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석사학위논문

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

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2021년 8월

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

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이 논문을 석사학위 논문으로 제출함

2021년 8월

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1. Introduction

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 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 diverticula, 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 SIH patients. 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, CT-myelography, and MRI-myelography. For RI cisternography, indium-111 is injected intrathecally via lumbar puncture. Following intrathecal RI injection, sequential scanning demonstrates dynamic changes of 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 complication of diagnostic, therapeutic, or inadvertent dural punctures. Similar with 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 occur within three days of diagnostic or therapeutic procedure [5,6]. Although using a smaller gauge with 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 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.

2. Materials and Methods

This study was performed in a retrospective manner after approval of the institutional review board of Keimyung University Dongsan Hospital (IRB No. 2021-01-070). Headache patients who had been referred for consultation to pain clinics for an EBP from February 2019 to November 2020 were included. Patients who had received an EBP for headache prevention prior to any symptom development were excluded. Identification and analysis of such headache patients were performed using a program of Clinical Data Warehouse version 2.5 (CDW, Planit Healthcare, Seoul, Korea). The search word that we used with the CDW for analysis was “epidural blood patch”.

2.1. EBP performance:

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

2.2. 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.

2.3. Review of medical records:

Careful evaluation was performed using electronic medical records of each patient. Evaluated data includes 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. non-targeted EBP. Targeted EBP means that it was performed at the corresponding CSF leakage level. Non-targeted EBP was performed irrespective of the level of CSF leakage. Patients in the group SIH 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 group PDPH 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 group PDPH was determined according to 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 three EBPs with minimal headache improvement).

2.4. 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, BMI, and headache intensities (VAS). The chi-squared test was used to compare differences between groups with respect to sex, headache features, associated phenomena, levels and types of CSF leakage, and the frequencies and outcomes of an EBP. All statistical values were two-tailed, and P-values < 0.05 were considered to be statistically significant. Statistical evaluations were performed using SPSS version 22.0 (IBM, NY, USA).

3. Results

Using the search word “epidural blood patch”, 78 patients were identified for analysis (February 2019~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 post-lumbar drainage, post-spinal tapping for CSF study, and post-spinal anesthesia. Among them, post-spinal tapping and post-spinal anesthesia were the most common. Among patients in the group SIH, 12% had a history of falling from a height before headache development. Otherwise, patients of the group SIH did not have prior trauma history. Patients in the group PDPH were younger significantly than in the group SIH ($P < 0.05$, Table 1).

Orthostatic headache was the most dominant clinical feature in both groups (91.7% in the group SIH vs 90.0% in the group PDPH). However, headache intensity was significantly higher in the group SIH than in the group PDPH ($P < 0.05$, Table 2). Associated phenomena 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 group SIH underwent cisternography or MRI-myelography. Thoracic and lumbar levels were most common in the group SIH and PDPH, respectively. Among patients in the group SIH, 66.7% of patients showed multiple level of CSF leakage, whereas only 4.5% of patients in the group PDPH showed multiple CSF leakage (Table 3).

The number of patients who needed repeated EBP was significantly higher in the group SIH than in the group PDPH. The maximum number of EBPs in the group SIH was three ($P < 0.01$). Targeted EBP was possible in 100% of patients in the group PDPH, whereas only in 66.7% of patients in the group SIH 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 group PDPH and group SIH, respectively ($P < 0.001$). The time interval from headache development to an EBP was significantly longer in the group SIH than in the group PDPH (15.0 vs 3.0 days, $P < 0.001$, Table 4).

Table 1. Demographic Characteristics and Etiologies

	Total patients (n=68)	Group SIH (n=24)	Group PDPH (n=44)	P-value
Age (years)	37.5 (55.0-30.3)	49.5 (34.0-64.5)	35.0 (28.3-44.8)	< 0.05
Sex				> 0.05
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)	> 0.05
Etiology				
Spontaneous		21 (88%)		
Traumatic		3 (12%)		
Post-lumbar drainage			1 (2%)	
Post-spinal tapping			28 (64%)	
Post-spinal anesthesia			15 (34%)	

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

Table 2. Headache Features and Associated Phenomena

	Total patients (n=68)	Group SIH (n=24)	Group PDPH (n=44)	P-value
History of previous headache	8 (11.8%)	3 (12.5%)	5 (11.4%)	> 0.05
Headache features				> 0.05
Orthostatic	62 (91.2%)	22 (91.7%)	40 (90.9%)	
Non-orthostatic	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)	< 0.05
Associated phenomena				
Nausea	25 (36.8%)	10 (41.7%)	15 (34.1%)	> 0.05
Vomiting	16 (23.5%)	6 (25.0%)	10 (22.7%)	> 0.05
Tinnitus	3 (4.4%)	1 (4.2%)	2 (4.5%)	> 0.05
Dizziness	17 (25.0%)	4 (16.7%)	13 (29.5%)	> 0.05
Diplopia	1 (1.5%)	1 (4.2%)	0 (0%)	> 0.05
Chilling sensation	14 (20.6%)	6 (25.0%)	8 (18.2%)	> 0.05

Values are number (%) or median (interquartile range).

PDPH: post-dural puncture headache; SIH: spontaneous intracranial hypotension.

Table 3. Levels and Types of CSF Leakage

	Total patients (n=68)	Group SIH (n=24)	Group PDPH (n=44)	P-value
Levels of CSF leakage				
Cervical	1 (1.5%)	1 (4.2%)	0 (0.0%)	> 0.05
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				
One level	43 (63.2%)	1 (4.2%)	42 (95.5%)	< 0.001
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; PDPH: post-dural puncture headache; SIH: spontaneous intracranial hypotension.

Table 4. Frequencies and Outcomes of an Epidural Blood Patch

	Total patients (n=68)	Group SIH (n=24)	Group PDPH (n=44)	P-value
Number of EBP				< 0.01
Once	55 (80.9%)	15 (62.5%)	40 (90.9%)	
Twice	10 (14.7%)	6 (25.0%)	4 (9.1%)	
More than three times	3 (4.4%)	3 (12.5%)	0 (0.0%)	
Direction of EBP*				< 0.001
Targeted	60 (88.2%)	16 (66.7%)	44 (100.0%)	
Non-targeted	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; PDPH: post-dural puncture headache; SIH: spontaneous intracranial hypotension.

* Targeted: epidural blood patch was performed at the CSF leakage level; Non-targeted: 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.

4. Discussion

This study showed that more than 90% of the group PDPH patients required only a single EBP to achieve a complete recovery of headache as compared to the group SIH. Previous study also demonstrated that the iatrogenic needle puncture group had a lower number of EBPs as compared to the spontaneous intracranial hypotension group [15]. The difference of outcome between these two groups is related to differences in the nature of the dural tear. Spontaneous CSF leakage found in the group SIH 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 level of CSF leakages throughout the spine in SIH patients [17]. Accordingly, this study showed 66.7% of multiple level of CSF leakage in the group SIH. If CSF is leaking in a multiple area, this means that more broad area should be faced by an injected blood. Hence, it seems that delayed

effect of injected blood as scar formation is relatively weak in the group SIH since more broad area of leakage within spinal canal should be faced by blood. Targeted EBP was possible in only 66.7% of the group SIH, whereas it was possible in 100% of the group PDPH. 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 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 of different efficacy between these two groups is because of longer intervals required until performance of an EBP in the group SIH as compared to the group PDPH. All patients in the group PDPH had an evident history of dural puncture before headache development. Therefore, we think that a prompter diagnosis of PDPH as compared to SIH was possible. Subsequently, immediate EBP could be performed after failure of conservative treatment. Previous study demonstrated that delay in EBP fewer than 4-days was associated with favorable outcome in patients of PDPH [9].

The response rate of first EBP in the group SIH, which means complete recovery of headache after single EBP, was 70.8%. Previous study demonstrated response rate of first EBP being 58.7% in SIH patients, 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 of SIH. Our study showed a response rate of 70.8% in the group SIH with

injection volume of 7~15 mL. Although the injected blood volume did not exceed 20 mL, we obtained similar results in 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 group SIH was higher than in the group PDPH. The orthostatic nature might become less evident over time. Some SIH patients 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 chilling sensation. Commonly reported cochlear-vestibular signs include tinnitus, ear fullness, dizziness, and vertigo. Hearing change was found in 70% of patients [12]. Presence of orthostatic headache, nausea, nuchal pain, and photophobia were associated with good predictors of an EBP [3].

As an etiology of the group SIH, most patients did not present any specific history of trauma before headache development. However, 3 patients in the group SIH had a trauma history. According to previous study, minor trauma such as tumble, was reported in 80% of these patients [17]. The group PDPH showed more frequent headache development following post-spinal tapping than post-spinal anesthesia. The neurology department of our institution uses 23-G spinal needle for spinal tapping. However, a 25-G 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 difference. Needle gauge is an important factor to reduce PDPH [7].

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 higher number of SIH patient is required to compare the efficacy of EBP. Second, not all patients who received an EBP had undergone examination to evaluate CSF leakage level. Especially, most patients of the group PDPH did not undergo such an examination. An EBP was administered at the expected spinal level of CSF leakage in the group PDPH. Third, the injected volume of blood was varied, ranging from 7 to 15 mL. Further study is required under a unified injected blood volume to identify the relationship between the effectiveness of EBP and blood volume.

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

5. Summary

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 headache patients, an epidural blood patch is the treatment of choice. The purpose of this study is to compare the clinical feature and efficacy of epidural blood patch for patients with spinal leakage of CSF.

Identification of orthostatic headache patients was performed using the program of Clinical Data Warehouse (CDW) version 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 two groups according to the cause of headache: spontaneous intracranial hypotension (group SIH) and post-dural puncture headache (group PDPH).

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

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

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(Abstract)

Cerebrospinal fluid (CSF) hypovolemia is a disease mainly caused by the leakage of spinal CSF. The leakage of CSF can be encountered spontaneously or after procedures such as spinal anesthesia, CSF tapping. The leakage of CSF can lead to intracranial hypotension, which is associated with an orthostatic headache. Spontaneous intracranial hypotension (SIH) and post-dural puncture headache (PDPH) present similar clinical characteristics, and both diseases require an epidural blood patch (EBP) if an initial conservative treatment has failed. The purpose of this study is to compare the clinical features and efficacy of EBP in patients with spinal leakage of CSF. Patients were divided into two groups according to the cause of headache: group SIH and group

PDPH. Headache intensity was significantly higher in the group SIH than in the group PDPH. Most patients in the group PDPH required a single EBP to achieve complete recovery of headache. However, patients in the group SIH required repeated EBP for complete pain relief.

뇌척수액의 척수 누출 환자에서 경막외 혈액 봉합술의 효능 비교

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(초록)

뇌척수액 누출은 자연적으로 혹은 경막외 마취, 척추 마취, 뇌척수액 검사 등의 술기 이후에 발생할 수 있다. 뇌척수액 누출의 주요 증상으로는 기립성 두통이 있다. 기립성 두통의 증상이 있는 환자에서 보존적 치료 실패 시, 경막외 혈액 봉합술이 가장 효과적인 치료법으로 알려져 있다. 이 연구에서는 기립성 두통 증상으로 신경 통증 클리닉으로 의뢰되어 경막외 혈액 봉합술을 시행한 환자들에서 두통의 임상 양상, 동반 증상, 경막외 혈액 봉합술의 효과 등을 경막 천자 후 두통군, 자발성 두개내압 저하증군으로 나누어 분석하였다. 그 결과, 경막 천자 후 두통군 환자의 대부분은 한 번의 경막외 혈액 봉합술 시행으로 두통 증상에서의 완전한 회복을 보였다. 반면, 자발성 두개내압 저하증군의 환자들은 두통의 완전한 증상 완화를 위해 반복적인 경막외 혈액 봉합술을 필요로 했고, 두통의 강도는 자발성 두개내압 저하증군의 환자들에게서 더 강한 것으로 나타났다.