# Spinal Cerebrospinal Fluid Drainage for prevention of Vasospasm in Aneurysmal Subarachnoid Hemorrhage: A Prospective, Randomized controlled study

## Abstract

**Introduction:** Cerebral vasospasm following aneurysmal subarachnoid hemorrhage (SAH) is a major cause of mortality and morbidity. Despite various treatment modalities, the optimal management of vasospasm remains elusive. In this regard; we undertook a prospective, randomized controlled study to evaluate the effectiveness of lumbar cerebrospinal fluid drainage (LCSFD) for prevention of cerebral vasospasm and its sequelae. **Materials and Methods:** Patients with aneurysmal SAH who met the inclusion criteria were randomized into two groups – Group I (30 patients) underwent LCSFD whereas Group II (30 patients) did not undergo LCSFD. All patients underwent aneurysmal clipping. Both the groups received standard neurosurgical treatment except for LCSFD. The outcome was measured in terms of (1) clinically evident vasospasm; (2) vasospasm-related cerebral infarction; (3) condition of the patient at the time of discharge; and (4) Glasgow outcome score (GOS) at 1- and 3-month follow-up. **Results:** LCSFD conferred a statistically significant benefit reducing the incidence of clinical vasospasm from 63% (in non-LCSFD group) to 30% (in LCSFD group) ($P = 0.01$) and incidence of vasospasm-related cerebral infarction from 53% (in non-LCSFD group) to 20% (in LCSFD group) ($P = 0.007$). Incidence of vasospasm was quantitatively lower in LCSFD group across all Hunt and Hess grades; however, it was statistically significant in SAH Grade III ($P = 0.008$). Mean duration of hospital stay was slightly lower in LCSFD group compared to non-LCSFD group; however, it did not reach statistical significance. A higher incidence of meningitis in LCSFD group was not statistically significant. A higher GOS was observed in LCSFD group at 1- and 3-month follow-up as compared to non-LCSFD group. **Conclusion:** Drainage of CSF through a lumbar drain following aneurysmal SAH caused a statistically significant reduction in the incidence of clinical and radiological vasospasm and its sequelae. It also shortens the overall duration of hospital stay and improves the outcome as evidenced by a better GOS score at 1- and 3-month follow-up. The results of this prospective, randomized study establish the efficacy of LCSFD in prevention of vasospasm following aneurysmal SAH.

**Keywords:** *Aneurysm, lumbar cerebrospinal fluid drainage, subarachnoid hemorrhage, vasospasm*

**Sachin Anil Borkar, Manmohanjit Singh, Shashank Sharad Kale, Ashish Suri, Poodipedi Sarat Chandra, Rajender Kumar, Bhawani Shankar Sharma, Shailesh Gaikwad[1], Ashok Kumar Mahapatra**

*Departments of Neurosurgery and [1]Neuroradiolgy, All India Institute of Medical Sciences, New Delhi, India*

## Introduction

Cerebral vasospasm is a prolonged cerebral arterial vasoconstriction that occurs from 3rd to 14th day following aneurysmal subarachnoid hemorrhage (SAH). Cerebral vasospasm continues to be the main cause of morbidity/mortality following aneurysmal SAH till date.

Many treatment modalities have emerged over the years to prevent cerebral vasospasm. Foremost among these modalities was the introduction of triple-H (3H) therapy in the early 1980s.[1,2] Nimodipine, which was introduced for widespread clinical use in 1985, reduced the overall percentage of patients with severe vasospasm from 30% to 20%; however, it does not seem to decrease the incidence of vasospasm identified on angiography.[3-5] In the late 1980s, endovascular techniques such as angioplasty and administration of intra-arterial chemical vasodilators such as papaverine and nimodipine enabled the neurological rescue of many patients, thereby further improving their overall outcome.[6,7] Despite all these advances, vasospasm continues to challenge. There is still no single effective mean to prevent vasospasm. Vasospasm currently accounts for a prolonged in-hospital stay and high-cost.[8-10]

Research has clearly shown that the pathophysiology of vasospasm is directly

*Address for correspondence:*
*Dr. Sachin Anil Borkar,*
*Department of Neurosurgery,*
*Cardio-Neuro Centre, All India*
*Institute of Medical Sciences,*
*Room No. 720, New Delhi,*
*India.*
*E-mail: sachin.aiims@gmail.com*

related to the presence of blood in the subarachnoid spaces surrounding the cerebral conductance vessels.[11,12] Because hemolysis of blood is the primary inciting agent for vasospasm, strategies to facilitate the clearance of blood from the subarachnoid spaces at the earliest would reduce the risk of cerebral vasospasm. This strategy has been studied by a number of investigators.[13-20]

Lumbar cerebrospinal fluid drainage (LCSFD) may represent a simple and effective way to increase the clearance of blood from the subarachnoid spaces and consequently decrease the incidence of clinically significant vasospasm. Draining CSF from the lumbar cistern would be expected to promote circulation of clear, newly formed CSF from the cerebral ventricles through the subarachnoid spaces, especially if the arachnoidal membranes were opened at the time of surgery. Moreover, lumbar drainage would also promote removal of the red cell mass from the intrathecal space, which represents the largest of all subarachnoid cisterns.

With this background, the authors undertook a prospective, randomized controlled trial assessing the efficacy of LCSFD for prevention of cerebral vasospasm in patients with aneurysmal SAH.

## Materials and Methods

This is a prospective, randomized control trial. Institutional ethics committee clearance was taken for the study. Patients of aneurysmal SAH (Hunt and Hess Grade II–IV), who got admitted during the study period and met the inclusion criteria, were randomly allocated to one of the two groups using computer-generated randomization chart.
• Group I: Underwent placement of Lumbar CSF drain
• Group II: Lumbar CSF drain was not placed.

### Inclusion criteria

1. All patients with aneurysmal SAH Hunt and Hess Grade II–IV with ictus within 10 days before admission.

### Exclusion criteria

1. Evidence of raised intracranial pressure in the perioperative period contradicting placement of lumbar intrathecal drains
2. Nonoperated patients where the aneurysm is not secured
3. Intracranial mass lesions, e.g., hematoma, cerebral edema, brain shift, etc.
4. Meningitis contradicting placement of intrathecal drains
5. Patients with Hunt and Hess Grade I and V SAH
6. Patients undergoing coiling.

### Clinical management

All patients were assigned a Hunt and Hess grade at the time of admission according to neurological parameters. The patients were also assigned a Fisher's grade based upon thickness of subarachnoid clot on computed tomography (CT) scan of head. At admission, all patients were resuscitated and stabilized. The patients with poor neurological status with poor respiratory effort were intubated. With the exception of CSF drainage, all patients received treatment according to a consistent protocol. This included early surgical occlusion of the ruptured aneurysm (within 3 days following admission). The LCSFD was placed at the time of induction before craniotomy and was kept in place for next 72 h postprocedure.

Patients in whom lumbar drain was placed were given antibiotics as per the protocol (Cefoperazone + sulbactam 1 gm 12 hourly, netilmicin 300 mg OD, Metrogyl 500 mg iv 8 hourly). Prophylactic 3H therapy was given depending on the clinical situation, administration of nimodipine, daily transcranial Doppler (TCD) ultrasonography examinations, rigorous monitoring, correction of electrolyte and blood gas abnormalities and management of hydrocephalus were carried out accordingly in both the groups.

Vasospasm was diagnosed using the criteria defined in the tirilazad trials:[9,10]
1. Deficits such as confusion, disorientation, drowsiness, or focal motor deficit during posthemorrhage days 4–14
2. Negative findings on CT scans obtained to rule out other causes of neurological deterioration such as hemorrhage, cerebral edema, or hydrocephalus
3. No other identifiable cause of neurological deterioration such as hyponatremia (Na <132 mEq/L), hypoxia, drug toxicity, infection, or seizures
4. Evidence of vasospasm on serial TCD examinations.

Cerebral infarction caused by vasospasm was diagnosed if either a delayed ischemic deficit became sustained beyond the risk period of cerebral vasospasm or if imaging studies revealed a region of cerebral infarction in a vascular territory consistent with the patient's vasospasm.

### Lumbar cerebrospinal fluid drainage methods

In all patients randomized under the LCSFD group, closed system lumbar CSF drain was typically placed in the operating room at the time of surgery through L3–L4 intervertebral space after induction and was clamped. Before the dural opening, lumbar drain was opened up to release CSF and to facilitate brain relaxation. LCSFD was continued for next 72 h. The CSF bag was typically kept at the level of head to avoid overdrainage of CSF.

### Outcome measures

There were four primary outcome measures in this study:
1. Clinically evident vasospasm
2. Vasospasm-related cerebral infarction
3. Condition of the patient at the time of discharge
4. Glasgow outcome score (GOS) score at 1- and 3-month follow-up.

Secondary outcome measures included duration of stay in Intensive Care Unit and overall hospital stay.

## Results

Sixty patients met the inclusion criteria and were randomly allocated to one of the two groups – thirty patients in Group I and thirty patients in Group II. With the exception of CSF drainage, all patients received treatment according to a standard protocol. This included early surgical clipping of the ruptured aneurysm (within 10 days following ictus).

There were thirty patients in each group. Both groups were matched with respect to age, sex, GCS on admission, and SAH grade at admission [Table 1].

Clinical evidence of vasospasm and rising TCD velocities suggestive of vasospasm developed in 30% (9/30) patients in LCSFD group compared to 63.3% (19/30) patients in non-LCSFD group and this difference was found statistically significant ($P = 0.01$). Although more number of patients (11/30) in Group II developed hemiparesis due to vasospasm compared to Group I (6/30), this difference was not found to be statistically significant. This may be because of small sample size.

Vasospasm-related cerebral infarction as evidenced by serial CT head occurred in 20% of Group I (6/30) compared to 53.3% (16/30) of Group II patients. This difference was also found to be statistically significant ($P = 0.007$) [Figure 1a-f].

We performed a subgroup analysis to look at the effect of LCSFD in individual SAH grade patients. We observed that the beneficial effect of LCSFD in preventing cerebral vasospasm was statistically significant in SAH Grade III patients ($P = 0.008$). In SAH Grade II and IV patients, although the incidence of vasospasm was lower in LCSFD group compared to non-LCSFD group, it did not reach statistical significance.
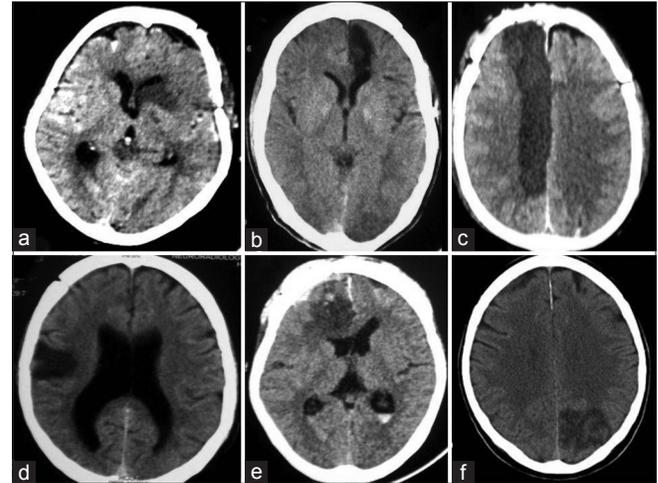


Figure 1: (a-f) Different locations of vasospasm-related cerebral infarction in the study population

### Table 1: Summarizing demographic profile of the two groups

| Parameters analyzed | Lumbar CSF drainage group | Non-Lumbar CSF drainage group | *P* |
|---|---|---|---|
| Number of patients | 30 | 30 | NA |
| Age in years (mean±SD) | 48.4±10.2 | 47.5±11.2 | 0.76 |
| Range | 30-70 | 18-75 | |
| Sex (male:female) | 13:17 | 14:16 | 0.79 |
| GCS on admission (minimum-maximum) | | | |
| Mean | 13.90±0.35 (12-15) | 14.05±0.65 (12-15) | 0.22 |
| Median | 14 (12-15) | 14 (12-15) | |
| Comorbid illness (%) | | | |
| HTN | 18 (60) | 14 (46.7) | 0.49 |
| DM | 1 (3.3) | 1 (3.3) | |
| Bronchial asthma | 0 | 1 (3.3) | |
| CAD | 1 (3.3) | 0 | |
| Valvular heart disease | 0 | 1 (3.3) | |
| SAH grade (%) | | | |
| II | 11 (36.7) | 15 (50) | 0.58 |
| III | 14 (46.7) | 11 (36.7) | |
| IV | 5 (16.7) | 4 (13.3) | |
| Aneurysmal bleed (%) | | | |
| ACom | 17 (56.7) | 17 (56.7) | 0.75 |
| DACA | 2 (6.7) | 4 (13.3) | |
| MCA | 7 (23.3) | 3 (10) | |
| PCom | 0 | 1 (3.3) | |
| ICA | 5 (16.7) | 5 (16.7) | |
| AICA | 1 (3.3) | 1 (3.3) | |

ACom – Anterior communicating artery; DACA – Distal anterior cerebral artery; MCA – Middle cerebral artery; PCom – Posterior communicating artery; ICA – Internal carotid artery; AICA – Anterior inferior cerebellar artery; CAD – Coronary artery disease; GCS – Glasgow coma scale; SAH – Subarachnoid hemorrhage; LP – Lumbar puncture; SD – Standard deviation

However, LCSFD was associated with a higher incidence of meningitis (5/30, 16.7%) compared to non-LCSFD group (2/10, 6.7%) although this difference was not statistically significant (*P* = 0.42). One patient in LCSFD group died due to fulminant meningitis and ventriculitis. The other complications in Group I included postoperative pneumonia in four patients (13.3%), dyselectrolytemia in 2 (6.7%), and septicemia in one patient (3.3%). In Group II, the perioperative complications were – pneumonia in four patients (13.3%), dyselectrolytemia in two patients (6.7%), urinary tract infection (UTI) in one patient (3.3%), and septicemia in two patients (6.7%). The incidences of postoperative pneumonia, UTI, dyselectrolytemia, and septicemia were almost similar in both groups and were not statistically significant. One peculiar complication observed in two of the patients in LCSFD group was development of intracranial hematoma – extradural hematoma in one patient and subdural hematoma in another. Both these patients were promptly diagnosed and operated emergently and made good recovery.

The patient outcome as quantified by GOS at the time of discharge was better in LCSFD group (median GOS = 4) as compared to non-LCSFD group (median GOS = 3) and this difference was found to be statistically significant (*P* = 0.01). Median GOS at 1- and 3-month follow-up was 5 in Group I compared to 4 in Group II and this difference was statistically significant (*P* = 0.04).

Two patients in each group died. In LCSFD group, one patient died of fulminant meningitis and ventriculitis

and other died of acute renal failure and septicemia. In non-LCSFD group, one patient expired due to ventilator-associated pneumonia during in-hospital stay whereas other patient expired 1 month after discharge probably due to aspiration pneumonitis.

Follow-up was present at 3 months postdischarge for 23/28 patients in Group I (82%) and 22/28 patients in Group II (79%) [Tables 2 and 3].

## Discussion

The management of patients with aneurysmal SAH should achieve two main goals: Prevention of rebleeding and treatment of cerebral vasospasm.[17] Early surgical clipping or endovascular coiling of aneurysm prevents the subsequent aneurysmal rebleeding. Despite the developments in the management of aneurysmal SAH, cerebral vasospasm remains an important cause of the morbidity and mortality.

Cerebral vasospasm usually develops 3–4 days after SAH and continues for 10–14 days. Ischemic neurological deficits from clinically evident vasospasm occur in approximately half of patients whose angiograms demonstrate vasospasm.[3,21] Severe symptomatic vasospasm occurs in approximately 25–37% of patients and causes permanent ischemic neurological deficit or death in 7–17%.[17,22]

Exact pathophysiologic mechanisms underlying cerebral vasospasm are not fully established and multifactorial

| Table 2: Summarizing the results in two groups | | | |
|---|---|---|---|
| Parameters analyzed | Lumbar CSF drainage group (%) | Non-Lumbar CSF drainage group (%) | *P* |
| Clinical effect of vasospasm | 9/30 (30) | 19 (63.3) | 0.01 |
| Focal neurological deficit | | | |
| Hemiparesis | 6/30 (20) | 11 (36.7) | 0.15 |
| Quadriparesis | 0 | 1 (3.3) | 1 |
| Monoparesis | 0 | 1 (3.3) | 1 |
| Paraparesis | 0 | 1 (3.3) | 1 |
| TCD effect of vasospasm | 9/30 (30) | 19 (63.3) | 0.01 |
| Radiological effect of vasospasm (vasospasm- related cerebral infarction) | 6/30 (20) | 16/30 (53.3) | 0.007 |
| SAH grade and risk of vasospasm | | | |
| II | 2/11 (18.2) | 7/15 (46.7) | 0.22 |
| III | 4/14 (28.6) | 9/11 (81.8) | 0.008 |
| IV | 3/5 (60.0) | 3/4 (75.0) | 1 |
| Perioperative complications | | | |
| Meningitis | 5/30 (16.7) | 2 (6.7) | 0.42 |
| Pneumonia | 4/30 (13.3) | 4 (13.3) | 1 |
| UTI | 0 | 1 (3.3) | 1 |
| Septicemia | 1/30 (3.3) | 2/30 (6.7) | 1 |
| Dyselectrolytemia | 2/30 (6.7) | 2/30 (6.7) | 1 |
| Hypoxia | 0 | 0 | - |
| Development of extradural/subdural hemorrhage/effusion requiring evacuation | 2/30 (6.7) | 0 | 0.5 |
| Development of hydrocephalus | 3/30 (10) | 2/30 (6.7) | 1 |
| Mortality | 2/30 (6.7) | 2/30 (6.7) | 1 |

SAH – Subarachnoid hemorrhage; LP – Lumbar puncture; UTI – Urinary tract infection; TCD – Transcranial Doppler

### Table 3: Summarizing the outcome between the two groups

| Parameters analyzed | Lumbar CSF drainage group (%) | Non-Lumbar CSF drainage group (%) | *P* |
|---|---|---|---|
| GCS at the time of discharge (range) | | | |
| Mean | 14.93±0.27 (14-15) | 14.48±1.43 (9-15) | 0.11 |
| Median | 15 (14-15) | 15 (9-15) | |
| GOS at the time of discharge | | | |
| Mean | 3.93±1.02 (1-5) | 3.27±0.80 (1-5) | 0.01 |
| Median | 4 (1-5) | 3 (1-5) | |
| Median duration of ICU stay in days (range) | 7.5 (3-20) | 8 (3-14) | 0.91 |
| Median duration of hospital stay in days (range) | 12 (7-31) | 12 (6-45) | 0.74 |
| GOS at 1 month follow-up | | | |
| Mean | 4.4±1.07 (1-5) | 3.86±0.93 (1-5) | 0.04 |
| Median | 5 (1-5) | 4 (1-5) | |
| GOS at 3 months follow-up | | | |
| Mean | 4.4±(1-5) | 3.86±0.93 (1-5) | 0.04 |
| Median | 5 (1-5) | 4 (1-5) | |

GOS – Glasgow outcome score; ICU – Intensive Care Unit; GCS – Glasgow coma scale

processes that contain oxygen-free radicals, endothelin, vascular endothelial growth factor, arachidonic acid derivatives, lipid peroxidation, inactivation of nitrous oxide, activation of protein kinase C system released from blood clots in the subarachnoid spaces and cisterns have been implicated to induce the muscular contraction and damage to the vessel leading to cerebral vasospasm.[23-26] However, the definite molecular mechanism which induces cerebral vasospasm is not yet clear. Thus, the optimal management for cerebral vasospasm is not fully established.

Introduction of 3H therapy in the early 1980s and calcium channel blockers such as nimodipine in later years decreased the patients with severe cerebral vasospasm from 30% to 20%.[4,17,19,21,22] In the late 1980s, endovascular treatments including angioplasty and injection of intra-arterial chemical vasodilators such as papaverine enabled to improve their overall outcome.[6] However, because these medications and endovascular intervention are unable to eliminate the blood clots, cerebral vasospasm still contributes to poor outcome in approximately 10–40% of patients with dense SAH.

There are numerous clinical studies which revealed that early surgical removal of blood clots and irrigation of subarachnoid spaces may reduce the risk of cerebral vasospasm;[15,18,22,27,28] however, the clinical results have not been satisfactory because it is very difficult to remove the clot completely in the acute stage after SAH and may even be hazardous.[17,21] It has also been well documented that the amount of subarachnoid clot is closely related to the incidence and severity of vasospasm.[17,22,27,28] In his original article published in 1980, Fisher had shown that the amount of blood within the basal cisterns on a CT scan correlated with the development of angiographic vasospasm.[29] When the subarachnoid blood was not detected or <1 mm thick (Fisher Grade I, II), severe vasospasm was rare (1 of 18 cases). In Fisher Grade III, severe spasm followed

almost invariably (23 of 24 cases).[29] This was confirmed by subsequent studies.[30,31] More recently, it was found that the relative risk for symptomatic vasospasm was 5.1 for patients with Fisher Grade III SAH (95% confidence interval, 2.0–13.1; *P* = 0.008).[32] Experimental studies in which a primate model was used showed that clot removal within 48 h of SAH prevented vasospasm.

The theoretical foundation of draining CSF in aneurysmal SAH is based on the fact that various substances derived from subarachnoid blood are related to mechanisms of development of cerebral vasospasm. Inagawa *et al*.[15] in their 140 surgically treated aneurysmal SAH patients undergoing cisternal CSF drainage concluded that the incidence of symptomatic and angiographic vasospasm was lower in patients with cisternal CSF drainage.

Several authors have combined cisternal CSF drainage with administration of fibrinolytic agents (urokinase [UK], recombinant tissue plasminogen activator [t-PA], etc.) which help in clot lysis. Mizoi *et al*.[18] assessed the efficacy of postoperative intrathecal injections of t-PA in preventing cerebral vasospasm in cases, with a diffuse severe SAH (Fisher Grade III aneurysmal SAH). None of the patients in their study developed angiographic vasospasm or delayed ischemic neurological deficit.

Hiroshima *et al*.[33] in their retrospective cohort study involving 95 patients with aneurysmal SAH concluded that effective CSF space irrigation with UK can prevent both symptomatic vasospasm and late hydrocephalus.

Yamada *et al*.[34] retrospectively studied effect of cisternal drainage and intrathecal UK injections in preventing symptomatic vasospasm after aneurysmal SAH in 69 patients with aneurysmal SAH (World Federation of Neurological Surgeons Grade I to IV, Fisher's Grade III, undergoing surgery, or coil embolization within 72 h of the onset). This study concluded that combining continuous

cerebrospinal drainage and intermittent intrathecal UK injection therapy is a relatively simple and effective method for symptomatic vasospasm prophylaxis in patients with aneurysmal SAH.

Kinouchi *et al*.[35] also concluded that intraoperative cisternal irrigation with t-PA combined with cisternal drainage is safe and effective for the prevention of symptomatic vasospasm following SAH. Hänggi *et al*.,[28] in a recently published prospective randomized clinical trial, have concluded that a multimodal approach with translumbar lysis with UK in combination with kinetic therapy using head shaking followed by intrathecal nimodipine lavage proved to be effective against cerebral vasospasm and for better clinical outcome.

However, there are some studies in literature which show that postoperative cisternal CSF drainage does not affect the incidence of cerebral vasospasm or the clinical outcome in patients with aneurysmal SAH.[27]

Results from several reports have indicated that direct ventricular CSF drainage resulted in preventing the vasospasm after aneurysmal SAH.[11] On the other hand, direct CSF draining from lateral ventricle may cause stasis blood clots within subarachnoid spaces so that ventricular drainages such as external ventricular drainage may, in fact, increase the risk of cerebral vasospasm.[17] LCSFD seems to be an easy and efficacious method to wash out the blood clots from subarachnoid spaces and cisterns, consequently preventing vasospasm. Moreover, LCSFD would be expected to promote circulation of clear and newly generated CSF from cerebral ventricles through subarachnoid spaces and also elimination of blood clots from intrathecal space with reduction in intracranial pressure.[17]

Several authors proposed that LCSFD after surgical clipping show positive influences on incidence of cerebral vasospasm, GOS score, cerebral infarct, and mean hospital stay.[16,17]

Klimo *et al*.[17] in a prospective nonrandomized trial involving 167 patients concluded that the LCSFD was superior to ventricular CSF drainage in the management of vasospasm. Symptomatic vasospasm occurred in 17% and 51% of patients with and without LCSFD, respectively, indicating that external clearance of spasmogenic substances reduces vasospasm in patients with thick SAH. Shunting of CSF through a lumbar drain conferred a statistically significant advantage with respect to marked reduction in the risk of clinically evident vasospasm and its sequelae, shortening of hospital stay, and improvement in outcome. In comparison with ventricular CSF drainage, LCSFD is more safe without being a direct cause of brain parenchymal damages such as intracranial hemorrhage.

Kasuya *et al*.[20] retrospectively studied the influence of continuous CSF drainage on vasospasm and hydrocephalus in 150 patients with aneurysmal SAH (32 cases of Grade I, 85 cases of Grade II, and 33 cases of Grade III by the Hunt and Hess classification). One-hundred seven of these cases received CSF drainage (cisternal, ventricular, lumbar, or a combination of these). There was a statistically significant reduction in vasospasm in the patients in which continuous CSF drainage was carried out ($P < 0.05$).

Kwon *et al*.[23] also established the effectiveness of LCSFD in preventing clinical vasospasm and its sequelae after endovascular coiling on aneurysmal SAH. The incidence of clinical vasospasm in the lumbar drain group was 23.4% compared to 63.3% the control group. Moreover, the risk of death in the lumbar drain group was 2.1% compared to 15% in the control group.

Hoekema *et al*.[14] studied the safety of LCSFD in aneurysmal SAH patients and concluded that LCSFD is safe when used in the setting of aneurysmal SAH if appropriate patient selection and good technique are employed. Of the 25 patients treated with a lumbar drain, only one suffered a reversible neurological event. No other complications occurred.

Table 4 summarizes the results of various studies regarding spinal CSF drainage for prevention of vasospasm following aneurysmal SAH.

Lumbar CSF drainage may be associated with various complications. Spinal nerve root injury and postdural puncture headache are reported as complications of LCSFD. Overaggressive CSF drainage from lumbar puncture drain can cause development of intracranial hemorrhage including extradural and subdural hematoma as evidenced by two cases in the present study.

In addition, cerebral herniation causing death or severe neurological impairment is the most serious complication of LCSFD, especially in patients with increased intracranial pressure.[12] The incidence of meningitis following continuous LCSFD varied from 2% to 10.5% as per various published series.[36-39]

## Limitations of the study

The major limitation of the study is its small sample size. We observed that the beneficial effect of LCSFD in preventing cerebral vasospasm was statistically significant in SAH Grade III patients ($P = 0.008$). In SAH Grade II and IV patients, although the incidence of vasospasm was lower in LCSFD group compared to non-LCSFD group, it did not reach statistical significance probably due to small sample size.

## Conclusion

This prospective, randomized controlled study has demonstrated the efficacy of LCSFD to significantly reduce clinical vasospasm and vasospasm-related cerebral infarction in patients with aneurysmal SAH, thereby

**Table 4: Studies regarding role of lumbar cerebrospinal fluid drainage for prevention of vasospasm in aneurysmal subarachnoid hemorrhage**

| Author | Year of publication | Study design | Inclusion criteria | Number of patients in LP CSF drain group | Number of patients in the control group | Results | Additional remarks |
|---|---|---|---|---|---|---|---|
| Klimo *et al.* | 2004 | Nonrandomized, retrospective, controlled-cohort study, surgically treated | Fisher Grade III, Grade IV | 81 | 86 | Statistically significant protective and beneficial effect across all outcome measures in Lumbar CSF drainage group, reducing the incidence of clinical vasospasm, the need for angioplasty and the occurrence of vasospastic infarction from 27% to 7% (all $P$=0.001-0.008). Mean duration of hospital stay was lower and GOS score at follow-up was better in Lumbar CSF drainage group | Lumbar CSF drainage conferred statistically significant protective effect in prevention of vasospasm across all Fisher grades |
| Hanggi *et al.* | 2008 | Prospective nonrandomized Phase II study Surgically treated | Fisher Grade III, Grade IV WFNS Grade II-IV | 20 | 20 | Combination of lumboventricular lavage and mechanical head motion reduces vasospasm on TCD ultrasonography, the incidence of DIND, and secondary infarctions on CT and improves clinical outcome ($P$=0.00002-0.005) | No obvious effect could be found on the rate of angiographic vasospasm |
| Kwon *et al.* | 2008 | Prospective nonrandomized, endovascular treatment only | Fisher Grade II-IV | 47 | 60 | Statistically significant protective effect in Lumbar CSF drainage group, reducing the incidence of clinical vasospasm and mortality. GOS score better in Lumbar CSF drainage group | No statistical significances in mean hospital stay and shunt procedures between the two groups |
| Kasuya *et al.* | 1988 | Retrospective Surgically treated | Fisher Grade II-IV | 107 | - | Statistically significant dose-response (drainage volume-vasospasm) relationship ($P$<0.005) | Study also includes alternative forms of CSF drainage (cisternal, ventricular, or a combination of these) |
| Present study | 2016 | Prospective randomized study Surgically treated | Fisher GradeII-IV Hunt and Hess Grade II-IV | 30 | 30 | Lumbar CSF drainage caused a statistically significant reduction in the incidence of clinical and radiological vasospasm and its sequelae. It also shortened the overall duration of hospital stay and improved the outcome as evidenced by a better GOS score at 1- and 3- month follow-up | The beneficial effect of Lumbar CSF drainage in preventing cerebral vasospasm was statistically significant in SAH Grade III patients ($P$=0.008). In SAH Grade II and IV patients, although the incidence of vasospasm was lower in Lumbar CSF drainage group compared to non-Lumbar CSF drainage, it did not reach statistical significance |

CSF – Cerebrospinal fluid; GOS – Glasgow outcome score; SAH – Subarachnoid hemorrhage; LCSFD – Lumbar CSF drainage; TCD – Transcranial Doppler; CT – Computed tomography; DIND – Delayed ischemic neurological deficit; WFNS – World Federation of Neurological Surgeons

contributing to a better outcome. Lumbar CSF drainage is are believed to decrease cerebral vasospasm by promoting circulation of CSF and clearance of blood from the subarachnoid spaces. LCSFD can be associated with meningitis. Proper care and appropriate antibiotics are warranted to prevent infection in patients who undergo LCSFD.

## Financial support and sponsorship

Nil.

## Conflicts of interest

There are no conflicts of interest.

## References

1. Awad IA, Carter LP, Spetzler RF, Medina M, Williams FC Jr. Clinical vasospasm after subarachnoid hemorrhage: Response to hypervolemic hemodilution and arterial hypertension. Stroke 1987;18:365-72.

2. Origitano TC, Wascher TM, Reichman OH, Anderson DE. Sustained increased cerebral blood flow with prophylactic hypertensive hypervolemic hemodilution ("triple-H" therapy) after subarachnoid hemorrhage. Neurosurgery 1990;27:729-39.

3. Allen GS, Ahn HS, Preziosi TJ, Battye R, Boone SC, Boone SC, *et al.* Cerebral arterial spasm – A controlled trial of nimodipine in patients with subarachnoid hemorrhage. N Engl J Med 1983;308:619-24.

4. Barker FG 2nd, Ogilvy CS. Efficacy of prophylactic nimodipine for delayed ischemic deficit after subarachnoid hemorrhage: A metaanalysis. J Neurosurg 1996;84:405-14.

5. Feigin VL, Rinkel GJ, Algra A, Vermeulen M, van Gijn J. Calcium antagonists in patients with aneurysmal subarachnoid hemorrhage: A systematic review. Neurology 1998;50:876-83.

6. Elliott JP, Newell DW, Lam DJ, Eskridge JM, Douville CM, Le Roux PD, *et al.* Comparison of balloon angioplasty and papaverine infusion for the treatment of vasospasm following aneurysmal subarachnoid hemorrhage. J Neurosurg 1998;88:277-84.

7. Eskridge JM, McAuliffe W, Song JK, Deliganis AV, Newell DW, Lewis DH, *et al.* Balloon angioplasty for the treatment of vasospasm: Results of first 50 cases. Neurosurgery 1998;42:510-6.

8. Corsten L, Raja A, Guppy K, Roitberg B, Misra M, Alp MS, *et al.* Contemporary management of subarachnoid hemorrhage and vasospasm: The UIC experience. Surg Neurol 2001;56:140-8.

9. Findlay JM, Kassell NF, Weir BK, Haley EC Jr., Kongable G, Germanson T, *et al.* A randomized trial of intraoperative, intracisternal tissue plasminogen activator for the prevention of vasospasm. Neurosurgery 1995;37:168-76.

10. Kassell NF, Torner JC, Haley EC Jr., Jane JA, Adams HP, Kongable GL. The international cooperative study on the timing of aneurysm surgery. Part 1: Overall management results. J Neurosurg 1990;73:18-36.

11. Macdonald RL. Pathophysiology and molecular genetics of vasospasm. Acta Neurochir Suppl 2001;77:7-11.

12. Weir B, Macdonald RL, Stoodley M. Etiology of cerebral vasospasm. Acta Neurochir Suppl 1999;72:27-46.

13. Hirashima Y, Kurimoto M, Hayashi N, Umemura K, Hori E, Origasa H, *et al.* Duration of cerebrospinal fluid drainage in patients with aneurysmal subarachnoid hemorrhage for prevention of symptomatic vasospasm and late hydrocephalus.

Neurol Med Chir (Tokyo) 2005;45:177-82.

14. Hoekema D, Schmidt RH, Ross I. Lumbar drainage for subarachnoid hemorrhage: Technical considerations and safety analysis. Neurocrit Care 2007;7:3-9.

15. Inagawa T, Kamiya K, Matsuda Y. Effect of continuous cisternal drainage on cerebral vasospasm. Acta Neurochir (Wien) 1991;112:28-36.

16. Kasuya H, Shimizu T, Kagawa M. The effect of continuous drainage of cerebrospinal fluid in patients with subarachnoid hemorrhage: A retrospective analysis of 108 patients. Neurosurgery 1991;28:56-9.

17. Klimo P Jr., Kestle JR, MacDonald JD, Schmidt RH. Marked reduction of cerebral vasospasm with lumbar drainage of cerebrospinal fluid after subarachnoid hemorrhage. J Neurosurg 2004;100:215-24.

18. Mizoi K, Yoshimoto T, Takahashi A, Fujiwara S, Koshu K, Sugawara T. Prospective study on the prevention of cerebral vasospasm by intrathecal fibrinolytic therapy with tissue-type plasminogen activator. J Neurosurg 1993;78:430-7.

19. Sasaki T, Ohta T, Kikuchi H, Takakura K, Usui M, Ohnishi H, *et al.* A phase II clinical trial of recombinant human tissue-type plasminogen activator against cerebral vasospasm after aneurysmal subarachnoid hemorrhage. Neurosurgery 1994;35:597-604.

20. Kasuya H, Shimizu T, Okada T, Takahashi K, Summerville T, Kitamura K. A study of continuous cerebrospinal fluid drainage in patients with subarachnoid hemorrhage. No Shinkei Geka 1988;16 5 Suppl: 475-81.

21. Sasaki T, Kodama N, Kawakami M, Sato M, Asari J, Sakurai Y, *et al.* Urokinase cisternal irrigation therapy for prevention of symptomatic vasospasm after aneurysmal subarachnoid hemorrhage: A study of urokinase concentration and the fibrinolytic system. Stroke 2000;31:1256-62.

22. Kawamoto S, Tsutsumi K, Yoshikawa G, Shinozaki MH, Yako K, Nagata K, *et al.* Effectiveness of the head-shaking method combined with cisternal irrigation with urokinase in preventing cerebral vasospasm after subarachnoid hemorrhage. J Neurosurg 2004;100:236-43.

23. Kwon OY, Kim YJ, Kim YJ, Cho CS, Lee SK, Cho MK. The utility and benefits of external lumbar CSF drainage after endovascular coiling on aneurysmal subarachnoid hemorrhage. J Korean Neurosurg Soc 2008;43:281-7.

24. Vatter H, Mursch K, Zimmermann M, Zilliken P, Kolenda H, Seifert V, *et al.* Endothelin-converting enzyme activity in human cerebral circulation. Neurosurgery 2002;51:445-51.

25. Asano T, Takakura K, Sano K, Kikuchi H, Nagai H, Saito I, *et al.* Effects of a hydroxyl radical scavenger on delayed ischemic neurological deficits following aneurysmal subarachnoid hemorrhage: Results of a multicenter, placebo-controlled double-blind trial. J Neurosurg 1996;84:792-803.

26. Kamezaki T, Yanaka K, Nagase S, Fujita K, Kato N, Nose T. Increased levels of lipid peroxides as predictive of symptomatic vasospasm and poor outcome after aneurysmal subarachnoid hemorrhage. J Neurosurg 2002;97:1302-5.

27. Otawara Y, Ogasawara K, Kubo Y, Sasoh M, Ogawa A. Effect of continuous cisternal cerebrospinal fluid drainage for patients with thin subarachnoid hemorrhage. Vasc Health Risk Manag 2007;3:401-4.

28. Hänggi D, Eicker S, Beseoglu K, Behr J, Turowski B, Steiger HJ. A multimodal concept in patients after severe aneurysmal subarachnoid hemorrhage: Results of a controlled single centre prospective randomized multimodal phase I/II trial on cerebral vasospasm. Cent Eur Neurosurg 2009;70:61-7.

29. Fisher CM, Kistler JP, Davis JM. Relation of cerebral vasospasm to subarachnoid hemorrhage visualized by computerized tomographic scanning. Neurosurgery 1980;6:1-9.

30. Rabb CH, Tang G, Chin LS, Giannotta SL. A statistical analysis of factors related to symptomatic cerebral vasospasm. Acta Neurochir (Wien) 1994;127:27-31.

31. Inagawa T. Cerebral vasospasm in elderly patients treated by early operation for ruptured intracranial aneurysms. Acta Neurochir (Wien) 1992;115:79-85.

32. Lasner TM, Weil RJ, Riina HA, King JT Jr., Zager EL, Raps EC, *et al.* Cigarette smoking-induced increase in the risk of symptomatic vasospasm after aneurysmal subarachnoid hemorrhage. J Neurosurg 1997;87:381-4.

33. Hirashima Y, Endo S, Kato R, Takaku A. Indications for cisternal irrigation with urokinase in postoperative patients with aneurysmal subarachnoid haemorrhage. Br J Neurosurg 1996;10:477-81.

34. Yamada K, Yoshimura S, Enomoto Y, Yamakawa H, Iwama T. Effectiveness of combining continuous cerebrospinal drainage and intermittent intrathecal urokinase injection therapy in preventing symptomatic vasospasm following aneurysmal subarachnoid haemorrhage. Br J Neurosurg 2008;22:649-53.

35. Kinouchi H, Ogasawara K, Shimizu H, Mizoi K, Yoshimoto T. Prevention of symptomatic vasospasm after aneurysmal subarachnoid hemorrhage by intraoperative cisternal fibrinolysis using tissue-type plasminogen activator combined with continuous cisternal drainage. Neurol Med Chir (Tokyo) 2004;44:569-75.

36. Shapiro SA, Scully T. Closed continuous drainage of cerebrospinal fluid via a lumbar subarachnoid catheter for treatment or prevention of cranial/spinal cerebrospinal fluid fistula. Neurosurgery 1992;30:241-5.

37. Findler G, Sahar A, Beller AJ. Continuous lumbar drainage of cerebrospinal fluid in neurosurgical patients. Surg Neurol 1977;8:455-7.

38. Kitchel SH, Eismont FJ, Green BA. Closed subarachnoid drainage for management of cerebrospinal fluid leakage after an operation on the spine. J Bone Joint Surg Am 1989;71:984-7.

39. Marshman LA, Hardwidge C, Donaldson PM. *Bacillus cereus* meningitis complicating cerebrospinal fluid fistula repair and spinal drainage. Br J Neurosurg 2000;14:580-2.