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# Comparison of the Effect of Prophylactic Ephedrin, Ringer's Lactate, and Colloid Applied During Spinal Anaesthesia on Hemodynamic Parameters in Geriatric Patients

Geratrik Hastalarda Uygulanan Spinal Anestezide Proflaktik Efedrin, Ringer Laktat ve Kolloid Uygulamalarının Hemodinamik Parametreler Üzerine Etkilerinin Karşılaştırılması

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**Cite as:** Uzun Sarıtaş P, Yelken B. Comparison of the Effect of Prophylactic Ephedrin, Ringer's Lactate, and Colloid Applied During Spinal Anaesthesia on Hemodynamic Parameters in Geriatric Patients. J Tepecik Educ Res Hosp 2023;33(1):128-35

## Abstract

**Objective:** Spinal anesthesia, especially in the elderly population, may cause a range of problems from hypotension, cerebral ischemia and myocardial infarcts, to acute renal failure and cardiac arrest. In our study, we researched the effect of ephedrine, ringer lactate, and colloid solutions administered prophylactically on hemodynamic parameters in geriatric patients administered spinal anesthesia.

**Methods:** This prospective, randomized, double-blind study included 75 patients aged 65 years and older in the American Society of Anesthesiologists I-II risk group undergoing urogenital system surgery. Patients were randomly divided into 3 groups called R, C and E. Group R was administered 1000 mL ringer lactate + 2 mL 0.9% NaCl, group C were administered 500 mL hydroxyethyl starch solution, and group E were administered 1000 mL ringer lactate + 10 mg ephedrine (with 2 mL volume). All patients had 5 mL/kg/hr ringer lactate administered for maintenance. The patients' systolic (SBP), diastolic (DBP) and mean blood pressure (MBP), heart rate (HR), and SpO<sub>2</sub> data were recorded. The values before administering fluids were taken as control values and a 30% fall in systolic blood pressure or systolic blood pressure <90 mmHg was accepted as hypotension, and 5 mg IV ephedrine was administered.

**Results:** In all groups, the SBP, DBP, and MBP were identified to have statistically significant increases at prepuncture (PP) and intraoperative 5<sup>th</sup> minute (I5) times. In group C, the hemodynamic changes after the increase at PP and I5 were less for SBP, DBP and MBP compared to groups R and E. In terms of HR, only group R had a statistically significant fall. One case in group R had bradycardia was identified.

**Conclusion:** All three methods can be used safely in the geriatric population; however, we concluded that patients with colloid infusion had more stable hemodynamic parameters.

**Keywords:** Spinal anesthesia, crystalloid, colloid, ephedrine, elderly



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**Received/Geliş tarihi:** 11.12.2022

**Accepted/Kabul tarihi:** 03.02.2023

## Öz

**Amaç:** Özellikle yaşlı hasta popülasyonunda uygulanan spinal anestezi; hipotansiyondan, serebral iskemi, myokard infarktüsü, akut renal yetmezlik ve kardiyak arreste kadar varabilen bir dizi problemlere sebep olabilir. Çalışmamızda geriyatrik hastalarda uygulanan spinal anesteziye profilaktik olarak uygulanan efedrin, ringer laktat ve kolloid solüsyonlarının hemodinamik parametreler üzerine olan etkilerini araştırmayı amaçladık.

**Yöntem:** Bu prospektif randomize çift-kör çalışmaya ürogenital sistem cerrahisi uygulanacak, Amerikan Anestezi Derneği I-II risk grubunda bulunan 65 yaş ve üstü 75 hasta dahil edildi. Hastalar rastgele 3 gruba ayrıldı. Gruplar R, K ve E olarak isimlendirildi. Grup R'ye 1000 mL ringer laktat + 2 mL %0,9'luk NaCl, grup K'ya 500 mL HES solüsyonu, grup E'ye 1000 mL ringer laktat + (2 mL volümde) 10 mg efedrin verildi. Tüm hastaların idamesi 5 mL/kg/saat olacak şekilde ringer laktat ile sağlandı. Hastaların sistolik (SKB), diyastolik (DKB) ve ortalama kan basıncı (OKB) kalp atım hızı (KAH) ve SpO<sub>2</sub> verileri kayıt edildi. Hastaların sıvı verilmeden önceki değeri kontrol değeri olarak baz alınarak sistolik kan basıncındaki %30'luk düşme ve sistolik kan basıncının <90 mmHg olması hipotansiyon olarak kabul edilerek 5 mg i.v. efedrin ile müdahale edildi.

**Bulgular:** Tüm gruplarda SKB, DKB ve OKB'nin ponksiyon öncesi (PÖ) ve intraoperatif 5. dk (İ5) değerlerinde istatistiksel olarak anlamlı artış tespit edildi. Grup K'da SKB, DKB ve OKB'de PÖ ve İ5 değerindeki artıştan sonraki hemodinamik değişimler, grup R ve E'ye göre daha az oldu. KAH bakımından sadece grup R'de istatistiksel olarak anlamlı bir düşme meydana geldi. Grup R'de 1 olguda müdahale edilmesi gereken bradikardi tespit edildi.

**Sonuç:** Yaşlı popülasyonda her üç yöntemin de güvenle kullanılabileceği fakat kolloid infüzyonu uygulanan hastalarda hemodinamik parametrelerin daha stabil seyrettiği sonucuna vardık.

**Anahtar Kelimeler:** Spinal anestezi, kristaloid, kolloid, efedrin, geriyatri

## Introduction

Sympathetic denervation and hypotension are the most commonly observed side effects of spinal anesthesia (SA) (10-40%)<sup>(1)</sup>. As a result, precautions taken with the aim of preventing hypotension that may develop during and after SA are more important than treatment. To date, physical methods increasing venous return and various volume expanders and vasopressor agents have been used for prophylaxis or treatment of hypotension<sup>(2)</sup>.

The administration of crystalloid and colloid fluids before SA is among the most commonly applied methods with the aim of preventing hypotension. The administration of crystalloid solutions before block is recommended in terms of reducing the incidence of hypotension. However, the value of crystalloid solutions for this topic is controversial. Ephedrine infusion may be an effective alternative to crystalloid infusion<sup>(3)</sup>. In geriatric patients, surgical and anesthetic management is more complicated and difficult compared with young patients. The functional capacity of organ systems reduces because of physiological changes developing linked to aging. Hence, elderly patients are more sensitive to surgical stress and perioperative weakening of organ functions<sup>(4-7)</sup>.

In our study, we researched the effects of ephedrine, ringer lactate, and colloid solutions given prophylactically on the hemodynamic parameters of geriatric patients administered SA.

## Materials and Methods

This study was approved by the institutional review board and ethics committee of Eskişehir Osmangazi University

Faculty of Medicine (approval number: 2009/315, date: 28.07.2009), and written informed consent was obtained from the patient's next of kin.

This prospective, randomized, double-blind study was completed in Eskişehir Osmangazi University Faculty of Medicine Department of Anesthesiology and Reanimation from September 2009 to May 2010. The study included 75 cases aged 65 years and older, in group I-II according to the American Society of Anesthesiologists classification, undergoing urogenital system surgery with no contraindications for SA. The main exclusion criteria were as follows: age <65 years, class III obesity, hypertension, severe heart failure, renal failure, and coagulopathy. Patients did not have premedication administered. All patients had an intravenous route opened with 20-G cannula before the operation. Patients had systolic blood pressure (SBP), diastolic blood pressure (DBP) and mean arterial blood pressure (MBP), heart rate (HR), electrocardiogram, pulse oximetry and peripheral oxygen saturation (SpO<sub>2</sub>) parameters monitored and control values noted. Patients were randomly divided into 3 groups of 25 patients. Groups were named R, C and E. Twenty minutes before the operation, each group had the following administered with the infusion pump: Group R 1000 mL ringer lactate + 2 mL 0.9% NaCl, group K 500 mL hydroxyethyl starch solution (HES), and group E 1000 mL ringer lactate + 10 mg ephedrine (with 2 mL volume). All patients had maintenance with 5 mL/kg/hr ringer lactate. Standard SA in the lateral decubitus position for all patients used a needle (22 Quincke) to enter the subarachnoid space through the L3-L4 or L4-L5 interval, with 7.5 mg Marcaine®

Spinal Heavy (Bupivacaine 5 mg/mL) (Sanofi İlaç San.ve Tic. A.Ş. Kırklareli/Turkey) solution administered after clear cerebrospinal fluid was seen. Following administration, all patients were laid in the supine position.

### Control Values

Patients had SBP, DBP, MBP, HR, and SpO<sub>2</sub> values monitored immediately after reaching the operation table.

### Loading Values (Pre-puncture Fluid Infusion, 20 min Duration)

Patients had SBP, DBP, MBP, HR and SpO<sub>2</sub> loading values at 5, 10, 15 and 20 minutes recorded after infusion began with the infusion pump (L5, L10, L15 and L20).

### Prepuncture (PP)

PP hemodynamic values (SBP, DBP, MBP, HR and SpO<sub>2</sub>) were recorded and then the standard SA technique was applied and the patients were laid in the supine position.

### Intraoperative Values

After being placed in the supine position, patients had SBP, DBP, MBP, HR and SpO<sub>2</sub> values recorded at 5-minute intervals (I5, I10, I15 and I20). Basal values were taken as those before administration of fluids and a fall of 30% in SBP or <90 mmHg SBP was accepted as hypotension and 5 mg IV ephedrine was used for intervention.

Patients were monitored for complications that may develop such as nausea, vomiting, bradycardia, tachycardia, hypotension-hypertension and headache. Sensorial block level was assessed according to dermatoma level using the pinprick method, while motor block degree was assessed using the Bromage scale.

### Statistical Analysis

All data in our study were analyzed with the SPSS 18.0 and SigmaStat 3.5 programs. Continuous quantitative data are expressed as n, mean, and standard deviation, while qualitative data are given as n and percentage. Data from repeated groups normal distribution were analyzed the one-way repeated measures Analysis of Variance (the Tukey method was used for multiple comparisons with this test), while data from variables without normal distribution were analyzed the Friedman repeated measures analysis of variance on ranks (the Holm-Sidak method was used for multiple comparisons with this test). Probability values of  $p < 0.05$  were accepted as significant. When conducting the

a priori power analysis, it was calculated such that for the analysis of variance on repetitive measurements between factors, it was necessary to have a total of 150 measurements (50 measurement in each group), to have 80% power for detecting a size effect ( $f=0.27$ ) for the partial  $\eta^2=0.07$ , a total of 72 patients, 24 in each group, were calculated as being necessary. However, considering related studies, the sample size was planned as a total of 75 patients and 25 in each group.

### Results

The study included 75 patients. Of the patients, 97% were male and 3% were female. The mean age of the patients was  $69.1 \pm 5.2$  years.

### Comparison of the Control Values Within the Groups (R, K, E)

Compared to control values, SBP was found to be statistically significantly high in group R at PP and I, in group C at PP, I5, and I10; and in group E at PP and I5 ( $p < 0.05$ ) (Figure 1).

Compared to control values, DBP was statistically significantly increased in group R at PP and I5; in group C at PP, I5, I15, and I20; and in group E at PP ( $p < 0.05$ ).

Compared to control values, MBP was statistically significantly increased in group R at PP and I5; in group C at PP, I5, I10, I15 and I20; and in group E at PP ( $p < 0.05$ ) (Figure 2).

Compared to control values, HR was statistically significantly decreased in group R at I10, I15, and I20 times ( $p < 0.05$ ). There was no statistically significant difference found for any value in group C and group E ( $p > 0.05$ ) (Figure 3).

Compared to control values, SpO<sub>2</sub> was statistically significantly increased in group R at I20, and in group C at I5, I10 and I20 ( $p < 0.05$ ). In group E, there was no statistically significant difference found for SpO<sub>2</sub> values ( $p > 0.05$ ).

### Comparison Between the Groups

In groups R, C and E, there were no statistically significant differences found between SBP, MBP, DBP, HR and SpO<sub>2</sub> values (Tables 1, 2). No case in our study had side effects such as nausea, vomiting and headache. Only 1 case in Group R had bradycardia identified and was administered 0.5 mg atropine.

### Discussion

In our study, while hemodynamic variations were observed in all patients administered prophylactic colloid,

crystalloid and ephedrine infusions, all groups were found to have significantly high SBP, DBP and MBP before spinal administration and in the intraoperative 5<sup>th</sup> minute. Although there was no statistically significant difference between the groups, it was observed that the elevation in arterial blood pressure values continued for a longer duration in the group administered colloid. Although SA is frequently chosen for urologic interventions in elderly cases, hypotension is a significant problem developing in the intraoperative

period. Hypotension may be observed more severely due to the reduction in the protective compensation mechanism in elderly individuals<sup>(6)</sup>. Severe hypotension may cause cerebral ischemia, thrombosis, and edema, especially in atherosclerotic elderly patients, which may lead to mental disorder, or myocardial ischemia in cases with a high risk of coronary artery disease. In the geriatric population, the resting sympathetic tonus degree is higher compared to young people and this explains significant falls in systemic

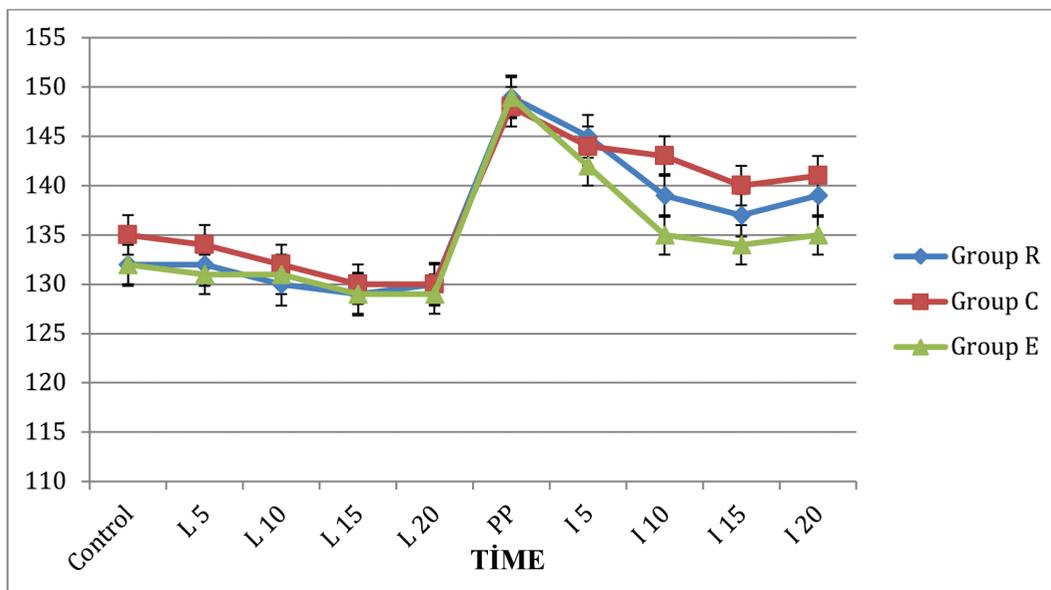


Figure 1. Comparison of the SBP values between groups over time

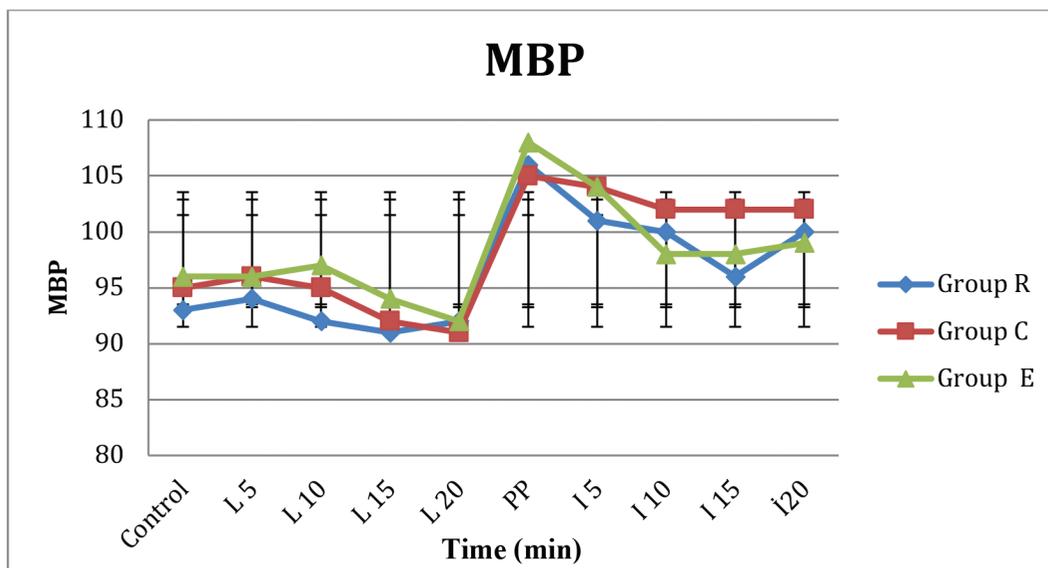


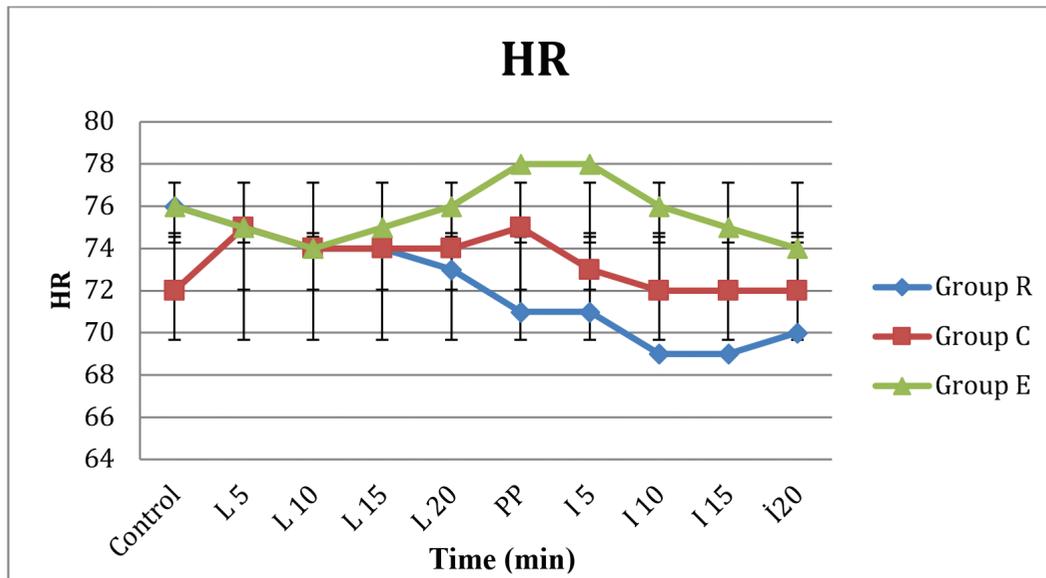
Figure 2. Distribution of mean blood pressure values in cases according to groups (mean ± SD)

SD: Standard deviation

vascular resistance (SVR) with sympathetic blockage<sup>(6)</sup>. As a result, the spinal-related hypotension mechanism is different in the elderly population compared with young people<sup>(9)</sup>. IV fluid treatment is recommended to reduce hypotension<sup>(10,11)</sup>. With sensorial block at T4-T6 levels, SVR reduced by 23-26%, central venous pressure by 2-3 mmHg, and left ventricular end diastolic volume by 20%.

One of the most frequently encountered side effects of SA is hypotension, which is accepted as SBP below 90 or 100 mmHg<sup>(12-14)</sup>, 20-30% falls from initial values<sup>(15-18)</sup> or sudden

fall in SBP of more than 30 mmHg<sup>(19)</sup>. In our study, we accepted hypotension as 30% fall in SBP taking the control value before administration of fluids to patients as a basis, or SBP <90 mmHg and intervened with 5 mg IV ephedrine. Carpenter et al.<sup>(19)</sup> stated that hypotension developed in 33% of 952 patients with SA administered without rehydration. A study in the geriatric patient population found that this rate was 76%<sup>(20)</sup>. Critchley et al.<sup>(21)</sup> identified hypotension in 70% of elderly patients with SA administered and stated that hypotension was a significant cause of morbidity and mortality<sup>(19)</sup>. Vena cava measurement with ultrasonography



**Figure 3.** Distribution of heart rate in cases in groups (mean ± SD)

SD: Standard deviation, HR: Heart rate

**Table 1. Comparison of the MBP values between groups over time**

		Group R	Group C	Group E	p
Control	Median (%25/%75)	93 (84.2/102)	95 (88/102)	93 (84.5/106.2)	0.82 <sup>ns</sup>
Loading 5	(Mean ± SD)	94.6±11.7	96.4±13.2	96.8±12.6	0.81 <sup>†</sup>
Loading 10	(Mean ± SD)	92.3±11.7	95.8±12.6	97.3±13.7	0.37 <sup>†</sup>
Loading 15	(Mean ± SD)	91.7±10.1	92.6±11.5	94.1±12.5	0.74 <sup>†</sup>
Loading 20	Median (%25/%75)	91 (85/98)	91 (86/97)	91 (85.7/101.5)	0.99 <sup>ns</sup>
PP	Median (%25/%75)	105 (96.7/118.2)	108 (97.2/117)	111 (97.5/116.5)	0.62 <sup>ns</sup>
I 5	(Mean ± SD)	101.5±13.9	104.6±13.4	104.6±14.6	0.68 <sup>†</sup>
I 10	(Mean ± SD)	100±12.8	103±10.2	99.9±11.6	0.56 <sup>†</sup>
I 15	(Mean ± SD)	96.7±14	102.8±8.9	99±12.3	0.31 <sup>†</sup>
I 20	(Mean ± SD)	102±13.3	105±11	100±12.1	0.67 <sup>†</sup>

<sup>†</sup>One-way Repeated Measures Analysis of Variance ANOVA (Mean ± SD)

<sup>ns</sup>Friedman Repeated Measures Analysis of Variance on Ranks (median- 25-75%)

L: Loading, PP: Prepuncture, I: Intraoperatif, SD: Standard deviation, MBP: Mean arterial blood pressure

of fluid treatment to prevent arterial hypotension after SA by Ceruti et al.<sup>(9)</sup> observed arterial hypotension at rates of 35% after SA. Among the methods used to prevent or reduce the incidence or severity of hypotension, intravenous fluid administration and the use of vasopressor material are important. Prophylactic fluid administration with this aim is easy to administer, effective, and very commonly used<sup>(22,23)</sup>. Studies have shown that crystalloids do not reduce the degree and incidence of hypotension; in fact, increased central venous pressure and pulmonary edema resulting from lowered colloid oncotic pressure after administration of large amounts of crystalloids was shown to cause severe delusional anemia, which may reduce oxygen transport capacity. The alternative fluid of colloids is accepted by most as reducing the incidence of hypotension<sup>(24,25)</sup>. Xie et al.<sup>(26)</sup> in a study of elderly patients undergoing total hip surgery concluded that patients colloid pre-loading had more effective cardiac output and hemodynamic stability compared with those crystalloid pre-loading. Sharma et al.<sup>(27)</sup> identified that hypotension developed in 52% of patients administered crystalloids and 16% of patients administered colloids to prevent hypotension developing because of SA and stated that the difference was significant. The multicenter CAESER<sup>(28)</sup> study concluded that hypotension associated with SA and symptomatic hypotension was lower in the colloid (HES) group in 167 pregnant cases with SA administered. A similar study of pregnant cases administered SA<sup>(29)</sup> concluded that the crystalloid group had statistically higher hypotension and bradycardia incidence compared with the colloid group. In our study, no group had hypotension observed, but the colloid group appeared to have more stable hemodynamic parameters, although the difference was not statistically significant. We think the reason for the

lack of observation of hypotension is the administration of low-dose (maximum 7.5 mg) heavy bupivacaine. In our study, group R was administered 1000 mL crystalloid, group C was administered 500 mL colloid, and group E was administered 1000 mL crystalloid + 10 mg ephedrine. No statistically significant hypotension was observed in groups R, C, and E compared to control values. In all groups, statistically significant increases were identified in SBP, DBP, and MBP at PP and I5 times. We concluded that this increase shows that premedication may be effective in controlling intraoperative pressure increases in the elderly population, especially. In group C, the hemodynamic variations after the increase at PP and I5 times in SBP, DBP and MBP were less compared to groups R and E. In our study, we concluded that the hemodynamic parameters were more stable in the group administered colloids. The debates about which fluid should be given, when and in what amount continue in relation to prophylactic fluid administration. Rout et al.<sup>(30)</sup> administered rehydration fluids for 10 and 20 min for hypotension prophylaxis linked to SA and showed the rapid infusion was insufficient to reduce hypotension incidence; however, it was effective to increase central venous pressure. Ngan Kee<sup>(31)</sup> et al. in a study identified that 15 mL/kg 4% gelatin solution with the aim of rehydration at 15 minutes infusion rate reduced vasopressor requirements in patients with blood pressure and unstable HR. The multicenter CAESAR study used 500 mL colloid (HES) + 500 mL ringer lactate as rehydration fluid in the colloid group and 1000 mL ringer lactate in the crystalloid group and administered fluid 15-30 min before SA<sup>(28)</sup>. In our study, we took care to administer rehydration fluids over 20 min in all groups due to the age of our patients. Gajraj et al.<sup>(32)</sup> in a study examining the effect of ringer lactate and ephedrine infusion on spinal-related

**Table 2. Comparison of the HR values between groups over time**

	Group R	Group C	Group E	p
Control	76.57±8.46	72.89±9.8	76.64±7.7	0.195
Loading 5	75.6±8.87	75.24±8.3	75.24±7.48	0.988
Loading 10	74±9.86	74.48±9.9	74.76±7.39	0.467
Loading 15	74.08±10.34	74.84±10.8	75.84±8.77	0.824
Loading 20	73.6±9.71	74.5±10.12	76.16±9.5	0.647
PP	71.7±12.57	75.9±12.96	78.56±14.4	0.195
I 5	71.69±12.79	73.1±11.6	78.28±14.36	0.173
I 10	69.5±13.42	72±12.83	76.04±14.12	0.467
I 15	69.8±11.15	72.68±13.9	75.84±12.22	0.776
I 20	70.4±12.56	72.56±12.4	74.40±12.1	0.319

p<0.05, HR: Heart rate

hypotension found that hypotension incidence was 55% in the crystalloid group and 22% in the ephedrine group, with a statistically significant difference and concluded that ephedrine infusion was effective in preventing hypotension. In this study, there was no comparison with colloids. In our study, the colloid group had more stable hemodynamics. Kang et al.<sup>(33)</sup> compared a group with ephedrine infusion with a bolus ephedrine group with the aim of preventing hypotension developing linked to SA. They concluded that the infusion group had more stable maternal SBP and that prophylactic ephedrine infusion was effective and reliable in prevent hypotension without inducing side effects such as significant maternal tachycardia, hypertension, and vomiting. In our study, in parallel with this study, patients with ephedrine infusion did not have clear tachycardia or hypertension; however, an increase occurred in the HR in group E, though not at statistically significant levels, and this increase should be considered in the geriatric population. A statistically significant fall occurred in the HR in group R. In group C, HR was more stable, although without a statistically significant difference, with no reductions or increases in HR. Moslemi et al.<sup>(34)</sup> examined the effects of prophylactic phenylephrine and ephedrine infusion on hypotension in cases undergoing SA for cesarean. They did not identify significant differences between the two groups in terms of systolic and DBP, but identified that the ephedrine group required more vasopressors. Naghibi et al.<sup>(35)</sup> compared the effects of phenylephrine and ephedrine administered immediately after SA in cases with lower abdominal surgery with a control group. They found significantly lower falls in systolic and DBP in the phenylephrine and ephedrine groups, with significant tachycardia observed in the ephedrine group. In our study, an increase was identified in HR in the group using ephedrine, although this was not statistically significant.

### Study Limitations

Our study had several limitations. First, 1000 mL loading fluid was administered as a standard to the geriatric patient population, and we think the administration of loading fluid in mL/kg for every patient will prevent volume loading. Second, hypotension was not observed in the group due to using low-dose heavy bupivacaine linked to the short duration of the operations, and the effect in preventing hypotension may not have been clearly assessed in the groups. Third, we used a single-center design and a small patient population.

### Conclusion

The results of our study show that all three methods can be used reliably in the geriatric population; however, we concluded that patients administered colloid infusion had more stability of hemodynamic parameters.

### Ethics

**Ethics Committee Approval:** This study was approved by the institutional review board and ethics committee of Eskişehir Osmangazi University Faculty of Medicine (approval number: 2009/315, date: 28.07.2009).

**Informed Consent:** Written informed consent was obtained from the patient's next of kin.

**Peer-review:** Externally peer-reviewed.

### Authorship Contributions

Surgical and Medical Practices: P.U.S., B.Y., Concept: P.U.S., B.Y., Design: P.U.S., B.Y., Data Collection or Processing: P.U.S., Analysis or Interpretation: P.U.S., B.Y., Literature Search: P.U.S., B.Y., Writing: P.U.S., B.Y.

**Conflict of Interest:** No conflict of interest was declared by the authors.

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

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