0	23.0	82.0	
5th minute ANI values	general anesthesia	20	76.0	25.0	83.0	>0.05
	spinal anesthesia	20	70.0	31.0	81.0	
	sedation	20	73.5	47.0	81.0	
	Total	60	73.5	25.0	83.0	
10th minute ANI values	general anesthesia	20	75.0	29.0	83.0	>0.05
	spinal anesthesia	20	73.0	33.0	81.0	
	sedation	20	73.0	49.0	83.0	
	Total	60	73.0	29.0	83.0	
15th minute ANI values	general anesthesia	20	73.0	25.0	80.0	>0.05
	spinal anesthesia	20	73.5	27.0	83.0	
	sedation	20	70.5	47.0	81.0	
	Total	60	72.5	25.0	83.0	
20th minute ANI values	general anesthesia	20	74.0	25.0	80.0	>0.05
	spinal anesthesia	20	72.5	30.0	83.0	
	sedation	20	71.5	50.0	82.0	
	Total	60	73.0	25.0	83.0	
25th minute ANI values	general anesthesia	20	75.0	27.0	81.0	>0.05
	spinal anesthesia	20	71.0	32.0	81.0	
	sedation	20	69.5	51.0	81.0	
	Total	60	71.0	27.0	81.0	
30th minute ANI values	general anesthesia	20	74.0	29.0	78.0	>0.05
	spinal anesthesia	20	69.5	33.0	81.0	
	sedation	20	73.0	29.0	79.0	
	Total	60	71.0	29.0	81.0	
60th minute ANI values	general anesthesia	20	73.0	29.0	79.0	>0.05
	spinal anesthesia	20	69.0	31.0	83.0	
	sedation	20	68.0	56.0	80.0	
	Total	60	70.0	29.0	83.0	
90th minute ANI values	general anesthesia	20	71.0	29.0	79.0	>0.05
	spinal anesthesia	20	68.0	33.0	79.0	
	sedation	20	69.0	55.0	79.0	
	Total	60	70.0	29.0	79.0	
120th minute ANI values	general anesthesia	20	72.0	29.0	81.0	>0.05
	spinal anesthesia	20	69.5	33.0	79.0	
	sedation	20	70.5	55.0	79.0	
	Total	60	70.5	29.0	81.0	

p<0.05 was considered statistically significant.

Table 3. Comparison of the medians of the postoperative ANI value at 0.5,10,15,30,60 minutes according to the study groups

Postoperative time-ANI values	Group	n	Median	Min.	Max.	P
5th minute ANI values	general anesthesia	20	68	23	97	>0.05
	spinal anesthesia	20	68	23	81	
	sedation	20	68	41	81	
10th minute ANI values	general anesthesia	20	64	21	78	>0.05
	spinal anesthesia	20	70	28	81	
	sedation	20	69	49	81	
15th minute ANI values	general anesthesia	20	65.0	25.0	77.0	>0.05
	spinal anesthesia	20	69.0	31.0	79.0	
	sedation	20	66.5	47.0	81.0	
30th minute ANI values	general anesthesia	20	65	26	78	>0.05
	spinal anesthesia	20	71	30	83	
	sedation	20	65	46	81	
60th minute ANI values	general anesthesia	20	66.0	26.0	77.0	>0.05
	spinal anesthesia	20	72.0	29.0	81.0	
	sedation	20	65.0	39.0	83.0	

p<0.05 was considered statistically significant.

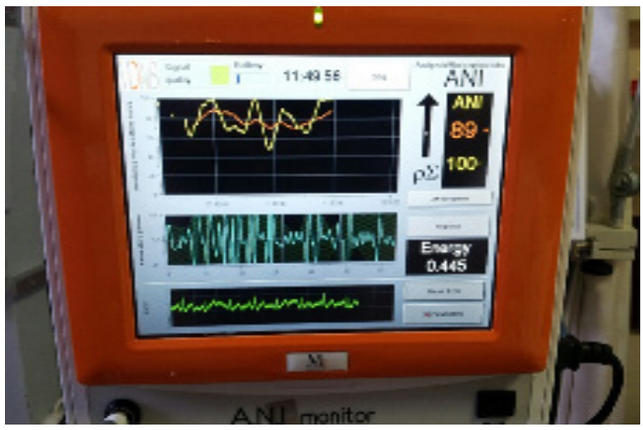


Figure 1. ANI parameters

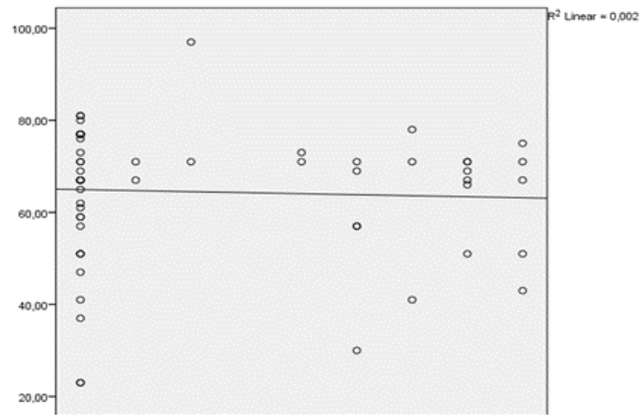


Figure 2. Relationship between VAS value and ANI value at postoperative 5th minute

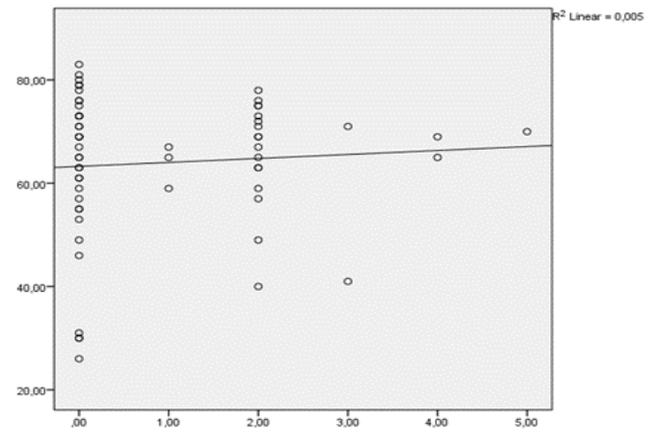


Figure 3. Relationship between VAS value and ANI value at the postoperative 30th minute

Discussion

The analgesic nociceptive index is a form of monitoring that has been used and popularized in the last few years. It has been frequently used and studied intraoperatively and postoperatively, especially in general anesthesia patients. Studies on ANI are increasing day by day, and publications are mostly made for the evaluation of pain during general anesthesia and postoperative pain. Publications on regional anesthesia have been limited to caudal and epidural anesthesia [6,7].

In our study, 60 elective urological cases were evaluated. They are divided into 3 groups as general anesthesia, spinal anesthesia, and spinal anesthesia under sedation. Intraoperative and postoperative ANI values have been measured. No significant difference was found intraoperatively in the measurements. No significant difference was found in the postoperative measurements. However, there was a low or insignificant negative correlation between postoperative ANI value and postoperative VAS value, but it was not statistically significant.

Logier et al. found the ANI index with the technique they described for the measurement of heart rate variability. The calculation of ANI is to build on the respiratory cycle flow over the R-R interval obtained from the ECG. Therefore, if the parasympathetic tonus is dominant, there will be a little decrease in heart rate with each inspiration and an increase in the R-R interval, which will cause respiratory arrhythmia. Filtered R-R analysis yields great variability. However, if the parasympathetic tonus is reduced, the effect of each respiratory cycle is diminished. Therefore, the effect of parasympathetic tonus on the R-R interval can be used to predict parasympathetic tonus, and consequently, the setting of analgesia and nociception can be predicted. Parasympathetic tonus decreases due to increased nociception depending on decreased analgesia or increased sympathetic activity, which leads to a decrease in ANI. ANI can provide a greater technological advantage, as it uses the wavelet formula (filters allow detection of individual frequency domains without phase shift, which allows distinguishing between sympathetic and parasympathetic effects), which is more mathematical than past pain parameters [8].

Le Guen et al. have evaluated labor pain by comparing ANI

values with VAS values in 45 pregnant women who had an epidural catheter. Regular measurements were made during uterine contractions and also every 5 minutes, and obtained results were parallel to VAS values [6].

Migeon et al. used ANI monitoring for the early assessment of pain after skin incision in 58 pediatric cases over 2 years of age who underwent caudal anesthesia and supplemented with sevoflurane inhaled anesthetic. They have stated that the patients are administered regional anesthesia during sevoflurane inhalation and that an increase of more than 10% during the surgical incision showed that the block is ineffective. Nineteen cases were evaluated as an unsuccessful block. They have found that pupil diameter monitoring (PD) changes were consistent with ANI [7].

In their study of 120 patients, Abdullayev et al. accepted the numerical rating scale (NRS) as the subjective component of pain and ANI values as the objective component of pain. They stated that there was a negative linear relationship between ANI and NRS and stated that higher NRS values meant lower ANI scores in case of pain [9].

In the study by Dostalova et al., seventy-two adults scheduled for elective neurosurgery spinal procedures were randomized into the ASA I-III patient ANI group, the Surgical Plethysmographic Index (SPI) group, and the control group, and it was stated that the intraoperative use of anesthesia and opioids was managed according to a strict protocol. They reported that both ANI and SPI guidance significantly changed intraoperative opioid use, but no changes were observed in postoperative cortisol levels and postoperative pain [10].

Jiao et al. presented a meta-analysis of ten studies examining the effects of Analgesia Nociception Index, Surgical Plet Index (SPI), and pupillometry monitoring methods in terms of intraoperative opioid administration and analgesia method. In the meta-analysis, it has been found that nociception measurement-guided analgesia reduces intraoperative opioid consumption compared to conventional analgesia, and that SPI-guided intraoperative opioid administration was less than traditional analgesia, and that the difference between ANI-guided analgesia and standard clinical care was not statistically significant [11].

Although it was stated in previous studies that ANI monitoring is effective in detecting the need for intraoperative opioids in the early period and monitoring postoperative pain, our results support the work of Dostalova and Jiao. Considering the VAS values, we have evaluated that ANI is not an effective monitoring technique in the intraoperative and postoperative pain follow-up of patients, since it has a low and insignificant negative correlation with ANI.

Our study has had several limitations. Although ethical committee approval and voluntary participant consent were obtained, no clinical trial registration was made. We have had three groups as general, spinal, spinal + sedation. Our results may have been influenced by the choice of anesthesia and the opioid strategy used in the groups. Differences in the unmeasured depth of anesthesia may have affected the observed results. Due to the limited sample size, our study was not powerful enough to detect more subtle differences between groups in the postoperative period.

Conclusions

As a consequence, we found that the use of ANI as a form of pain monitoring that can provide an independent, continuous, non-invasive measurement of intraoperative and postoperative pain is not significant in urological cases under general anesthesia, spinal anesthesia, and sedated spinal anesthesia.

Although it is concluded in our study that the use of ANI monitoring in both intraoperative and postoperative pain control monitoring is not significant, it should be supported by new studies to be carried out in this direction, and thus, the use of ANI monitoring in patients receiving anesthesia will become more convenient.

Scientific Responsibility Statement

The authors declare that they are responsible for the article's scientific content including study design, data collection, analysis and interpretation, writing, some of the main line, or all of the preparation and scientific review of the contents and approval of the final version of the article.

Animal and human rights statement

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. No animal or human studies were carried out by the authors for this article.

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Conflict of interest

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