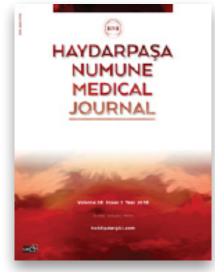
HAYDARPAŞA NUMUNE MEDICAL JOURNAL

DOI: 10.14744/hnhj.2018.71676
Haydarpasa Numune Med J 2019;59(2):128–135



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ORIGINAL ARTICLE

Comparison of Brain Natriuretic Peptide (BNP) Levels in Patients Under General or Spinal Anesthesia

Nurettin Kurt[1], Mustafa Murat Kaşıkçı[2], Özcan Pişkin[3], Volkan Hancı[4], Mustafa Sakın[5]

[1]Department of Anesthesiology and Reanimation, Darica Farabi Public Hospital, Kocaeli, Turkey
[2]Department of Anesthesiology and Reanimation, Fulya Acibadem Hospital, Istanbul, Turkey
[3]Department of Anesthesiology and Reanimation, Zonguldak Karaelmas University Faculty of Medicine, Zonguldak, Turkey
[4]Department of Anesthesiology and Reanimation, Dokuz Eylul University Faculty of Medicine, Izmir, Turkey
[5]Department of Anesthesiology and Reanimation, Rize Public Hospital, Rize, Turkey

Abstract

Introduction: Many hemodynamic parameters are affected according to selected anesthesia type in patients under general or spinal anesthesia. In recent years, brain natriuretic peptide (BNP) has been frequently used in clinical follow-up. It is released from the heart ventricles and is directly proportional to increased ventricular dilatation and pressure load, suggesting cardiac performance. We aimed to compare the cardiac effects of general and spinal anesthesia with BNP values in noncardiac small surgical operations where hypovolemia is unexpected.

Methods: The study was conducted between January and May 2009 after obtaining the approval from the ethics committee at the Haydarpaşa Numune Training and Research Hospital. Our patient group consisted of 44 patients (15 women and 29 males), aged between 45 and 80 years, scheduled for ASA 2-3, NYHA 2-3, describing exercise dyspnea at the end of 5 min walking test, with an ejection fraction of 40%–55%, hypovolemia unexpected small surgery planned (inguinal hernia, urinary incontinence, rectocele, cystocele, etc.). Patients were randomly assigned to two groups to receive general anesthesia and spinal anesthesia. Venous blood was taken, and the BNP levels were measured 30 min before the operation, 25 min after anesthesia, and 8 h after the operation.

Results: In General and Spinal Anesthesia group, there was no significant change in the 25th-min BNP level according to the preoperative BNP level ($p>0.05$); the increase in the 8th-hour BNP level was statistically significant ($p<0.01$). There was no statistically significant difference between the groups in terms of percent change in 25-min BNP level according to preop ($p>0.05$), while the percent change in BNP level at 8th hour according to preop of spinal anesthesia group was significantly higher than general anesthesia group ($p<0.05$).

Discussion and Conclusion: In our study, postoperative BNP increase was observed in patients who underwent both general and spinal anesthesia. This increase is statistically more significant in spinal anesthesia. This difference shows that the cardiac performance of patients in the spinal anesthesia group is more affected.

Keywords: Brain natriuretic peptide (BNP); general anesthesia; spinal anesthesia.

In patients undergoing general or spinal anesthesia, the type of anesthesia selected affects many hemodynamic parameters. Heart rate, rhythm, myocardial contractility, and changes in vascular tone are mediated by the autonomic nervous system. In patients undergoing general anesthesia, increase in catecholamine levels due to intubation and excessive excitation during induction phase and hypertension depression of myocardial contractility, myocardial ischemia, and hypertension related to postoperative pain related may be seen. In patients undergoing

Correspondence (İletişim): Nurettin Kurt, M.D. Kocaeli Darica Farabi Egitim ve Arastirma Hastanesi, Anesteziyoloji ve Reanimasyon Klinigi, Kocaeli, Turkey
Phone (Telefon): +90 505 678 22 55 **E-mail (E-posta):** nurettinkurt@gmail.com

Submitted Date (Başvuru Tarihi): 20.02.2018 **Accepted Date (Kabul Tarihi):** 19.04.2018

spinal anesthesia, cardiac output may be reduced dependent on the level of the block, and bradycardia due to hypotension and blockade of sympathetic fibers may occur.

The value of laboratory and diagnostic methods used in predicting perioperative cardiac morbidity is of great importance, and related studies are underway.

Brain natriuretic peptide (BNP) has been frequently applied in clinical follow-up in recent years. It is released from the heart ventricles and increases in proportion to ventricular enlargement and pressure load and gives an idea about cardiac performance. Type B natriuretic peptide is released from cardiac ventricles in response to ventricular volume expansion and pressure overload; This neurohormone regulates blood pressure, electrolyte balance, and fluid volume. Several studies have shown that the amount of released BNP is directly proportional to ventricular volume expansion, pressure overload, and heart failure [1–3].

This study aimed to compare the cardiac effects of general and spinal anesthesia in consideration of BNP values in noncardiac minor surgical operations in which hypovolemia is not anticipated.

Materials and Methods

The study was carried out between January and May 2009 at Haydarpaşa Numune Training and Research Hospital general surgery operating room. Our study population consisted of 44 ASA 2-3, NYHA 2-3 (15 female and 29 male) patients aged 45–80 years, with ejection fraction of 40%–55%, who were scheduled for minor surgery for inguinal hernia, urinary incontinence, rectocele, cystocele, and so on. The patients without any expectation for hypovolemia described exertional dyspnea at the end of 5-min walking test.

Patients with serum creatinine levels above 2 mg/dl, and those with established diagnoses of decompensated heart failure, cardiomyopathy, newly onset myocardial infarction, morbid obesity, neuromuscular disease, and pregnants, also individuals in whom spinal anesthesia was contraindicated, or patients who do not accept the procedure and those who will undergo surgeries lasting more than 110 min criteria were not included in the study.

The patients were given 0.5 mg IV atropine and 5 mg IV diazem as premedication 45 min before surgery. During the preoperative visit, all patients were informed about the study, and their written approvals were obtained.

Venous blood samples of 5 ml were obtained from the patients at 30 min before surgery, at the 25th min of induction of anesthesia, and at the 8th hour after surgery in the EDTA containing tubes. The BNP measurements were performed using Centaur BNP kits, in Beckman Coulter Access 2 immunoassay analyzer.

Vascular access was opened using a 20 G intravenous cannula in the preoperative preparation room. The patients were monitored by Petas Monitor NOKMA 265 R; and systolic arterial pressure (SAD), diastolic arterial pressure (DAB), mean arterial pressure (MAP), heart rate (HR), and oxygen saturation (SpO_2) measurements were noninvasively performed. Crystalloid 0.9% NaCl was initiated as 15 ml/kg/h infusion rate and continued until the end of the operation.

The patients were randomly divided into two groups for general and spinal anesthesia.

Patients undergoing spinal anesthesia were brought to a sitting position. Insertion site of spinal needle was cleaned under sterile conditions. A suitable intervertebral space (L3-4 or L4-5) was detected, and a 25 G or 26 G spinal needle was inserted into the spinal space from the midline. After clear cerebrospinal fluid (CSF) flow was observed, 3 ml (5 mg/ml) 0.5% hyperbaric bupivacaine was slowly injected into intrathecal space. The patients were brought into the supine position, and their head sides were elevated for 30°. Sensory block levels of the patients were evaluated with pinprick test and dermatome level. The level is planned to be in the T8-T6 dermatome area. Postoperative hemodynamic parameters (SAB, DAB, OAB, SPO_2, CAD) were recorded at 1, 5, 10, 25, 45, 60 min after induction of anesthesia.

Preoxygenation was performed with 100% oxygen for 3–5 min in patients undergoing general anesthesia. Anesthesia was induced with 1 mcg/kg fentanyl, 5 mg/kg thiopental, and 0.1 mg/kg vecuronium. Endotracheal intubation was performed after muscle relaxation. Controlled ventilation was performed at tidal volume of 8–10 ml/kg and respiratory frequency of 10–12/min. Anesthesia was maintained with 50% O_2 and 1% MAC sevoflurane in 50% N_2O. Muscle relaxation was achieved with 0.01 mg/kg vecuronium. Hemodynamic parameters (SAB, DAB, OAB, SPO_2, HR) were recorded at 1, 5, 10, 25, 45, 60 min after induction and postoperatively. At the end of the surgery, muscle relaxants were antagonized, and the patients were extubated while they were fully awake to reduce the risk of aspiration.

Statistical Analysis

For the statistical evaluation of study data, the NCSS 2007 & PASS 2008 Statistical Software (Utah, USA) program was used. Descriptive statistical methods (mean, standard deviation) were employed to evaluate the data. For the intergroup comparisons of quantitative data with normal distribution Student t test, and for intergroup comparisons of parameters with non-normal distribution, Mann–Whitney U test was employed. The paired sample t test was used for intragroup comparisons of the normally distributed parameters. Chi-square test was used to compare qualitative data. Spearman's Rho correlation test was used to examine the relationships between the parameters. The results were evaluated at 95% confidence interval and at a significance level of $p<0.05$.

Results

The study was carried out on 44 patients (29 male (65.9%) male and 15 female (34.1%)) aged between 45 and 80 years. The mean age of the cases was 59.48±9.98 years. The cases were divided into general anesthesia (n=22) and spinal anesthesia (n=22) according to the type of anesthesia given. The duration of operation varied between 40 min and 110 min (mean 64.52±14.59 min).

In the General Anesthesia Group

There was no statistically significant relationship between the age and percent change in BNP values at 25th min and 8th hour in comparison with preoperative values, and percent change in 8th-hour BNP values relative to 25-min values and age ($p>0.05$).

In the Spinal Anesthesia Group

There was no statistically significant relationship between the age and percent change in BNP values at 25th min and 8th hour in comparison with preoperative values, and percent change in 8th-hour BNP values relative to 25-min values and age ($p>0.05$).

No statistically significant difference was found between the percent change in BNP levels at the 25th min and 8th hour compared to preoperative values and also between 8th-hour and 25th-min BNP values according to gender ($p>0.05$).

No statistically significant difference was found between the groups according to MAP levels in the preoperative period ($p>0.05$).

The MAP levels at the 5th min of general anesthesia were statistically significantly higher than the patients undergoing spinal anesthesia ($p<0.05$).

The MAP levels at the postoperative 25th and 40th min were significantly higher than the patients undergoing spinal anesthesia ($p<0.01$).

In the General Anesthesia Group

No statistically significant change was observed between 5-min, 25-min, 40-min, and postop MAP levels relative to preoperative MAP levels ($p>0.05$).

In the Spinal Anesthesia Group

Decreases in the 5-min, 25-min, 40-min, and postop MAP levels were statistically significant when compared with preoperative MAP levels ($p<0.01$).

General Anesthesia Spinal Anesthesia

No statistically significant intergroup difference was found as for mean pulse rates in the preoperative period, 5 min, 25 min, 40 min, and in the postoperative period ($p>0.05$).

In the General Anesthesia Group

No statistically significant change was seen in the mean pulse rates detected in the preoperative period, and at 5 min, 25 min, 40 min, and in the postoperative period ($p>0.05$).

In the Spinal Anesthesia Group

No statistically significant change was seen in the mean pulse rates detected in the preoperative period, and at 5 min, 25 min, 40 min, and postoperative period ($p>0.05$).

General Anesthesia Spinal Anesthesia

There was no statistically significant difference between the groups in terms of mean BNP values at the 25th and 8th hours, and in the preoperative period ($p>0.05$).

General and Spinal Anesthesia Group

There was no significant change in BNP levels at the 25th min relative to preoperative BNP levels ($p>0.05$). The increase in BNP levels at 8th hour was statistically significant ($p<0.01$).

There was no statistically significant difference between the groups at the 25th min BNP level relative to preoperative levels ($p>0.05$).

The percent change in the BNP level at the 8th hour of the spinal anesthesia group was significantly higher when compared with the general anesthesia group ($p<0.05$).

There was no statistically significant difference between the groups in terms of percent change in the BNP levels at the 8th hour relative to the 25th-min BNBP values ($p>0.05$).

Discussion

A careful evaluation of risk factors for preoperative cardiac disease in patients with heart failure or cardiovascular disease is important for the selection of anesthetic agents to be administered using an appropriate method of anesthesia. The method of anesthesia and agent selected must be appropriate and tolerable by the patient and surgical intervention.

Many parameters assess the extent of known cardiovascular effects of general and spinal anesthesia. In our study, we aimed to evaluate the cardiovascular effects of anesthetic methods according to preoperative, perioperative, and postoperative BNP values of the patients. BNP is a protein consisting of 32 amino acids released from cardiac ventricles in response to myocyte tension. It is the strongest hormonal determinant of left ventricular dysfunction, and its plasma levels are correlated with left ventricular filling pressures. For these reasons, we planned our study predicting that there may be a relationship between the cardioprotective effects of the selected anesthesia method and BNP level.

In our study, there was no significant difference between the spinal and general anesthesia groups in terms of age, BMI (body mass index), duration of operation, and gender distribution (Table 1). The importance of this is that measured BNP levels are affected by age, BMI, and gender as well as cardiac performance. To evaluate the effect of the selected anesthesia method on BNP, we aimed to have other parameters affecting the BNP at the comparable levels.

In our study, there was no statistically significant correlation between BNP percent changes according to age and gender (Tables 2, 3, 4).

General anesthetics, especially inhalation anesthetics, may cause impaired renal function as a result of their multiple effects. Sympathetic blockade associated with regional anesthesia (spinal or epidural) may similarly lead to increased venous capacity and hypotension due to arterial vasodilation. However, it is not as severe as seen in general anesthesia, and it is parallel to the extent of sympathetic blockade. Causes of high plasma BNP levels in patients with renal dysfunction may include extracellular fluid increase, concomitant cardiac disease, and decreased renal natriuretic peptide clearance [4].

Considering that the measured BNP values increased in renal failure, we excluded patients with creatinine levels above 2 mg/dl. In the assessment of cardiac function and volume burden in CRF, the BNP levels in patients with renal insufficiency were found to be higher in patients with renal insufficiency compared to those without renal failure [5].

The BNP levels are affected by age, gender, BMI, and renal function, and may lead to misinterpretation of cardiac dysfunction when used per se. We think that the evaluation should be supported by physical examination, other biochemical markers, and cardiac tests.

Dobson et al. compared spinal and general anesthesia hemodynamically in patients who underwent transurethral resection of prostate (TURP), and detected greater number

Table 1. Evaluation of general characteristics according to groups

	General anesthesia	Spinal anesthesia	p
+Age	56.95±9.78	62.00±9.73	0.094
+BMI	24.33±3.88	26.59±4.26	0.073
+Duration of operation	66.55±15.32	62.50±13.86	0.364
	n (%)	**n (%)**	
++Gender			
Male	15 (68.2)	14 (63.6)	0.750
Female	7 (31.8)	8 (36.4)	0

+Student t test; ++Chi-square test.

Table 2. Correlation of age and BNP percent change levels

	Age			
	General Anesthesia		**Spinal Anesthesia**	
	r	**p**	**r**	**p**
Percent change in BNP at 25 min relative to preoperative values	0.164	0.466	0.075	0.740
Percent change in BNP at 8 h relative to preoperative values	0.218	0.329	-0.093	0.682
Percent change in BNP at 8 h relative to 25 min	-0.021	0.926	-0.102	0.652

Spearman's Rho test was used.

Table 3. Evaluation of percent change in BNP values according to gender of the patients

	Male Mean±SD (Median)	Female Mean±SD (Median)	p
Percent change in BNP at 25 min relative to preoperative values	-0.97±23.73 (-2.40)	-7.70±30.61 (-3.59)	0.814
Percent change in BNP at 8 h relative to preoperative values	90.36±89.08 (66.10)	68.09±80.97 (35.45)	0.250
Percent change in BNP at 8 h relative to 25 min	94.04±74.56 (88.37)	111.89±131.67 (68.00)	0.629

Mann–Whitney U test.

of hemodynamic changes in general anesthesia they performed using fentanyl, etomidate, vecuronium bromide when compared with spinal anesthesia performed with hyperbaric bupivacaine. In the general anesthesia group, they attributed decreases in stroke volume due to the controlled respiration, decrease in venous return, and HR [6]. In our study, we thought that hypotension in patients undergoing spinal anesthesia was due to sympathetic block applied at higher levels (Table 5, Fig. 1). We revealed that spinal anesthesia induced hemodynamic changes more frequently than a balanced general anesthesia practice.

The mean pulse rates of the groups were compared. In the general anesthesia group, no statistically significant change was observed in the average pulse rates measured at 5 min, 25 min, 40 min, and in the postoperative period when compared with the preoperative measurements. The decrease in the mean postoperative pulse rate in the spinal anesthesia group was found to be statistically significant when compared with the preoperative values (Table 6, Fig. 2). With these findings, it can be said that hemodynamic changes in spinal anesthesia lead a more aggressive course than general anesthesia. Hemodynamic differences can be attributed to the high level of the sympathetic block in spinal anesthesia.

To reduce postoperative mortality and morbidity, it is important to determine the high-risk group of patients preoperatively. Cardiovascular diseases play an important role in mortality and morbidity. BNP is an important biochemical parameter used in determining cardiovascular risk [7]. In the study conducted by J. Dernellis and M. Panaretou, 1590 patients who had undergone noncardiac surgery were evaluated, and it was revealed that only increased BNP levels indicated cardiac risk. In their study, they emphasized that BNP is a noninvasive and easily performed biochemical test, and the results have important implications [8]. In their study with 41 patients undergoing non-

Table 4. Evaluation of preoperative BNP values according to gender

	Male Mean±SD	Female Mean±SD	p
Preop BNP	89.48±35.95	105.13±42.25	0.814

Student t test.

Table 5. Evaluation of mean arterial pressure (MAP) values in groups

MAP	General anesthesia Mean±SD	Spinal anesthesia Mean±SD	+p
Preop	102.64±18.99	106.23±13.30	0.472
5 min	107.00±18.49	95.45±12.30	0.019*
25 min	101.95±17.42	88.18±10.99	0.003**
40 min	106.73±15.88	89.36±13.69	0.001**
Postop	100.95±14.05	87.14±13.64	0.002**
Preop-5 min ++p	0.457	0.001**	
Preop-25 min ++p	0.882	0.001**	
Preop-40 min ++p	0.287	0.001**	
Preop-postop ++p	0.603	0.001**	

+Student t test; ++Paired sample t test; *p<0.05; **p<0.01.

Table 6. Evaluation of pulse rates according to groups

Pulse	General anesthesia Mean±SD	Spinal anesthesia Mean±SD	+p
Preop	75.14±13.89	77.95±13.46	0.498
5 min	79.09±16.28	78.36±12.68	0.869
25 min	71.41±12.76	74.32±15.33	0.498
40 min	71.41±12.19	74.64±15.12	0.440
Postop	70.86±11.26	73.00±14.30	0.585
Preop-5 min ++p	0.205	0.802	
Preop-25 min ++p	0.240	0.112	
Preop-40 min ++p	0.211	0.135	
Preop-postop ++p	0.122	0.028*	

+Student t test; ++Paired sample t test; *p<0.05; **p<0.01.

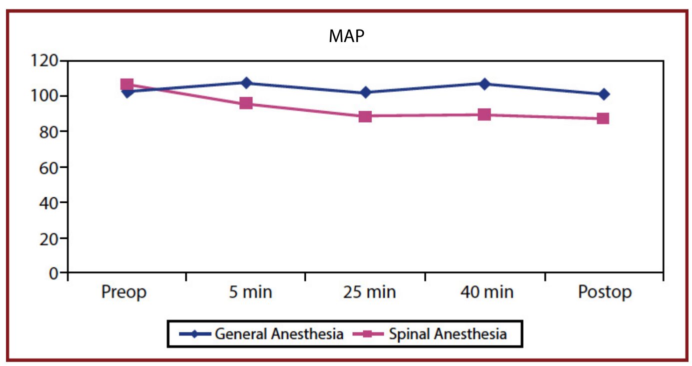

Figure 1. MAP graph.

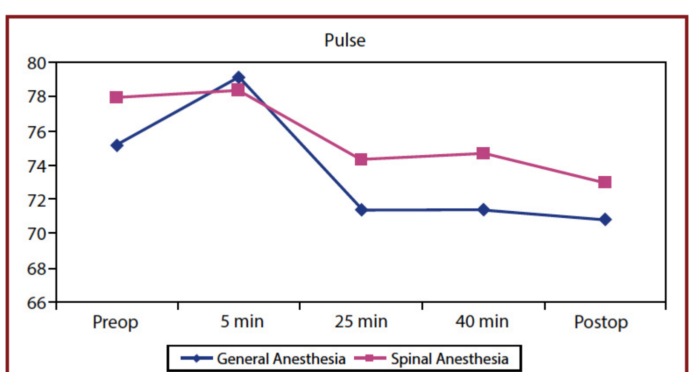

Figure 2. Pulse rate graph.

cardiac surgery, S. C. Gibson et al. [9] found that patients with high BNP levels preoperatively had a higher cardiac risk and were more exposed to postoperative cardiac problems. We did not encounter preoperatively high BNP values in our study because the patients had no advanced cardiac problems. Preoperatively, the highest level of BNP value was 148 pg/ml in our study. The postoperative 8th-hour BNP value of this patient was 324 pg/ml. The patient was receiving medical treatment because of preoperative diagnosis of HT and DM. Any adverse event was not observed during the postoperative clinical follow-up of this patient who was under our clinical surveillance.

It is obvious that every surgical procedure that patients are exposed to has certain cardiac risks with the contribution of anesthetic methods and drugs. Numerous studies have been carried out to reveal the relationship between risks and anesthetic methods. In a study of 423 patients who underwent peripheral vascular surgery, Bode et al. [10] compared epidural, spinal, and general anesthesia methods. Although small hemodynamic changes were detected among the groups, they showed that the selected anesthesia method had no effect on mortality and morbidity. N.D. Edwards et al. [11] showed that the incidence of postoperative myocardial ischemia increased in 100 patients who had to undergo transurethral surgery. However, when the general and spinal anesthesia methods used in these patients were compared, no significant difference was found as for the frequency of postoperative myocardial ischemia. N. Şenoğlu et al. [12] studied the effect of general and spinal anesthesia on maternal cardiac enzymes (CK-MB, myoglobin, troponin I, pro BNP) in 50 cesarean cases without cardiac disease. They found no significant increase in myocardial damage and enzyme levels between general and spinal anesthesia groups and concluded that the choice of anesthesia should be done according to the patient's wishes. In our study, the increase in BNP levels at the 8th hour relative to BNP level in the preoperative period in both general and spinal anesthesia patients was statistically significant (Table 7, Fig. 3). We thought that the reason for this elevation may be due to the volume added to the circulation after perioperative peripheral vasodilatation occurred in patients under general and spinal anesthesia. In addition, we concluded that crystalloid fluid replacement for patients may also contribute to this hypervolemia. Considering these factors, we can say that cardiac problems due to anesthesia may occur in patients with apparent cardiovascular disease, and BNP is an important cardiac marker to detect this abnormality.

S. Roult et al. [13] investigated maternal and fetal enzyme levels in 15 cesarean cases who received spinal anesthesia. They detected a 'non-acute' increase in maternal ANP and BNP levels and correlated this increase to the crystalloid fluid replacement they applied to prevent development of hypotension. In our study, no significant difference was found between the spinal anesthesia group and the general anesthesia group as for the 25th-min BNP levels compared to the preoperative levels (Table 8). There was no

Table 7. Evaluation of BNP values in groups

BNP	General anesthesia Mean±SD	Spinal anesthesia Mean±SD	$^{+}$p
Preop	100.14±42.82	89.50±33.70	0.365
25 min	95.50±49.48	89.36±44.35	0.667
8 hour	145.45±58.02	165.59±61.42	0.270
Preop-25 min $^{++}$p	0.275	0.979	
Preop-8 hour $^{++}$p	0.001**	0.001**	

$^{+}$Student t test; $^{++}$Paired sample t test; *p<0.05; **p<0.01.

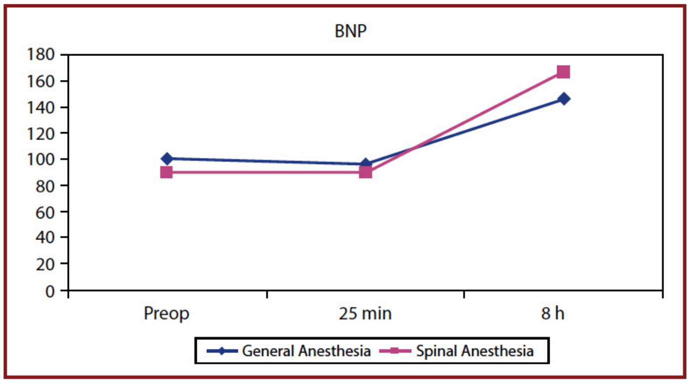

Figure 3. BNP graph.

Table 8. Evaluation of BNP percent changes in groups

	General Anesthesia Mean±SD (Median)	Spinal Anesthesia Mean±SD (Median)	P
Percent change in BNP at 25 min relative to preoperative values	-5.99±23.76 (-3.72)	-0.53±28.59 (-0.82)	0.656
Percent change in BNP at 8 h relative to preoperative values	63.60±94.14 (50.39)	101.94±74.51 (85.75)	0.044*
Percent change in BNP at 8 h relative to 25 min	85.65±102.46 (57.62)	114.61±90.46 (94.41)	0.091

Mann Whitney U test; *p<0.05.

difference between the groups in terms of MAP and pulse rates at the 25th min (Tables 5, 6).

When the half-life of BNP is considered to be 20 min, and if one thinks that hypotension due to sympathetic blockage emerging 25 min after the spinal anesthesia, and peripheral vascular pooling developing due to the effects of cardiac depression and peripheral vasodilatation caused by general anesthesia exert similar effects, naturally a significant difference was not seen between BNP levels in both groups.

However, the percent change in the BNP level at the 8th hour in the spinal anesthesia group was significantly higher than in the general anesthesia group (Table 8). This difference manifesting postoperatively gives an idea concerning the difference between groups regarding cardiac functions and demonstrates that cardiac performances of the patients receiving spinal anesthesia are more severely affected. Any changes were not observed during clinical and ECG monitorizations. We believe that this is because the patient group we selected consisted of patients with low cardiac risk. We think in spinal anesthesia, increase in BNP levels is due to the addition of greater volumes fluid into the circulation compared to general anesthesia indicates a significant difference between groups. In addition, we can say that crystalloid fluid replacement also contributes to volume increase. The high level of sympathetic block in spinal anesthesia together with more prominent hypotension and peripheral vascular pooling compared to general anesthesia induced hypervolemia. R. Ohara et al. [14] reported that BNP is an important marker of blood volume in patients who had undergone cesarean delivery under spinal anesthesia and BNP increased as the volume increased.

It should be kept in mind that perioperative deep hypotension may cause postoperative cardiac risks in patients with higher BNP levels preoperatively. K. Terasako showed that in patients with preoperatively higher BNP levels who had arthroplasty and cement placement perioperative hypotension and later on cardiac problems were more frequently observed [15]. The choice of anesthesia method and perioperative fluid replacement regimen is becoming more important in high-risk patients who will undergo surgery.

Conclusion

BNP is one of the important markers that predict postoperative cardiac risk in patients with cardiovascular problems who will undergo surgery.

In our study, increase in BNP levels was observed postoperatively in patients who had undergone general or spinal anesthesia. In both anesthesia techniques, we think that perioperative hypotension, peripheral vascular pooling due to peripheral vasodilatation and the addition of this volume to the circulation together with crystalloid fluid replacement is effective in the increase in BNP levels. This increase was statistically more significant in spinal anesthesia. This difference shows that the cardiac performance is more severely affected in the spinal anesthesia group.

Considering the fact that our study was performed with a low number of cases, we believe that larger scale relevant studies should be conducted.

Peer-review: Externally peer-reviewed.

Authorship Contributions: Concept: N.K.; Design: M.M.K.; Data Collection or Processing: M.S.; Analysis or Interpretation: Ö.P.; Literature Search: V.H.; Writing: N.K.

Conflict of Interest: None declared.

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

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