Retrospective Study

# Comparison of Efficacy of an Epidural Blood Patch in Patients with Spinal Leakage of Cerebrospinal Fluid

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**Background:** The leakage of cerebrospinal fluid (CSF) can be encountered spontaneously or after procedures such as epidural or spinal anesthesia, intrathecal chemotherapy, CSF tapping, or other various spinal procedures. The leakage of CSF can lead to intracranial hypotension, which is associated with an orthostatic headache. For such patients with this type of headache, an epidural blood patch is the treatment of choice.

**Objective:** The purpose of this study is to compare the clinical features and efficacy of an epidural blood patch for patients with spinal leakage of CSF.

**Study Design:** Retrospective study.

**Setting:** University hospital inpatients referred for consultation to the pain clinic

**Methods:** Identification of patients with orthostatic headache was performed using the program Clinical Data Warehouse (CDW) v 2.5. Search word in CDW for analysis was "epidural blood patch." We carefully evaluated the demographics, etiology, clinical features of headache, associated phenomena other than headache, level and types of CSF leakage, and frequencies and outcomes of epidural blood patches. We allocated patients into 2 groups according to the cause of headache: spontaneous intracranial hypotension (group SIH) and post-dural puncture headache (group PDPH).

**Results:** The number of patients needing repeated epidural blood patches was significantly higher in the SIH group SIH in the PDPH group ($P = 0.007$). In the PDPH group, a targeted epidural blood patch was possible in 100% of the cases, whereas it was possible in only 66.7% of the patients in the SIH group, indicated by previous examination ($P < 0.001$). Forty patients (90.9%) and 17 patients (70.8%) achieved complete recovery from headache after a single epidural blood patch in the PDPH group and SIH group, respectively ($P < 0.001$).

**Limitation:** The number of patients allocated to each group was not balanced because of the retrospective design.

**Conclusion:** Most patients in the PDPH group required a single epidural blood patch to achieve complete recovery from headache. However, patients in the SIH group required repeated epidural blood patches for complete pain relief.

**Key words:** CSF leakage, epidural blood patch, intracranial hypotension, orthostatic headache

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Cerebrospinal fluid (CSF) hypovolemia, which means a volume depletion of CSF, is a disease mainly caused by the leakage of spinal CSF. The causes of CSF hypovolemia can include a traumatic CSF leakage, spontaneous CSF leakage, and iatrogenic CSF leakage by a needle puncture (1).

Spontaneous intracranial hypotension (SIH) results from CSF leakage from the spinal column. Underlying dural sac weakness associated with meningeal diver-

ticula, minor trauma in conditions of dural weakness, ventral dural tears of intervertebral disc material, and CSF-venous fistulas are frequent causes of SIH. However, in some cases, the cause of SIH is completely unknown (1,2). Headache is the most common manifestation of patients with SIH. Headaches are mostly orthostatic, with various clinical presentations such as nausea, vomiting, photophobia, hearing impairment, and dizziness (3). Diagnostic measures for suspected SIH are radioisotope (RI) cisternography, computed tomography (CT) myelography, and magnetic resonance imaging (MRI) myelography. For RI cisternography, indium-111 is injected intrathecally via lumbar puncture. Following intrathecal RI injection, sequential scanning demonstrates dynamic changes in parathecal activity. The appearance of parathecal activity following RI injection is considered direct evidence of CSF leakage, indicating the approximate leakage site (1-4).

Post-dural puncture headache (PDPH) is one of the most common complications of diagnostic, therapeutic, or inadvertent dural punctures. Similar to SIH, the hallmark symptom of PDPH is the onset of headache within 15 minutes of standing or sitting. The headache resolves within 15 minutes of lying down. In most cases, the symptom of PDPH occurs within 3 days of the diagnostic or therapeutic procedure (5,6). Although using a smaller gauge with an atraumatic needle demonstrates a preventive effect in reducing PDPH, some procedures, such as postoperative lumbar drainage, always require a large gauge needle for catheter insertion. In such cases, headache is frequently observed (7).

Conservative treatment for SIH and PDPH includes bed rest, theophylline, intravenous fluid infusion, caffeine, and epidural blood patch (EBP). Among such treatment, EBP is considered the treatment of choice for those patients who have failed to respond to an initial conservative treatment (2,3,8-12).

The efficacy of an EBP varies, ranging from 36% to 90% with different injection methods and blood volumes (11-14). SIH and PDPH present similar clinical characteristics, and both diseases require an EBP if an initial conservative treatment has failed. However, there are limited studies comparing clinical features and efficacy of an EBP. The purpose of this study is to compare the clinical features and efficacy of an EBP in patients with SIH or PDPH.

## Methods

### Patients

This study was performed in a retrospective manner after approval from our institutional review board (2021-01-070). Patients with headache who had been referred for consultation to pain clinics for an EBP from February 2019 through November 2020 were included. Patients who had received an EBP for headache prevention prior to any symptom development were excluded. Identification and analysis of these patients were performed using the program Clinical Data Warehouse v 2.5 (CDW, Planit Healthcare, Seoul, Republic of Korea). The search word that we used with the CDW for analysis was "epidural blood patch."

### EBP Performance

EBP was performed by a C-arm-guided technique by a single physician with experience performing more than 6,000 C-arm-guided injections. For epidural entry at a specific spinal level, a midline approach via loss-of-air resistance was used. Autologous blood ranging from 7 - 15 mL was injected using a 22G Tuohy epidural needle. Blood was injected very slowly to minimize any discomfort during the injection. Before injection of blood, the epidural space was confirmed by using 3 mL of contrast medium.

### Group Allocation

Included patients were classified into 2 groups depending on the cause of headache. Patients who received an EBP due to SIH were classified into the group SIH. Patients who received an EBP due to PDPH were classified into the group PDPH. These groups were compared with respect to demographic characteristics, etiologies, headache features, level and types of CSF leakage, frequencies, and clinical outcomes of an EBP.

### Review of Medical Records

Careful evaluation was performed using the electronic medical records of each patient. Evaluated data included demographics, etiology of headache, history of previous headache, headache features and intensity, associated phenomena other than headache, level and types of CSF leakage, and frequencies and outcomes of an EBP. For the determination of level of CSF leakage, the results of cisternography or myelography were evaluated. Single level or multiple CSF leakage level was also determined by the result of cisternography or myelography. Pain intensity was evaluated using a visual analog scale (VAS; 0 = no pain and 10 = most severe pain imaginable) before EBP and one day after EBP. When an EBP was performed, it was divided into targeted vs nontargeted EBP. Targeted EBP means that it was performed at the corresponding CSF leakage level. Nontargeted EBP was performed irrespective of the level of CSF leakage. Pa-

tients in the SIH group who did not show any CSF leakage after examination, and those who had not undergone such examination, received an EBP at the cervicothoracic junction, since this level is known to be the most frequent level of spontaneous CSF leakage (8,15). Patients in the PDPH group did not undergo any examination since the punctured spinal level was very clear following a diagnostic or therapeutic procedure. Therefore, the level of CSF leakage in the PDPH group was determined according to the punctured spinal level during the procedure.

Clinical outcomes after an EBP were classified into excellent (complete headache relief without recurrence after the first EBP); good (headache relief after the first EBP, but subsequent recurrence of headache with spontaneous remission); fair (headache relief after second EBP); and poor (more than 3 EBPs with minimal headache improvement).

### Statistical Analysis

After a normality test, Student t-test or Mann-Whitney U test was performed to analyze differences between the groups with respect to age, body mass index, and headache intensities measured by VAS. The $\chi^2$ test was used to compare differences between groups with respect to gender, headache features, associated phenomena, levels and types of CSF leakage, and the frequencies and outcomes of an EBP. All statistical values were 2-tailed, and $P$ values < 0.05 were considered to be statistically significant. Statistical evaluations were performed using computer program SPSS v 22.0 (IBM Corporation, Armonk, NY).

## Results

Using the search word "epidural blood patch," 78 patients were identified for analysis (February 2019 through November 2020). Among these 78 patients, 10 patients were excluded since an EBP had been performed for the prevention of headache. Therefore, the remaining 68 patients were analyzed.

The causes of PDPH in that group included postlumbar drainage, postspinal tapping for CSF study, and postspinal anesthesia. Among them, postspinal tapping and postspinal anesthesia were the most common. Among patients in the SIH group, 12% had a history of falling from a height before headache development. Otherwise, patients in the SIH group did not have a prior history of trauma. Patients in the PDPH group were significantly younger than those in the SIH group ($P$ = 0.014, Table 1).

Orthostatic headache was the most dominant clinical feature in both groups (91.7% in the SIH group vs 90.0% in the PDPH group). However, headache intensity was significantly higher in the SIH group than in the PDPH group ($P$ = 0.047, Table 2). Associated phe-

Table 1. *Demographic characteristics and etiologies.*

| | Total Patients (n = 68) | SIH Group (n = 24) | PDPH Group (n = 44) | *P* value |
|---|---|---|---|---|
| Age (years) | 37.5 (55.0-30.3) | 49.5 (34.0-64.5)- | 35.0 (28.3-44.8) | 0.014 |
| Gender | | | | 0.667 |
| Male | 26 (38%) | 10 (42%) | 16 (36%) | |
| Female | 42 (62%) | 14 (58%) | 28 (64%) | |
| BMI (kg/m$^2$) | 22.0 (3.2) | 22.0 (2.8) | 22.9 (3.9) | 0.310 |
| Etiology | | | | |
| Spontaneous | | 21 (88%) | | |
| Traumatic | | 3 (12%) | | |
| Postlumbar drain | | | 1 (2%) | |
| Postspinal tapping | | | 28 (64%) | |
| Postspinal anesthesia | | | 15 (34%) | |

Values are number (%), mean (SD), or median (interquartile range). BMI, body mass index; SIH, spontaneous intracranial hypotension; PDPH, postdural puncture headache.

Table 2. *Headache features and associated phenomena.*

| | Total Patients (n = 68) | SIH Group (n = 24) | PDPH Group (n = 44) | *P* value |
|---|---|---|---|---|
| History of previous headache | 8 (11.8%) | 3 (12.5%) | 5 (11.4%) | 0.889 |
| Headache features | | | | 0.916 |
| Orthostatic | 62 (91.2%) | 22 (91.7%) | 40 (90.9%) | |
| Nonorthostatic | 6 (8.8%) | 2 (8.3%) | 4 (9.1%) | |
| Headache intensity (0-10) | 5.0 (4.0-6.0) | 5.0 (4.3-6.0) | 4.0 (4.0-6.0) | 0.047 |
| Associated phenomena | | | | |
| Nausea | 25 (36.8%) | 10 (41.7%) | 15 (34.1%) | 0.536 |
| Vomiting | 16 (23.5%) | 6 (25.0%) | 10 (22.7%) | 0.833 |
| Tinnitus | 3 (4.4%) | 1 (4.2%) | 2 (4.5%) | > 0.999 |
| Dizziness | 17 (25.0%) | 4 (16.7%) | 13 (29.5%) | 0.241 |
| Diplopia | 1 (1.5%) | 1 (4.2%) | 0 (0%) | 0.353 |
| Chilling sensation | 14 (20.6%) | 6 (25.0%) | 8 (18.2%) | 0.542 |

Values are number (%) or median (interquartile range). SIH, spontaneous intracranial hypotension; PDPH, postdural puncture headache.

nomena other than headache included nausea, vomiting, tinnitus, dizziness, diplopia, and chilling sensation. Among them, nausea and vomiting were the most common in both groups (Table 2).

To identify the level of CSF leakage, 20 patients (83%) in the SIH group underwent cisternography or MRI myelography. Thoracic and lumbar levels were most common in the SIH group and PDPH group, respectively. Among patients in the SIH group, 66.7% showed multiple levels of CSF leakage, whereas only 4.5% of patients in the PDPH group showed multiple CSF leakage (Table 3).

The number of patients who needed repeated EBP was significantly higher in the SIH group than in the PDPH group. The maximum number of EBPs in the SIH group was 3 ($P$ = 0.007). Targeted EBP was possible in 100% of patients in the PDPH group, whereas only in 66.7% of patients in the SIH group, as indicated by previous examination ($P$ < 0.001). Forty patients (90.9%) and 17 patients (70.8%) achieved complete recovery of headache with a single EBP in the PDPH group and SIH group, respectively ($P$ < 0.001). The time interval from headache development to an EBP was significantly longer in the SIH group than in the PDPH group (15.0 vs 3.0 days, $P$ < 0.001, Table 4)

Table 3. *Level and types of CSF leakage.*

| | Total Patients (n = 68) | SIH Group (n = 24) | PDPH Group (n = 44) | *P* value |
|---|---|---|---|---|
| Level of CSF leakage | | | | |
| Cervical | 1 (1.5%) | 1 (4.2%) | 0 (0.0%) | 0.353 |
| Thoracic | 15 (22.1%) | 13 (54.2%) | 2 (4.5%) | < 0.001 |
| Lumbar | 48 (70.6%) | 6 (25.0%) | 42 (95.5%) | < 0.001 |
| None | 7 (10.3%) | 7 (29.2%) | 0 (0.0%) | < 0.001 |
| Types of CSF leakage | | | | < 0.001 |
| One level | 43 (63.2%) | 1 (4.2%) | 42 (95.5%) | |
| Multiple level | 18 (26.5%) | 16 (66.7%) | 2 (4.5%) | |
| None | 7 (10.3%) | 7 (29.2%) | 0 (0.0%) | |

Values are number (%). CSF, cerebrospinal fluid; SIH, spontaneous intracranial hypotension; PDPH, postdural puncture headache.

## Discussion

This study shows that more than 90% of the patients in the PDPH group required only a single EBP to achieve a complete recovery of headache, compared to the patients in the SIH group. A previous study also demonstrated that an iatrogenic needle puncture group had a lower number of EBPs compared to the spon-

Table 4. *Frequencies and outcomes of an epidural blood patch.*

| | Total Patients (n = 68) | SIH Group (n = 24) | PDPH Group (n = 44) | *P* value |
|---|---|---|---|---|
| Number of EBPs | | | | 0.007 |
| One | 55 (80.9%) | 15 (62.5%) | 40 (90.9%) | |
| Two | 10 (14.7%) | 6 (25.0%) | 4 (9.1%) | |
| More than 3 or more | 3 (4.4%) | 3 (12.5%) | 0 (0.0%) | |
| Direction of EBP | | | | < 0.001 |
| Targeted | 60 (88.2%) | 16 (66.7%) | 44 (100.0%) | |
| Nontargeted | 8 (11.8%) | 8 (33.3%) | 0 (0.0%) | |
| Outcome of EBP | | | | < 0.001 |
| Excellent | 50 (73.5%) | 11 (45.8%) | 39 (88.6%) | |
| Good | 10 (14.7%) | 6 (25.0%) | 1 (2.3%) | |
| Fair | 5 (7.4%) | 4 (16.7%) | 4 (9.1%) | |
| Poor | 3 (4.4%) | 3 (12.5%) | 0 (0.0%) | |
| Onset-EBP intervals (days) | 4.0 (3.0-13.5) | 15.0 (10.0-21.75) | 3.0 (2.0-4.0) | < 0.001 |

Values are number (%) or median (interquartile range). EBP, epidural blood patch; SIH, spontaneous intracranial hypotension; PDPH, post-dural puncture headache. Targeted, epidural blood patch was performed at the CSF leakage level; nontargeted epidural blood patch was performed irrespective of CSF leakage level; Excellent, complete headache relief without recurrence after first epidural blood patch; Good, headache relief after the first epidural blood patch but subsequent recurrence of headache with spontaneous remission; Fair, headache relief after second epidural blood patch; Poor, more than three epidural blood patches with minimal headache improvement.

taneous intracranial hypotension group (15). The difference of outcome between these 2 groups is related to differences in the nature of the dural tear. Spontaneous CSF leakage found in the SIH group is considered to develop in the weak areas of the dura mater. Various dural weaknesses, either congenital or acquired, allow CSF to leak into the epidural space. Moreover, such spontaneous tears tend to present a larger hole than those created by iatrogenic needle punctures (4,16).

The mechanism by which EBP improves orthostatic headache can be explained in 2 stages. In the early stage, elevated epidural pressure by injection of autologous blood subsequently leads to an elevation of CSF pressure. Accordingly, intracranial CSF volume is replaced by redistribution of CSF. In the later stage, injected autologous blood forms a blood clot or fibrosis to seal the CSF leakage with resultant prevention of further leakage (9,15). Immediate effects correspond to the changes during the earlier stage of EBP, whereas delayed and long-lasting effects can be expected during the later stage of EBP (9).

CT myelography or radionuclide cisternography often reveals multiple levels of CSF leakage throughout the spine in patients with SIH (17). Accordingly, this study shows 66.7% of patients in the SIH group had multiple levels of CSF leakage. If CSF is leaking in multiple areas, this means that a more broad area should be treated with injected blood. Hence, it seems that a delayed effect of injected blood as scar formation was relatively weak in the SIH group since a more broad area of leakage within the spinal canal should be treated with blood. Targeted EBP was possible in only 66.7% of the SIH group, whereas it was possible in 100% of the PDPH group.

We consider that injecting blood at the corresponding spinal level is important for the sealing effect caused by scar formation or fibrosis of blood. However, due to the invasive nature of cisternography or myelography, not all patients in the SIH group could undergo such an examination. Those patients who were not evaluated with examination received an EBP at the cervicothoracic level. This failure of targeted EBP in the SIH group might explain differences in efficacy. In a large cohort study of EBP, site-directed EBP correlated well with a greater likelihood of first EBP efficacy (10). Another reason for different efficacy between these 2 groups is because of longer intervals required until performance of an EBP in the SIH group compared to the PDPH group. All patients in the PDPH group had an evident history of dural puncture before headache development. Therefore, we think that a prompter diagnosis of PDPH compared to SIH was possible. Subsequently, immediate EBP could be performed after failure of conservative treatment. A previous study demonstrated that a delay in EBP fewer than 4 days was associated with a favorable outcome in patients with PDPH (9).

The response rate of the first EBP in the SIH group, which means complete recovery of headache after a single EBP, was 70.8%. A previous study demonstrated a response rate of the first EBP was 58.7% in patients with SIH, which is lower than our result. However, among patients with an injected blood volume more than 22.5 mL, the response rate was higher (67.9% vs 47.0%) (8). This result implies that a higher volume of blood might be required to get a good response from EBP in patients with SIH. Our study showed a response rate of 70.8% in the SIH group with an injection volume of 7-15 mL. Although the injected blood volume did not exceed 20 mL, we obtained similar results to a previous study with a higher blood volume group (8). Therefore, further study is required to clarify the relationship between injected blood volume and subsequent treatment outcomes.

Both groups showed orthostatic headache as the most dominant clinical feature. However, pain intensity in the SIH group was higher than in the PDPH group. The orthostatic nature might become less evident over time. Some patients with SIH can progress to chronic daily headache with anxiety or depression (17). Associated phenomena that were found, other than headache, were nausea, vomiting, dizziness, tinnitus, diplopia and a chilling sensation. Commonly reported cochlear-vestibular signs include tinnitus, ear fullness, dizziness, and vertigo. Hearing change was found in 70% of patients (12). The presence of orthostatic headache, nausea, nuchal pain, and photophobia were associated with good predictors for an EBP (3).

As an etiology of the SIH group, most patients did not present any specific history of trauma before headache development. However, 3 patients in the SIH group had a trauma history. According to a previous study, minor trauma, such as a tumble, was reported in 80% of these patients (17). The PDPH group showed more frequent headache development following postspinal tapping than postspinal anesthesia. The neurology department of our institution uses a 23G spinal needle for spinal tapping. However, a 25G spinal needle is used for the purpose of spinal anesthesia in the operating room. Therefore, using a smaller gauge of needle for spinal

anesthesia can explain such a difference. Needle gauge is an important factor to reduce PDPH (7).

### Limitations

This study includes several limitations. First, since this study is retrospectively designed, there was an imbalance in the number of patients allocated to each group. Further study with a higher number of patients with SIH is required to compare the efficacy of EBP. Second, not all patients who received an EBP had undergone examination to evaluate the CSF leakage level. Especially, most patients of the PDPH group did not undergo such an examination. An EBP was administered at the expected spinal level of CSF leakage in the PDPH group. Third, the injected volume of blood was varied, ranging from 7 mL to 15 mL. Further study is required with an identical injected blood volume to identify the relationship between the effectiveness of EBP and blood volume.

## Conclusion

In conclusion, both groups demonstrated similar clinical features. Most of the patients in the PDPH group required a single EBP to achieve complete recovery from headache. However, patients in the SIH group required repeated EBPs to achieve complete pain relief.

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