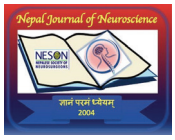
The efficacy of intracisternal irrigation of papaverine on cerebral blood flow in patients with subarachnoid hemorrhage



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Abstract

Background: Cerebral vasospasm remains the most common cause of death in patients after subarachnoid hemorrhage despite various treatments. This study was conducted to find the efficacy of intracisternal washing with papaverine on cerebral blood flow.

Materials and Methods: This study was performed on 40 patients and totally 120 arteries in 2022. Cerebral blood flow velocity changes before and after washing with papaverine were measured and analyzed.

Results: Twenty (20) patients with anterior communicating artery (ACOM) aneurysm and 20 patients with middle cerebral artery (MCA) aneurysm were assessed. Mean blood flow velocity before aneurysm and before washing in ACOM and MCA was 66.2±13.8cm/s and 62.86±7.3cm/s, respectively, which reached 20.45±4.17 cm/s and 32.1±7.7 cm/s, respectively after washing (P value = 0.016 and 0.024).

Mean blood flow after aneurysm and before washing in ACOM and MCA was 93.2±10.9 cm/s and 69.44±12.2 cm/s, respectively, which reached 33.29±4.2cm/s and 40.01±5.28 cm/s, respectively after washing (P value = 0.001 and 0.01).

Conclusion: Intracisternal irrigation with papaverine significantly reduces cerebral blood flow and relieves vasospasm.

Key words: Intracisternal washing, papaverine, subarachnoid hemorrhage, vasospasm

Introduction

Subarachnoid hemorrhage occurs in 6-8 per 100000 population. The mortality is high in first 24 hours which comprises of one fourth of the people diagnosed with SAH. Mortality within one month of diagnosing SAH is around 45%[1]. The most common cause of morbidity and mortality in patients with SAH is cerebral vasospasm and delayed cerebral ischemia[1-4]. Following haemorrhage, vasospasm is detected angiographically in 30-70% during the first 5 to 14 days[5,6]. Delayed cerebral ischemia was detected in 50% patients with angiographically detected vasospasm of which 20% suffer from stroke or die[7,8]. Vasospasm occurs following SAH due to endogenous spasmogens including oxyhemoglobin and endothelin. These spasmogens inhibit Nitric oxide synthetase(NOS) and subsequently reduce the endogenous vasodilators producing vasospasm[9,10]. Clinical improvements were elicited with nimodipine prophylaxis, hypervolemia, hemodilution, control of hypertension (HHH therapy) but this HHH therapy can't completely remove the effect of vasospasm[11-13]. Several clinical report suggest Intra arterial papaverine in reversing cerebral vasospasm both in acute and long term setting. However it was associated with hemodynamic instability like bradycardia and hypotension. Recent studies have suggested papaverine washing of aneurysmal vessel and subarachnoid space prevents aneurysmal vasospasm and also avoids hemodynamic complications[4]. The present study is conducted to evaluate the impact of intracisternal papaverine irrigation in the subarachnoid space on the amount of cerebral blood flow.

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Materials and methods

This study is conducted in Institute of Neurosurgery, Madras Medical College from January 2022 to December 2022. The inclusion criteria were the patients with cerebral aneurysm. Exclusion criteria were a) The patients whose

cerebral aneurysm was not confirmed during the operation. b) The patients who could not undergo the treatment due to anesthetic issues. c) The patients who did not consent to participate in the study. 20 patients with ACOM aneurysm and 20 patients with MCA aneurysm were enrolled in the study.

Method of sampling: The participants were selected through simple random sampling.

Informed and written consent were obtained from all 40 patients who were enrolled in the study. After dissecting out the aneurysm and before clipping of the aneurysm, 40 mg of papaverine, mixed with 20 cc of saline at 37°C was infused to the aneurysmal arteries in subarachnoid space. Blood flow velocity was measured by help of arterial ultrasound (DWL2000 Doppler Ultrasound machine) and a (2 mm, 16 MHz) probe was applied with measurement scale of cm/s. The blood flow velocity was also measured 20 min after washing with papaverine.

Hemodynamic parameters including blood pressure and pulse of the patients were recorded before and 20 min after infusion of papaverine.

The paired t test and SPSS 18 software were used to compare the blood flow velocity between the two groups.

Results

Mean age of the studied patients was 45.02 ± 5.56 years. Among the patients, 16 (40%) people were men and the rest were women. In anterior communicating group (ACOM), 8(40%) patients were men and in middle cerebral artery (MCA), 10 (50%) patients were men (P value = 0.5). Moreover, mean age of the patients in ACOM group and MCA group was 46.50 ± 3.62 years and 49.55 ± 2.56 years, respectively (P value = 0.1), the two groups were identical in terms of age and sex. Blood flow velocity was significantly reduced after washing with papaverine in all patients.

Blood flow velocity before and after papaverine infusion is shown in Table 1 for both groups.

Among the 40 studied patients, 3 (7.5%) of them suffered from bradycardia and 5 (12.5%) of them suffered from hypotension after papaverine infusion. There was no significant difference between the side effects and the aneurysmal artery [Table 3].

Table 1: Comparison of blood flow velocity before and after papaverine infusion

	Artery before aneurysm and before washing	Artery before aneurysm and after washing	
ACOM	66.2±13.8	20.45±4.17	0.016
MCA	62.86±7.3	32.1±7.7	0.02
	The first artery after aneurysm and before washing	The first artery after aneurysm and after washing	
ACOM	93.2±10.9	33.29±4.2	0.001
MCA	69.44±12.2	40.01±5.28	0.01
	The first artery after aneurysm and before washing	The first artery after aneurysm and after washing	
ACOM	65.4±12.16	45.2±7.8	0.01
MCA	53.5±6.8	43.5±8.1	0.005

ACOM: Anterior communicating; MCA: Middle cerebral artery

There was no significant difference in the reduction of blood flow velocity before and after washing with papaverine in the branches of ACOM and MCA [Table 2].

Table 2: Comparison of blood flow velocity reduction in the studied branches for the two arteries of ACOM and MCA

	Before washing	After washing	
Artery before aneurysm	42.3±15.4	28.56±15.67	0.4
The first artery after aneurysm	50.4±12.3	8.95±5.9	0.4
The second artery after Aneurysm	19.8±8.9	7.9±3.1	0.3

Table 3: Comparison of the side effects arising from papaverine for the two groups

	ACOM (%)	MCA (%)	
Bradycardia	2 (10)	1 (5)	0.5
Hypotension	3 (15)	2 (10)	0.1

ACOM: Anterior communicating; MCA: Middle cerebral artery

Discussions

Cerebral vasospasm is defined as cerebrovascular angiographic attenuation, which can be symptomatic and asymptomatic[1]. Various medications administered orally or intra-arterially are available for the management of cerebral perfusion pressure. The orally administered medications does not reach the therapeutic concentrations and also need a prolonged duration for action. When these drugs are administered intracisternally , the appropriate therapeutic concentration is achieved in much lesser time period. Papaverine which is an alkaloid acts directly on the smooth muscle cells of cerebral and cardiac vessel causing vasodilatation. Papaverine acts by inhibiting cyclic adenosine monophosphate and cyclic guanosine 3 and 5 monophosphate intra-arterially[2] thereby increasing NO and induces vasodilatation[1].

Various studies have evaluated the effect of intra-arterial papaverine, although very few studies were conducted on the effect of intracisternal use papaverine and vascular tone. Furthermore, intra-arterial injection of papaverine requires neuroradiological intervention and has hemodynamic side effects[14]

In this study, we found intracisternal irrigation of papaverine in the subarachnoid space significantly reduces the blood flow velocity in the studied vessels. In the study conducted by Segawa et al., in 15 patients with ruptured aneurysm wherein intracisternal irrigation of vessels by papaverine used during surgery. Intraoperative serial angiographic imaging of 7 patients showed a dilatation in anterior and middle cerebral arteries 30 min after injection of initial dose which lasted 60 min. 7 patients showed improvement in neurological symptoms, However 6 patients did not show any response and the 2 other patients encountered a hematoma[15]. A study conducted by Kosty (2005) mentioned the vasospasm as a main issue during clipping of aneurysms in subarachnoid hemorrhage. The above study mentioned that the actual cause of this phenomenon could not been identified. In this study they pointed to the old therapies of using calcium channel blockers and also considered newer therapy of intravascular injection of papaverine as an effective treatment.

They hoped that papaverine intracisternal injection may be effective too, however, it requires further research[16] In this regard, the present study proved the efficacy of washing the intracisternal space with papaverine in vasodilatation of vessels with a suitable sample size. Nevertheless, this study did not address the patients post operatively and the prophylactic use of this method in preventing vasospasm which requires a further study.

The various complications of intra-arterial injection of papaverine include mydriasis, confusion, convulsion, reversible depression of brainstem, increase in ICP, hypotension, bradycardia, and thrombocytopenia[14] and the intracisternal injection of papaverine can cause mydriasis, seventh nerve palsy, and malignant hyperthermia[16].

In our study, 7.5% of the patients suffered from temporary bradycardia and 12.5% of them suffered from hypotension which was corrected by IV fluids alone.

Conclusion

It was found that irrigation of papaverine in intracisternal space significantly reduces the blood flow velocity in the studied arteries and did not cause any serious complication to the patients.

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