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COMPARISON BETWEEN LOADING COLOID FLUID WITH PHENILEPHRINE PRETREATMENT ON HYPOTENSION OCCURRENCE IN GERIATRIC PATIENTS WITH SUBARACHNOID BLOCK

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ABSTRACT

Background: Although subarachnoid block (SAB) is the best option for geriatric patients undergoing surgery, it still has side effects, one of which is hypotension. This study aimed to compare colloid fluid loading with phenylephrine premedication on hypotension occurrence post-SAB.Methods: A randomized, double-blind, clinical trial was conducted at Wahidin Sudirohusodo General Hospital, Makassar, Indonesia and its network teaching hospitals in Makassar from January to April 2024. Patients were divided into two groups: patients who received colloid loading and patients who received phenylephrine premedication.Results: A total of 48 patients were included in this study and were divided equally into two groups. It was found that the mean arterial pressure value was higher in phenylephrine group compared to colloid group at 5-, 6-, 7-, 8-, and 12-minutes post-SAB ($p<0.05$). The frequency of hypotension and its onset showed statistically significant differences (frequency: $p = 0.041$; onset: $p = 0.044$) between the two groups, where the frequency of hypotension in phenylephrine group was less and the mean hypotension onset in phenylephrine group was also longer (7.20 minutes).Conclusion: Phenylephrine premedication might prevent hypotension better than colloid loading.
Keywords : subarachnoid block., geriatric., colloid., phenylephrine.

INTRODUCTION

Geriatric population possesses many physiological changes, including respiratory, cardiovascular, and nervous system function. These physiological changes have an impact on increasing the risk of comorbidities and mortality during anesthesia and surgery.1,2 Subarachnoid block (SAB) is more beneficial than general anesthesia for geriatric patients because it provides an adequate anesthetic effect and reduces the risk of complications that often occur after general anesthesia such as thromboembolism and respiratory depression.3,4 However, SAB still have many disadvantages when administered to geriatric patients. The number of post-SAB hypotension occurrence increases in geriatric patients, which creates a challenge for an anesthesiologist when performing SAB.5 This number is estimated to reach up to 80% and often occurs in geriatric patients who receive SAB. Post-SAB hypotension results from blockade of the sympathetic nervous system, leading to decreased stroke volume and peripheral vasodilation. This results in a decrease in minute cardiac output (CO) and systemic vascular resistance (SVR), which eventually reduces mean arterial pressure (MAP). Preventable MAP reduction that is not treated during SAB might increase the risk of morbidity and mortality in geriatric patients.[6,7]Management of post-SAB hypotension in geriatric patients could be performed by administering intravenous fluids such as crystalloids or colloids and administering vasopressor drugs.6 Providing intravenous fluid loading before SAB might prevent hypotension. However, geriatric patients generally cannot tolerate excessive administration of intravenous fluids, especially crystalloid fluids.8Administration of vasopressors is an excellent alternative when intravenous fluid administration to prevent hypotension due to SAB is still inadequate.[9]

Phenylephrine is a vasopressor that is often used to treat hypotension. Phenylephrine acts directly on the α1 receptor and causes arterial vasoconstriction and increases SVR and left ventricular contraction.10,11 Although phenylephrine might cause reflex bradycardia and result in cardiac output decrease, this could be prevented by maintaining preload dependency, which will be greatly influenced by blood volume to maintain stable stroke volume.[12,13]Today, no study has been conducted that compare colloid fluid loading with phenylephrine premedicationin geriatric patients regarding hypotension occurence after SAB. Therefore, this study aimed to compare colloid fluid loading and phenylephrine premedication regarding blood pressure reduction after SAB in geriatric patients.This study aims to determine the comparison of hypotension in geriatric patients after subarachnoid block between those who received colloid fluid loading, ephedrine pretreatment and phenylephrine pretreatment.

MATERIAL AND METHODS

This was a randomized, double-blinded, clinical trial carried out at Wahidin Sudirohusodo General Hospital and its network hospitals in Makassar, Indonesia from January

to April 2024. The population of this study was all geriatric patients with SAB. The study samples were geriatric patients with SAB who met the inclusion criteria and agreed to participate in this study. Inclusion criteria in this study were patients who received SAB, aged ⩾ 60 years, body weight (BW): 50-90 kg, height (TB): 150-175 cm, body mass index (BMI): 18.5-29 .9 kg/m2, American Society of Anesthesiologists (ASA) physical status (PS) I-II, and agreed to participate in this study. The exclusion criteria in this study were patients who refused to use SAB or had contraindications to SAB and patients who had contraindications to vasoconstrictors administration (allergy or hypersensitivity to vasoconstrictors, had a history of unstable angina, coronary artery bypass surgery, myocardial infarction refractory arrhythmias, untreated or uncontrolled severe hypertension , untreated or uncontrolled heart failure, uncontrolled hypothyroidism, sulfite sensitivity, uncontrolled diabetes, pheochromocytoma, use of cocaine, monoamine oxidase inhibitors, phenothiazine compounds, or tricyclic antidepressants). The drop out criteria in this study were patients who experienced complications during the study or patients withdrew from the study.

This study had received a certificate of ethical suitability (ethical clearance) from the Ethics Committee for Biomedical Research in Humans, Faculty of Medicine, Hasanuddin University. Informed-consent was carried out before the subject participated in this study, and we maintained the confidentiality of the study subject's identity, hence no party felt disadvantaged by the conducted study. Patients were then randomly divided into two groups: patients who received colloid loading and patients who received phenylephrine premedication. The researchers and patients did not know the group allocation.All patients were given premedication as followed: Dexamethasone 10 mg/intravenous (IV) in slow bolus for 3-5 minutes (diluted with NaCl 0.9% in 5-10 ml syringe), Ondansetron 5 mg/IV, Omeprazole 40mg/IV in slow bolus for 3-5 minutes (dilute with 0.9% Nacl in a 5-10 ml syringe), and Ketorolac 30 mg/IV in slow bolus for 3-5 minutes (diluted with NaCl 0.9% in 5-10 ml syringe). Patients in the colloid group received a loading of gelofusin colloid fluid 5 mL/kgBW/IV (Colloid group) with a maximum infusion rate and finished just before the SAB agent injection. The phenylephrine group received a bolus of phenylephrine 2 µg/kgBW/IV (Phenylephrine group) just before the SAB agent injection.SAB was performed in the L3-L4 or L4-L5 interspace in the Left Lateral Decubitus (LLD) position with a 25 G spinal needle. SAB was carried out with Bupivacaine 0.5% hyperbaric 10 mg (2 mL) and morphine adjuvant 2 µg/kgBW/IV at a rate of 1 mL/3-5 seconds. The patient was positioned supine and given oxygen 2 liters/minute via nasal cannula. The height of the block was assessed using the height of the autonomic block at the level of the thoracic VIII vertebra (cold test); thoracic X vertebra for sensory block (prick test); Bromage scale target for motor block was >2.Mean arterial blood pressure (MAP) was recorded every one minute after SAB for 15 minutes after SAB administration. T0 is the blood pressure before the SAB was performed, T1 was the blood pressure one minute after SAB was performed, T2 was the blood pressure two minutes after the SAB was performed, and so on up to T15.After obtaining data results from both groups, data analysis was carried out using the IBM SPSS Statistics version 25.0 program. A p value <0.05 indicates significance.

RESULTS

A total of 48 patients were included and further divided into two groups equally. There was no significant difference regarding the patients' characteristics between groups (p>0.05) (Table 1). Comparison of MAP (Table 2) 15 minutes post-SAB administration showed that MAP was the highest in phenylephrine group compared to colloid, especially at 5-, 6-, 7-, 8-, and 12- minutes post SAB (p<0.05). No significant differences were found between groups at other measurement times. The trend of decreasing MAP was analyzed using the Friedman test (Figure 1) and found a significant decreasing trend (p<0.05). Regarding hypotension incidence (Table 3), there was no statistically significant difference between groups (p > 0.05). The mean hypotension frequency in phenylephrine group was 4.4 times lower than in colloid group (Table 4). The mean hypotension onset in phenylephrine group was also longer (7.20 minutes) compared to colloid group (6.83). When tested, there were significant differences in terms of hypotension frequency and hypotension onset between groups (p = 0.041 and 0.044, respectively).

Table 1. Sample Demographics

Variable	Group K (n=24)	Group F (n=24)	*P* value
Sex[1]			
Men	13 (54,1%)	21 (87,5%)	0,090*
Women	11 (45,9%)	3 (12,5%)	
Age[2] (Year)	65,4±6,1	65,7±6,8	0,936*
Weight[2] (kg)	58,33 ± 10,61	56,71 ± 8,13	0,183*
Height[2] (cm)	157,66 ± 7,44	157,95 ± 6,23	0,077*
BMI[2] (kg/cm^2)	23,4±3,3	22,7±2,7	0,740*
Physical Status[1]:			1,000*

ASA PS I	2 (8,3%)	2 (8,3%)
ASA PS II	22 (91,7%)	22 (91,7%)

[1]Data is presented in frequency form and analyzed using the Chi square test. [2]Data are presented in the form of Mean ± SD and analyzed using the Kruskal Wallis test. *: Statistically significant

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Table 2. Comparison between MAPs based on time measured every minute

MAP	Group K (n=24)	Group F (n=24)	p value
Before SAB			
Mean ± SD	100,5 ± 10,8	101,6 ± 9,8	0.708[1]
Median	100,5	103,5	
Range	75,0-121,0	81,0-116,0	
Minutes 1			
Mean ± SD	98,5 ± 11,3	103,5 ± 10,6	0.129[1]
Median	97,0	104,0	
Range	79,0-120,0	71,0-121,0	
Minutes2			
Mean ± SD	95,4 ± 12,2	99,1 ± 10,2	0.204[2]
Median	96,0	100,5	
Range	74,0-116,0	71,0-112,0	
Minutes 3			
Mean ± SD	91,3 ± 10,9	96,5 ± 12,7	0.065[2]
Median	91,5	99,0	
Range	75,0-110,0	58,0-112,0	
Minutes 4			
Mean ± SD	88,9 ± 12,9	94,4 ± 14,1	0.127[2]
Median	87,5	96,5	
Range	69,0-110,0	52,0-112,0	
Minutes 5			
Mean ± SD	86,1 ± 10,8	94,0 ± 13,2	0.009[2]*
Median	85,5	93,5	
Range	67,0-108,0	50,0-111,0	
Minutes 6			
Mean ± SD	85,8 ± 10,3	92,7 ± 14,2	0.032[2]*
Median	85,5	92,5	
Range	71,0-111,0	58,0-123,0	
Minutes 7			
Mean ± SD	84,6 ± 12,6	92,5 ± 14,0	0.038[2]*
Median	86,0	90,5	
Range	61,0-110,0	55,0-121,0	
Minutes 8			
Mean ± SD	85, ± 11,1	94,0 ± 12,0	0.012[2]*
Median	84,0	91,0	
Range	70,0-113,0	75,0-122,0	
Minutes 9			
Mean ± SD	86,4 ± 11,3	92,7 ± 12,8	0.080[1]
Median	87,0	92,0	
Range	67,0-115,0	70,0-116,0	

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MAP	Group K	Group F	p value
Minutes 10			
Mean ± SD	86,04 ± 11,38	92,04 ± 13,46	0.102[1]
Median	86,0	91,0	
Range	69,0-118,0	64,0-119,0	
Minutes 11			
Mean ± SD	86,21 ± 12,95	93,0 ± 11,05	0.057[1]
Median	86,0	92,5	
Range	61,0-118,0	70,0-118,0	
Minutes 12			
Mean ± SD	86,2 ± 11,6	93,2 ± 11,8	0.046[1]*
Median	86,0	93,5	
Range	58,0-118,0	66,0-118,0	
Minutes 13			
Mean ± SD	87,4 ± 11,5	92,6 ± 11,7	0.128[1]
Median	87,0	92,5	
Range	66,0-120,0	66,0-120,0	
Minutes 14			
Mean ± SD	84,9 ± 11,4	90,7 ± 10,8	0.081[1]
Median	83,5	88,0	
Range	61,0-119,0	75,0-119,0	
Minutes 15			
Mean ± SD	85,8 ± 13,0	92,1 ± 10,4	0.074[1]
Median	85,5	90,5	
Range	58,0-120,0	74,0-120,0	

Mean arterial pressure data are presented in the form of mean ± SD, median and range of values. [1]Data was analyzed using the One Way Anova test if the data was normally distributed. [2]Data was analyzed using the Kruskal Wallis test if the data was not normally distributed. *statistically significant.

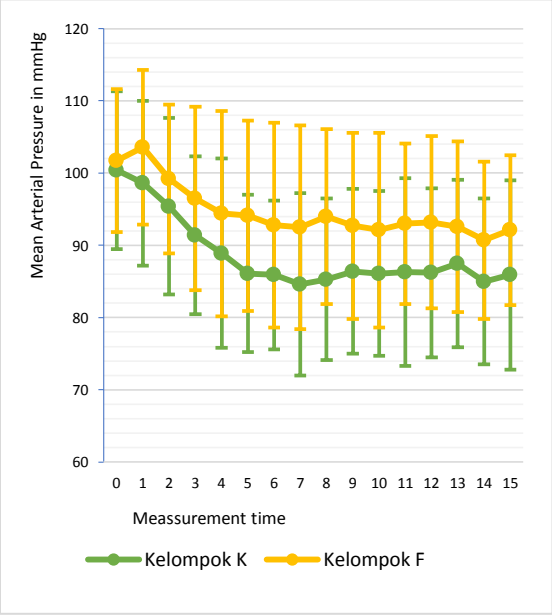

Figure 1. MAP Value 15 minutes after SAB

Group K: patients were given gelofusin, Group F: patients were given phenylephrine. Data on the graph is presented in the form of mean ± SD.

Table 3. Comparison of hypotension occurrence in the Colloid group compared to Phenylephrine group

Hypotension		Group		*P* value
		Group K	Group F	
Yes	n	12	5	0,090[ns]
	%	50,00%	20,80%	
No	n	12	19	
	%	50,00%	79,20%	
Total	N	24	24	
	%	100,00%	100,00%	

The data in the table is in percentage form, analyzed using the Chi square test. [ns] Not significant.

Tabel 4. Comparison of the onset of hypotension and the mean frequency of hypotension between groups

Variable	Group	N	Mean ± SD	Nilai *p*
Frequency Hypotension	K	24	4.50 ± 2.11	0.041*
	F	24	4.40 ± 2.19	
Onset Hypotension	Koloid	24	6.83 ± 3.24	0,044*
	Fenilefrin	24	7.20 ± 4.66	

Data in the table is in the form of mean ± SD, analyzed using the Mann-Whitney test. *statistically significant.

DISCUSSION

There were significant differences in MAP between groups at 5-, 6-, 7-, 8-, and 12-minutes post-SAB ($p<0.05$). In this study, MAP in colloid group was lower than phenylephrine group.The results of study were supported by a study conducted by Jhalandra et al. They found that there was no significant difference between colloid and crystalloid fluids in preventing hypotension caused by SAB. Furthermore, there was a significant reduction in blood pressure in colloid group in the first 20 minutes.14 This also occurred in a study conducted by Pinelopi et al, which stated that post-SAB hypotension could not be prevented by loading colloid or crystalloid 5 mL/kgBW in geriatric patients with hypertension or normotension comorbid.[15]

The FDA-approved indication for intravenous phenylephrine hydrochloride is to increase blood pressure in adults with clinically significant hypotension resulting primarily from vasodilation in settings such as septic shock or anesthesia.[16] The clinical use of phenylephrine in the operating room is quite extensive. Phenylephrine administration is commonly used in the setting of hypotension to counteract the vasodilatory effects of anesthetic agents. Phenylephrine might be used to treat hypotension after induction or during maintenance of anesthesia. In this setting, initial low doses of phenylephrine might increase preload and MAP through venous and arterial constriction, respectively.[17]Hypotension occurred less frequently in phenylephrine group compared to colloid group with a statistically significant difference. This is in line with a study which stated that giving phenylephrine 100 mcg before SAB was effective in preventing hypotension in geriatric patients in the first 15 minutes after SAB.[18]Another study comparing phenylephrine and ephedrine administration stated that the mean variation in stroke volume in ephedrine group tended to be lower than in phenylephrine group.8 The occurrence of post-SAB hypotension in geriatric patient was thought to be caused by a decrease in stroke volume and the inability to maintain cardiac output rather than a decrease in SVR. This is because the risk of hypotension increases due to increased basal sympathetic activity and decreased baroreceptor sensitivity in geriatric patients.[12]

Hypotension onset in phenylephrine group was slower than in colloid group, where phenylephrine group had a slower mean onset time of first hypotension after SAB. Mean hypotension frequency in phenylephrine group was also lower compared to colloid group. This is in accordance with a study which stated that phenylephrine 100 mcg administration was very effective in slowing hypotension onset and preventing recurrent hypotension in the first 15 minutes after SAB in pediatric patients.[14]Experimental studies have shown that optimal pharmacologic correction of the circulatory effects of SAB is achieved with phenylephrine, with phenylephrine best suited for use in hypotensive, tachycardic patients, and when the potential chronotropic effects of ephedrine are undesirable.[19] Phenylephrine, a fast-acting alpha-adrenergic agonist, appears to be the vasopressor of choice because it counteracts the decrease in systemic vascular resistance and thereby restores baseline hemodynamics. Ephedrine has a more delayed vasopressor effect than phenylephrine, and increases heart rate and cardiac output. During SAB, there is usually no need to increase cardiac output, as there is already a compensatory increase in response to the drastic reduction in systemic vascular resistance.[20]

CONCLUSION

Phenylephrine pretreatment might prevent hypotension occurrence better than colloid loading. The results of this study must be further confirmed using a larger sample size. In addition, studies on other types of anesthesia and surgery is needed to confirm these findings.

FINANCIAL SUPPORT AND SPONSORSHIP

Nil

1. CONFLICT OF INTEREST

There are no conflicts of interest.

2. ETHICAL ASPECT

Ethical approval was oobtained from the Health Research Ethics Committee, Faculty of Medicine, Hasanuddin University, No.

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