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# Comparison of the Effects of Colloid Preload and Ephedrine Bolus Administration on Left Ventricular Loading and Quality of Spinal Anesthesia

**Onur Özlü[1], Süreyya Aydin[2], Ebru Salman A[3]*, Mustafa Aksoy[4] and Mustafa Çağatay[5]**

[1]*Anesthesiology and Reanimation Depatment, Dışkapı Yıldırım Beyazıt Research and Educational Hospital, Ankara, Turkey*
[2]*Resident in Trainning, Anesthesiology and Reanimation Depatment, Dışkapı Yıldırım Beyazıt Research and Educational Hospital, Ankara, Turkey*
[3]*Anesthesiologist, Atatürk Research and Trainning Hospital, Ankara, Turkey*
[4]*Anesthesiologist, Anesthesiology and Reanimation Department, Dışkapı Yıldırım Beyazıt Research and Educational Hospital, Ankara, Turkey*
[5]*Microbiology Department, Dışkapı Yıldırım Beyazıt Research and Educational Hospital, Ankara, Turkey*

## Abstract

**Background:** We aimed to investigate the effects of colloid preload or ephedrine bolus on ventricular wall stress by measuring plasma N terminal-Brain natriuretic peptide (NT-ProBNP) concentrations in patients undergoing arthroscopic knee surgery under spinal anesthesia.

**Methods:** 60 patients ASA I-II, aged 20-60 were randomly assigned into two groups. Spinal anesthesia was induced with 0.5% 3 ml levobupivacaine. In Group K (n=30) patients received 500 ml of HES (130/0.4) solution 20 minutes prior to spinal anesthesia. In Group E (n=30) ephedrine 15 mg i.v was injected 1 minute after spinal anesthesia. SBP, DBP, MBP, HR were recorded before and 3,5,7,10,15,20,25,30,45,60,120,240 min. after spinal anesthesia spinal anesthesia and in both groups and in group K also recorded before preload. The plasma concentrations of NT-ProBNP were measured before and 1 and 3 hours after the spinal block.

**Results:** Mean both groups were similar with respect to MBP. In Group K, NT-proBNP concentrations were significantly higher at the first and third hours of spinal block than baseline values (p=0,003, p<0,001). Mean NT-proBNP concentrations were similar between the groups.

**Conclusion:** Colloid preload with 500 ml and ephedrine 15 mg i.v injection could be used for hypotension prophylaxis during spinal anesthesia with hemodynamic stability.

**Keywords:** Spinal anesthesia; Hypotension; Brain natriuretic peptide (BNP)

## Introduction

Spinal anesthesia, performed easily with low dose local anesthetic agent is used commonly for lower extremity surgery, because of rapid onset of action. It provides early ambulation with effective postoperative analgesia and reduced nausea and vomiting [1]. On the other hand, hypotension after spinal anesthesia remains a major clinical problem. Fluid preloading regimens with crystalloid or colloid solutions, vasopressor agents, physical methods to increase venous return by elevating the patient's legs or head down position are the methods used in combination or seperately for the management of hypotension with various success. The optimal form of hypotension management is contradictary [2,3].

Ephedrine which stimulates both α- and β-receptors is one of the most commonly used noncathecolamine sympathomimetic drug for treatment of hypotension associated with spinal anesthesia. Colloid preload for volume expansion is suitable, but volume overload could be hazardous in some patients. Both methods are associated with transient increase of left ventricular wall stress. Brain natriuretic peptide (BNP), which is mainly synthesized and secreted from the cardiac ventricle, is a sensitive indicator of cardiac ventricular volume load [4]. BNP is synthesized as proBNP and then metabolized to BNP and N terminal BNP (NT-BNP) [5]. It was speculated that perioperative cardiovascular risk increases as BNP concentration increases [6]. It was suggested in a recently published metaanalysis that an elevated preoperative BNP or NT-proBNP measurement is a powerful and independent predictor of cardiovascular events in the first 30 days after non-cardiac surgery [6]. Vanzetto, et al. also stated that even the small changes in ventricular function associated with myocardial ischemia produce measurable changes in plasma BNP [6].

We designed this study to compare the effects of colloid preload and administration of ephedrin bolus on left ventricular wall stress by measuring plasma NT-ProBNP concentration and urinary retention in patients undergoing arthroscopic knee surgery under spinal anesthesia.

## Material and Methods

After Hospital Ethical Committee Approval and written informed patient consent, 60, aged between 20-60, ASA status I-II patients undergoing knee arthroscopy under spinal anesthesia were included in this prospective randomized study. Patients with body mass index (BMI)> 40 $kgm^{-2}$, patients having allergic reactions to anesthetic drugs, renal or urinary tract disorders, neurological or cardiovascular disease and contraindication to spinal anesthesia were excluded from the study.

Patients were randomized by means of computer generated random

***Corresponding author:** Ebru Salman A, Anesthesiologist, Atatürk Research and Trainning Hospital, Ankara, Turkey, E-mail: ebru.salman@gmail.com

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number table into 2 groups. Groups were assigned according to sealed opaque envelopes containing information for group allocation. Eighteen gauge i.v cannula was insert on the dorsum of the nondependent hand. In Group K (n=30), patients received hydroxyethyl starch solution(HES), 500 ml, intravenously (Hemohes® 6% 500 ml, Braun Medical AG/ Sweden) 20 minutes prior to spinal anesthesia. In Group E (n=30) ephedrine 15 mg was injected intravenously 1 minute after the spinal anesthesia.

Patients were not premedicated. Noninvasive blood pressure, electrocardiography and peripheral oxygen saturation were monitorized.(Drager® Infinity Delta, USA). Spinal anesthesia was induced with intratechal %0,5 3 ml levobupivacaine injected over 20 seconds with a 22 G Quincke needle at the L3-L4 or L4-L5 interspace in the right or left lateral position in all patients. Nasal oxygen, 2 $L.min^{-1}$ was applied with a face mask to all patients. NaCl 0,9% solution was infused at a rate of 5 $ml.kg\text{-}1h^{-1}$ from the beginning of spinal anesthesia until to the end of surgery.

Blood samples were collected from the patients just after intravenous cannulation and at the first and third hours of spinal anesthesia. Plasma concentrations of NT-ProBNP were determined using Immulite 2000 NT-ProBNP kit (Siemens® Medical Solutions Diagnostics Corporate Offices, Los Angeles, USA) with chemiluminescent immunometric assay method [7].

SBP, DBP, MBP, and HR were recorded before spinal anesthesia and 3, 5, 7, 10, 15, 20, 25, 30, 45, 60, 120 and 240 minutes after the induction of spinal anesthesia in both groups; SBP, DBP, MBP and HR were also recorded before colloid preload in Group K.

Hypotension was defined as 30% decrease of SBP than baseline values or SBP less than 90 mmHg. Ephedrine 5 mg, iv was titrated to maintain baseline blood pressure and repeated as necessary. Total ephedrine used was recorded.

Sensorial and motor block levels were assessed 5 minutes after spinal anesthesia and later every 30 minutes using pinprick test and Bromage scale respectively until motor block disappeared. The patients were observed in the recovery room until sensorial block regression was at least 2 dermatomal level. Postoperative 0.9% $NaCl_2$ $mlkg^{-1}h^{-1}$ infusion was continued until motor block disappeared. The total amount of fluid infused was also recorded. Urinary retention was defined as patient experiencing discomfort in the setting of being unable to void [8]. Urinary retantion at the 3 hours after the onset of spinal anesthesia and the first postoperative voiding time were recorded postoperatively. Duration of surgery, total amount of fluid infused and side effects such as hypotension, bradycardia, nausea and vomiting were also recorded.

## Statistical Analysis

Data analysis was performed by using Statistical Package for Social Sciences (SPSS) version 11.5 software (SPSS Inc., Chicago, IL, United States). Shapiro-Wilk test was used to test the normality of distribution for continuous variables. Data were expressed as mean ± SD or median (min-max), where applicable.

While, the mean differences were compared by unpaired t test, otherwise, Mann Whitney U test was used for the comparisons of median values. Categorical data were analyzed by Pearson's Chi-square or Fisher's exact test, where applicable.

Repeated Measures of ANOVA was applied for evaluation of hemodynamic parameters. When the p-values from the Wilk's Lambda test are statistically significant to know which time differs from which others, Bonferroni adjusted multiple comparison test was used. Whether the differences among measurement times regarding for NT-proBNP were statistically significant or not was evaluated by Friedmant test. When the p-values from the Friedman test are statistically significant to know which time differs from which others, Bonferroni Adjusted Wilcoxon Sign Rank test was used.

A p value less than 0.05 was considered as statistically significant. The Bonferroni Adjustment was applied for all possible multiple comparisons controlling Type I error.

## Results

Patient age, gender, BMI and duration of surgery were similar between the groups (p>0.05) (Table 1). Mean MBP values were significantly decreased at 30, 45 min and 1, 2, 4. hr after induction in Group E and 4 hr after induction in Group K. (p<0,025) But the groups were similar with respect to mean MBP (Figure 1). Mean HR were similar within and between the groups (p>0.05) (Figure 2). Maximum sensorial block level, time to arrive maximum sensorial block level, total sensorial and motor block durations were similar in both groups (p>0.05) (Table 2). Mean NT-proBNP concentrations were significantly higher 1 and 3 hours of spinal anesthesia than baseline values in Group K (p=0,003, p<0,001). In Group E, mean NT-proBNP concentrations were similar throughout the study period (p >0.05). The groups were similar with respect to NT-proBNP (p >0.05 ) (Table 3).

Bradycardia, nausea and vomiting were not observed at all. Additional ephedrine was injected for only one patient in Group K. The amount of fluid infused intravenously in perioperative period was similar between the groups(p>0.05) (Table 4). The first voiding time was earlier in Group K than Group E.(p=0.004) (Table 4) Urinary retention was not observed in any of the patients.

| | Group E | Group K | p |
|---|---|---|---|
| Age (year) | 41.6 ± 10.7 | 39.1 ± 8.7 | 0.332 |
| Gender M/F | 15/15 | 16/14 | 0.796 |
| BMI | 26.9 ± 4.3 | 27.8 ± 4.4 | 0.421 |
| Duration of Surgery (min) | 39.4 ± 8.3 | 39.4 ± 8.3 | 0.982 |

**Table 1:** Demographic variables and duration of surgery (mean ± SD).

| | Group E | Group K | p |
|---|---|---|---|
| Max sensorial block level | T10 (T12-T8) | T10 (T12-T8) | 0.945 |
| Duration to reach maximum level (min) | 20 (9-30) | 20 (9-30) | 0.860 |
| Sensorial block duration (min) | 330 (240-420) | 330 (210-390) | 0.105 |
| Motor block duration (min ) | 270 (150-360) | 270 (180-330) | 0.448 |

(p >0.05 )

**Table 2:** Maximum sensorial block level and time to reach nescessary maximum block level. total motor and sensorial block durations ( median;min-maks).

| | Group E | Group K | p |
|---|---|---|---|
| 0.min | 43.4 (20-140) | 37.8 (20-209) | 0.468 |
| 60.min | 45.1 (20-137) | 42.7 (20-198)a | 0.842 |
| 180.min | 43.8 (20-142) | 39.9 (20-221)b | 0.728 |

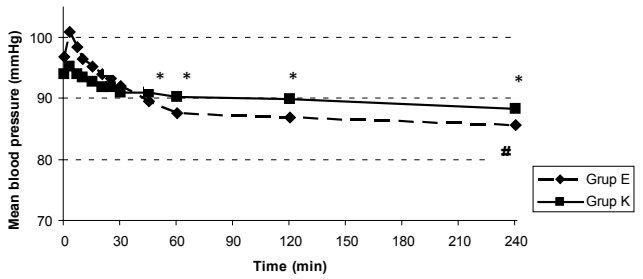
a. p=0.003; The difference between 0.min and 60.min was significantly important in Group K.
b. p<0.001; The difference between 0.min and 180.min was significantly important in Group K.

**Table 3:** NT-proBNP Concentrations ($pgml^{-1}$) (median; min-max).

| | Group E | Group K | p |
|---|---|---|---|
| Ephedrine (n.%) | 0 | 1 (3.3%) | 1.000 |
| Intraoperative fluid (ml) | 230 (155-520) | 265 (160-400) | 0.378 |
| Postoperative fluid (ml) | 550 (305-840) | 560 (300-900) | 0.717 |
| The first voiding time *(min) | 427 (262-670) | 366 (240-492) | 0.004 |

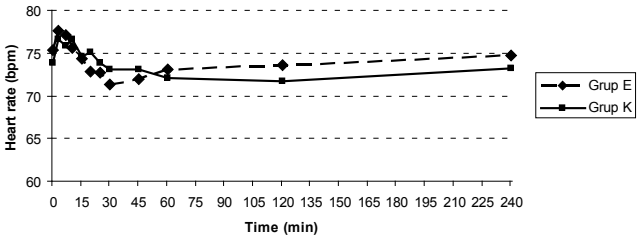
(p <0.05)

**Table 4:** Use of perioperative ephedrin. total intraoperative and postoperative fluid volume. the first voiding time (median; min-max).




*p<0.025. # p<0.025; There were significant difference at 30. 45 min and 1. 2. 4 hours after induction in Group E and 4 hours after induction in Group K comparing the baseline values.

**Figure 1:** Mean blood pressure.




p >0.05 There were no differences within and between the groups.

**Figure 2:** Median mean heart rate values.

## Discussion

In this study, we could not show any difference in between the colloid preload and ephedrine bolus administration in preventing spinal hypotension and left ventricular wall stress. Although the increse in plasma pro-BNP concentrations were higher in patients after colloid infusion, bolus ephedrine administration and colloid infusion had statistically similar effects on plasma pro-BNP concentrations.

Volume expansion with crystalloid or colloid solutions could be performed for the management of hypotension. Rout et al. failed to confirm the advantage of crystalloid fluid infusion for the prevention of hypotension [9]. Teoh et al. stated that colloid preload is more effective than crystalloid preload in prevention of hypotension associated with spinal anesthesia. They also emphasized that crystalloid coload is more effective than preload [10]. Large amounts of crystalloid may lead to tissue edema which can impair oxygen transport and delay tissue healing.

A further problem with quality of the spinal anesthesia is the increased incidence of urinary retantion and urethral catheterization. Although smaller volumes of colloid solutions decrease these problems, some of them could be antigenic [3,11]. The reason for what we used HES as colloid solution in this study is that HES has a lower incidence of anaphylactic reaction than dextran [12]. Atrial natriuretic peptide and brain natriuretic peptide (BNP) are responsible for regulation of blood pressure and fluid balance by counter-balancing the renin-angiotensin system. Since BNP in plasma is mainly produced in ventricles, it is more sensitive and specific indicator of ventricular disorders than other natriuretic peptides. BNP is continously released in response to increase in ventricular volume and pressure without circadian rhythm [13,14]. Terasako investigated the relationship between plasma concentration of atrial and brain natriuretic peptides and alterations in blood pressure in patients undergoing hip arthroplasty under general anesthesia [15]. They found that the level of plasma BNP concentration is higher during congestive heart failure and acute myocardial infarction compared with ANP in patients with left ventricular dysfunction after CABG. Measurement of perioperative natriuretic peptide levels correlating with impairment with may be an important indicator for diagnosis and follow up of early postoperative complications in terms of cardiovascular impairment [15]. Since high preoperative values of ANP and BNP are associated with more hypotension during cemented arthroplasty, BNP could be a marker for the patients with limited myocardial reserve [15].

Goertz et al. investigated the effect of ephedrine bolus administration on left ventricular loading and systolic performance during high thoracic epidural anesthesia combined with general anesthesia with transesophageal echocardiography[16] . They showed that the increase in arterial pressure was not related with the increased left ventricular afterload in contrary to the finding they reported that after bolus administration of phenylephrine increases end-systolic wall stress under similar conditions [16,17]. One limitation of our study is the lack of the control group which precludes determination of an absolute reduction in the incidence of hypotension.

Because durations of sensorial and motor block levels were similar for all patients, the degree of sympathetic block of local anesthetic were similar between two groups. As a result, we think that both methods have similar effect on ventricular wall stress of patients undergoing spinal anesthesia.

Atalay et al. have found in their study investigating three different anesthesia methods in patients with cardiac risk undergoing lower extremity surgery on the level of plasma BNP that BNP levels were lower in the patients thoracal epidural analgesia and lumbar epidural anesthesia and analgesia applied [18].

The dose of ephedrine was chosen depending on the result of a previous study. Igbal, et al. have shown that 15 mg bolus dose of prophylactic i.v ephedrine was the optimal dose significantly reduced the incidence of maternal hypotension without increasing the risk of reactive hypertension [19].

Postoperative urinary retantion (POUR) is associated with the risk of overdistension and an inability to void urine for 6 to 12 hours after the surgical procedure or experiencing discomfort because of being unable to void [8]. Because of persisting S2-S4 block, inability to void after spinal anesthesia could occur and the patients recover the ability to void normally when sacral block regresses. Spinal anesthesia is a risk factor for POUR and recovery of voiding depends on the duration of the local anesthetic action therefore, POUR is observed less with short acting local anesthetics [20,21]. Amount of fluid infused intraoperatively more than 750 ml is another important predictive factor for POUR [8]. In this study, median sensorial and motor block durations with levobupivacaine were approximately 5.5 hours and 4.5 hours respectively. In our study, median intraoperative fluid volume

was 230 ml in group E and 265 ml in group K. POUR could not be a serious problem possibly because of less fluid infusion intraoperatively.

In conclusion, both intravascular volume expansion with 500 ml HES solution given as preload and prophylactic ephedrine bolus 15 mg i.v administration provided hemodynamic stability without left cardiac ventricular wall strech.

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