



A case report on the management of severe vasospasm in subarachnoid hemorrhagic patients using intra-arterial nimodipine, intrathecal sodium nitroprusside and intra-arterial papaverine

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ABSTRACT

Management and prevention of vasospasm in subarachnoid haemorrhage are one of the complex dictums so far. Aneurysmal subarachnoid haemorrhage (aSAH) is the condition in which bleeding occurs in subarachnoid space. Vasospasm is a complex immunologically active phenomenon which requires a multimodality approach in the treatment of established vasospasm. Various treatment strategies for vasospasm and related disabilities include vasodilators such as nimodipine, sodium nitroprusside and papaverine. Intra-arterial nimodipine shows drastic improvement in several patients by resolving and preventing vasospasm. Intra-arterial administration of nimodipine can cause hypotension which can be easily managed. Papaverine is also an efficient drug-producing vasodilatory action on cerebral arteries. Papaverine is considered as the first intraarterial agent to reduce angiographic cerebral vasospasm which has the side effect of elevated intracranial pressure. Besides, the intrathecal administration of sodium nitroprusside has also demonstrated the effect in ischemic vasospasm after subarachnoid haemorrhage. Intraarterial administration of this drug can induce arterial hypotension which is not a recommended method. Vomiting is the main side effect of sodium nitroprusside, which can be managed with antiemetics such as ondansetron. Here we present a case of management of cerebral vasospasm in subarachnoid patients using the combination of these three effective drugs which showed a remarkable improvement in the resolution of aneurysmal vasospasm.



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INTRODUCTION

Cerebral vasospasm is the primary cause for disability as well as mortality in aneurysmal subarachnoid haemorrhage (aSAH). Risk factors for SAH include habits of cigarette smoking, alcohol, comorbid conditions such as hypertension, diabetes mellitus, hypercholesterolemia, family history of hemorrhagic strokes in first degree relatives, elder people (>60 years), estrogen compounds (Jithin *et al.*, 2016). About 30% of the patients show symptomatic vasospasm between 4th and 14th day after the initial bleeding, and that might be last up to 4th week (Alaraj *et al.*, 2010). Diagnosis is

by computed tomography or lumbar puncture or four-vessel angiography and CT angiogram (Kim *et al.*, 2009). The management and prevention of vasospasm and delayed cerebral ischemia are essential to improve the quality of life. The typical treatment pattern of cerebral vasospasm includes endovascular therapies with triple H (Hypertension, hemodilution, hypervolemia) and vasodilators. Nimodipine, a calcium channel blocker has been widely used as an intraarterial agent for vasospasm therapy since it is beneficial in reversing angiographic vasospasm. Nimodipine is FDA approved for treatment aneurysmal subarachnoid haemorrhage with vasospasm (Daou *et al.*, 2019). Intra-arterial nimodipine administration is through a microcatheter placed in the affected vessel as an infusion over 20-40 min. Nimodipine is infused at a rate of 6mg/h per affected vessel. If a patient develops hypotension, the infusion is temporarily stopped till its stabilized (Cho *et al.*, 2011). The nimodipine solution for intraarterial is prepared after dilution with 0.9% saline to attain the solution of 0.01 mg/ml. Angiograms were taken 10-30 min after the nimodipine administration. Papaverine is an effective vasodilator of the cerebral arteries which improves cerebral blood flow. Intra-arterial papaverine effectively improves angiographic vessel diameter, cerebral oxygenation, and cerebral circulation time. Sodium nitroprusside is another treatment option for cerebral ischemia with severe medically refractive vasospasm after subarachnoid haemorrhage (SAH). Intrathecal sodium nitroprusside is also a described method for delayed cerebral ischemia and cerebral vasospasm refractory to conventional treatment. Vomiting is the most familiar adverse effects of sodium nitroprusside. Here we are presenting a case report on the management of vasospasm in subarachnoid patients using intra-arterial papaverine, nimodipine and intrathecal sodium nitroprusside.

Case History

A 30-year-old male patient with aneurysmal subarachnoid haemorrhage (aSAH) with WFNS grade II and Fischer grade 4 was admitted to ICU and was started on SAH protocol. A CT angiogram was done on the day of admission, which shows a saccular aneurysm of size 0.6*0.6cm with wide neck measuring 4mm seen inferior posterior aspect of right Internal Carotid Artery(ICA). Another aneurysm measuring 0.5*0.5cm with the wide neck of size 4mm was seen involving the bifurcated form of a right middle cerebral artery. All the segmental branches are arising from the aneurysm. The patient was taken up for right pterional craniotomy and clipping of both aneurysms after ICU preoper-

ative stabilization. The patient was kept on triple H therapy (hypertension, hypervolemia and hemodilution) postoperatively. He developed left side hemiparesis with Grade 0 power in left upper limb and Grade 3 power in left lower limb and Upper Motor Nerve (UMN) facial palsy on eighth post-operative day suggestive of vasospasm with evident high velocities in the right MCA. CT Brain showed evidence ischemia right frontal lobe with post-operative clipping changes. He was stabilized in ICU, urgent external ventricular and lumbar drain insertion followed by Sodium nitroprusside infusion was started intrathecally. He was on ionotropic supports to maintain cerebral perfusion and with adequate fluid maintenance. He was taken up for urgent Digital Subtraction Angiography (DSA) which showed severe stenosis of the M1 segment of right middle cerebral artery secondary to vasospasm. Intraarterial nimodipine was given to the patient, and there were significant dilatation and reperfusion of the affected segment was observed in post-injection angiography. Clinical improvement of the power was seen the lower limb (grade 4) and upper limb (grade 2). Follow up CT head showed a reduction in the ischemic changes. DSA was repeated, and the same procedure was repeated, which showed reoccurrence of spasm in the M1 segment of the right MCA, which was not responding much with intra-arterial nimodipine infusion. Then a microcatheter was advanced into the spastic segment, and Papaverine infusion was tried through the microcatheter in the involved segment. Post injection angiogram showed recovery of vasospasm in the segment. Balloon angioplasty was not attempted because of the proximity of the aneurysm clips. The motor weakness showed further improvement in Grade 4+ in the lower limb and upper limb with residual weakness in the right wrist and fingers (Grade 2). A significant resolution of the infarct was observed in the follow-up CT. The patient was on aggressive physiotherapy and rehabilitation. The intravenous nimodipine was converted to oral nimodipine and continue till 3weeks of ictus.

DISCUSSION

Cerebral vasospasm is one most catastrophic sequelae of aneurysmal subarachnoid haemorrhage. Various drugs are available to treat and prevent vasospasm. Oral nimodipine is most commonly used to treat vasospasm, considering the risk of an adverse reaction such as hypotension, both the IV and IA routes are undertaken with the precaution of ionotropic support under close monitoring. In a study conducted by Asma *et al.*, retrospectively evaluated 25 subjects treated with Intra-

arterial nimodipine (IAN) infusion and found that IAN therapy was significantly adequate in lowering Cerebral angiographic vasospasm in 95.1 % of 41b treatment sessions (Bashir *et al.*, 2016). Some of the other studies discussed the effectiveness of the combination of intra-arterial nimodipine and papaverine or balloon angioplasty and found as an effective method to treat vasospasm (Kerz *et al.*, 2016). Papaverine is an alkaloid that produces vasodilatory induction of cerebral and cardiac vessels by directly acting on cells of the smooth muscle, which mainly inhibits the cyclic guanosine 3&5 monophosphate and cyclic adenosine monophosphate intrarterially which elevate NO and results in vasodilation. Intra-arterial Papaverine (IA PAPA) treatment was introduced by Kassell *et al.* (1992), described its successful efficacy in managing cerebral arterial vasospasm. Kaku *et al.* conducted a study with ten patients using balloon angioplasty and then followed by IA PAPA, resulting in 80% improvement clinically (Kassell *et al.*, 1992). Strict monitoring of blood pressure, pulse rate and intracranial pressure are required while the patient is on papaverine infusion (McAuliffe *et al.*, 1995). Sodium nitroprusside is also administered intravenously as an infusion to treat vasospasm by activating guanylate cyclase and which results in the relaxation of vascular smooth muscle. But it has been limited by various serious adverse reactions, including observation of intense hypotension caused by intravenous infusion. Intrathecal administration act directly on the adventitial surface of large blood vessels. Another action which includes the prolongation of Tpa activity could also be useful in the management of vasospasm. In a study conducted by Nihat, the effect of intrathecal sodium nitroprusside (ISP) evaluated in 14 animals. That study supports the hypothesis that ISP is an effective treatment for cerebral vasospasm. Those animals treated with continuous intrathecal SNP showed effective lessening in the mean diameter of the basilar artery, which was 29.25 +/- 4.54%. Also, the study reports that during sodium nitroprusside administration, continuous close monitoring of intracranial pressure (ICP) and arterial blood pressure is vital (Egemen *et al.*, 1993). In our patient, the combination of these three drugs, Nimodipine, Papaverine and sodium nitroprusside showed adequate improvement in the angiographic and clinical outcome.

CONCLUSION

Vasospasm is a complex immunologically active phenomenon which requires a multimodality approach in the treatment of established vasospasm. Multimodality approach in the treat-

ment of vasospasm has changed the outcome in this case significantly. Administration of Papaverine, Nimodipine and Sodium nitroprusside requires careful precautions and monitoring to manage the hemodynamic changes induced by these agents. Pharmacological agents used intra arterially are described as Chemical Angioplasty which is an effective and efficient method in preventing serious ischemic damage due to vasospasm. Intrathecal agents work as an additive measure working in the extravascular environment. Though further studies are required for the more scientific establishment of these measures, and we consider this as a positive step for developing a protocol in the management of severe vasospasm.

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Conflict of Interest

The authors declare that there is no conflict of interest.

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