의학석사 학위 논문

자발성 두개내 저압증 환자에서 시행하는 경막외 자가 혈액 봉합술의 결과에 미치는 예후 인자에 관련한 연구

Predictors of response to epidural blood patch in patient having spontaneous intracranial hypotension

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이 논문을 의학석사 학위 논문으로 제출함

2021 년 2 월

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ABSTRACT

Spontaneous intracranial hypotension (SIH) is recognized resulted by low cerebrospinal fluid pressure. An autologous epidural blood patch (EBP) in SIH treatment now widely accepted as a mainstay interventional treatment. Although its favor effectiveness, a single EBP often requires additional EBP delivering because of inadequate response in single trial. The aim of this study was to find out an associated factor of EBP outcome to estimate this additional EBP requirement. This single-center retrospective observational study used the institutional registry records of 321 patients who experienced epidural blood patch between September 2001 and March 2016. We divided the SIH patients into two groups according to their response upon EBP; an immediate responder and a delayed responder group. An immediate responder group showed their sufficient symptoms relieving 2times or less attempting EBP, on the other hand delayed responder group showed 3 times or more attempting EBP. Between the two groups, statistical differences in basic demographic characteristics were not found. There are many estimated associated factors for example; brain image, epidural blood patch site, laboratory data including platelet to lymphocyte ratio or neutrophil lymphocyte (NLR) ratio. Consequently, only the NLR showed statistical meaning. We reveal an elevated NLR ratio is an associated factor to favor outcome in multivariate logistic regression analysis.

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INTRODUCTION

Spontaneous intracranial hypotension (SIH) manifest various symptoms resulted by low cerebrospinal fluid pressure.[1,2] The most common symptom is an orthostatic headache, which represents diverse accompanied symptoms with or without neurologic deficit.[3] Other symptoms such as an nausea, vomiting, auditory problem, facial numbness and even visual problems are also reported.[4] For the reason of these various symptoms, diagnosis over SIH is usually confirmed under radiologic assistance and it often identify the leakage level or other structural change.[4] After confirmation of SIH, epidural blood patch (EBP) is widely performed as an interventional management to the level of leakage site or provisional leakage site it not identified their leakage level.

By this time, there are number of studies related to its etiologies and treatments for spontaneous spinal fluid leakage.[5] According to the result of these studies, a non-surgical treatment including EBP showed acceptable outcome.[6] Despite of its effectiveness, there is yet to well established methodology about EBP; for example aiming which target level, determining of blood volume, delivering interval or other related factors which affect its results. On a detail view of each clinical study, previous studies proved the EBP is an acceptable SIH treatment despite of its various success rate.[7] On the other hand, it relatively showed less effective than that for the post dural puncture headache (PDPH) treatment.[8-11] Refering to previous reports, repeated EBPs should be offered as least one-fourth of patients are not cured by one blood patch and about 50% cases require more than one blood patch.[7,12] This relatively weak effectiveness request repetitive EBP in SIH patient but there is yet a recommended guide line as like when and how to assess its response and to attempt additional EBP if it need.

In this study, we focused to reveal the associated factors between EBP response and other factors including laboratory findings. This evaluation may help to estimate the EBP response and eventually might support to build a recommendation of EBP in SIH treatment.

MATERIALS AND METHODS

This single-center retrospective observational study used the institutional registry records of 321 patients who experienced epidural blood patch because of SIH between September 2001 and March 2016. The ethics board of our institution approved this study (approval number, 2019–0832), and the necessity for obtaining informed consent was waived as we were only reviewing recorded data.

Patients

Patients who met all of the following criteria were included: (1) SIH diagnosed patients by the neurology department (2) who received autologous EBP, (3) both radioisotpe cisternography and brain MRI results were available, and (4) discharged with significant symptom improvement. The exclusion criteria were: (1) incomplete medical records, and (2) absence of record of radioisotpe cisternography and brain MRI.

Patients were diagnosed with spontaneous intracranial hypotension if they had at least 2 of the following 3 criteria: orthostatic headache, low cerebrospinal fluid (CSF) pressure, and diffuse pachymeningeal gadolinium enhancement on brain MRI.[13] Orthostatic headache was defined as a headache that occurs or worsens less than 15 minutes after assuming the upright position and disappears or improves less than 30 minutes after resuming the recumbent position.

Each patient was initially managed with supportive treatments by neurologist. If these initial supportive treatments failed within a week, patients were consulted via pain clinic, and delivered an autologous epidural blood patch by experienced pain clinicians.

Demographics and clinical profiles

Age, sex, height, weight, body mass index, underlying disease such as diabetes mellitus, hypertension, coronary arterial disease, cerebrovascular disease, or herniated intervertebral disc were collected and analyzed by reviewing electronic medical records (Fig. 1).

History of headache such as migraine, tension headache, and cluster headache, associate symptom such as nausea, vomit, photophobia, hearing impairment, tinnitus, vertigo, or diplopia, duration of headache, and headache intensity using 11 point $[0-10]$ numeric rating scale(NRS) were collected and analyzed from medical record.

Brain MRI reviews were based on formal reports of the radiologists. The flowing signs was recorded: pachymeningeal enhancement[14], engorgement of venous structure[15], brain sagging[16], pituitary hyperemia[15], midline shift[3], midbrain-pons angle[17], vein of Galen-Straight sinus

angle[18]. The midbrain-pons angle was defined as the angle between the line tangential to the anterior margin of the midbrain and the line tangential to the superior margin of pons on sagittal midline of brain MRI. The angle between the vein of Galen and straight sinus was measured as an index of downward stretching.

The radioisotope cisternography was also reviewed that the location of leakage, and number of leakage levels in cisternography were analyzed. The leakage levels were classified according to the spine anatomy in 3 types, which as cervical, thoracic, and lumbar.[19] Early bladder activity was defended by the presence of radioactivity in the urinary bladder 1 to 3 hours after a lumbar intrathecal injection of a radioactive tracer.[20]

Epidural blood patch

Targeted autologous EBPs were performed using a 21-gauge Tuohy needle via a midline or paramedian approach under fluoroscopy C-arm system (OEC 9800, General Electric Healthcare, Little Chalfont, United Kingdom) guidance with the patient in prone position. The epidural space was identified using the loss of resistance technique, and accurate localization was confirmed by ensuring the spread of the injected contrast medium over the targeted epidural space. Thereafter, autologous blood was slowly injected until the patient began to appeal any back or radicular pain. The target level of autologous EBP was determined as well the level of most increased paraspinal activity on radioisotope MRI cisternography.

Target volume of vein blood in epidural injection was 20ml. however administration had ceased when patients start to feel any discomfort during procedure even if yet to fulfill the target volume. An additional autologous EBP was delivered in the case of multiple leakage site over 2 days after the first EBP. A second EBP attempted to another level over the first delivered site in multiple leakage case. Otherwise, the second attempting was delivered in identical target level in single leakage-sustaining symptom case. Subsequently, there was another additional EBP attempting until the symptoms get fully regression.

Hospitalization period

The hospitalized period of subjects was investigated for the secondary outcome . All individual subjects were hospitalized as an inward patient until they acquired fully symptoms resolved. The period was defined as that from the begin as episode of SIH care to discharge day without other complications.

Treatment response

The successful response was defined as a remission of all symptoms within 72 hours after the EBP attempting as like other study.[21] In cases there symptoms remained, the repetitive EBP was delivered just after their EBP response assessing. Their response to repeated EBP assessed in the same manner as the first EBP. We categorized as the immediate responder who showed successful response no more than 2 times EBP attempting.[12] Other subjects were categorized as the delayed responder group who showed successful responses more than 3 times EBP delivered.

Statistical analysis

Continuous variables are presented as means with standard deviation (SD) or medians with the interquartile range (IQR), if skewed. Categorical variables are presented as absolute numbers and percentages.

To analyze differences between delayed and immediate responders post-EBPs, continuous variables were compared using Student's *t*-test or the Mann–Whitney *U* test, as appropriate. Categorical data were compared using the chi-square test to assess differences between the two groups. The most relevant factors associated with a EBP response were included in a univariate logistic regression analysis. The inclusion of variables into the final multivariate logistic regression analysis to evaluate independent factors associated with a delayed response upon post-procedure was based on biological plausibility, clinical importance and statistical considerations ($P < 0.10$). Statistical analyses were performed using SPSS 21.0 for Windows (SPSS Inc., Chicago, IL, USA). A two-tailed P value of < 0.05 was considered to indicate a statistically significant difference.

RESULTS

From September 2001 to March 2016, 321 inpatients who diagnosed SIH and performed epidural blood patch. Twenty-three patients were excluded from analysis. Fifteen patients were excluded due to incomplete medical record. Eight patients were excluded because of absence of record of radioisotpe cisternography and brain MRI. In total, 298 patients fulfilled both the inclusion and exclusion criteria (Figure 1).

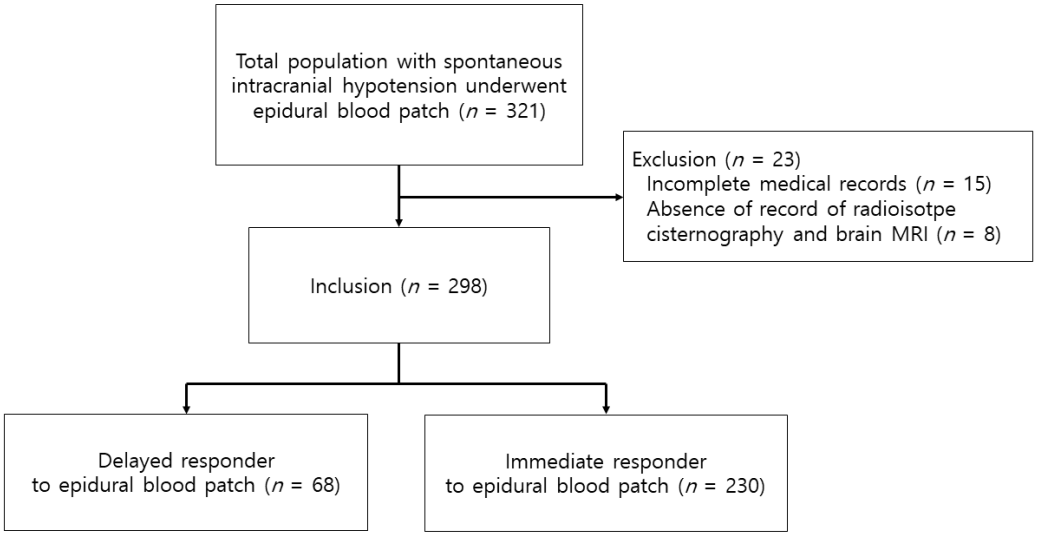

Figure 1. Flow diagram of the study

Delayed responders were defined as the patients who was performed epidural blood patch above three times. Immediate responders were defined as the patients who were performed epidural blood patch below two times

Demographics and clinical profiles

The baseline patient demographic characteristics are shown in Table 1, categorized into total patients, delayed responders, and immediate responders. There were 68 (22.8%) delayed responders and 230 (77.2%) immediate responders. None of the baseline characteristics differed between two groups except hypertension (Table 1). The delayed responders had more hypertension compared to immediate responders (15 [6.5%] vs. 0 [0.0%], P = 0.027). Age, sex, height, weight, body mass index, diabetes mellitus, coronary arterial disease, cerebrovascular accident, herniated intervertebral disc, migraine, tension headache, cluster headache, associate symptom such as nausea, vomit, photophobia, hearing

impairment, tinnitus, vertigo, and diplopia, duration of headache, and severity of headache were no significantly different in both groups.

Table 1. Demographics and clinical features in spontaneous intracranial hypotension patients undergone epidural blood patch

	Total patients (n = 298)	Delayed responders (n = 68)	Immediate responders (n = 230)	*P* value
Age (years)	38.0 (33.0–46.0)	38.0 (34.0 –46.0)	38.0 (33.0–46.0)	0.952
Sex				
Male/ Female	108 (36.2)/ 190 (63.8)	27 (39.7)/ 41 (60.3)	81 (35.2)/ 149 (64.8)	0.499
Height (cm)	164.6 ± 22.3	165.4 ± 8.9	164.4 ± 8.2	0.365
Weight (kg)	58.0 (52.3–68.0)	58.5 (52.1–69.0)	58.0 (52.4–67.9)	0.816
Body mass index (kg/m^2)	22.3 ± 2.9	21.9 ± 2.8	22.4 ± 2.9	0.270
Underlying disease				
Diabetes mellitus	12 (4.0)	1 (1.5)	11 (4.8)	0.310
Hypertension	15 (5.0)	0 (0.0)	15 (6.5)	0.027
CAD	6 (2.0)	3 (4.4)	3 (10.3)	0.130
CVA	1 (0.3)	0 (0.0)	1 (0.4)	>0.999
HIVD	10 (3.4)	2 (2.9)	8 (3.5)	>0.999
History of headache				0.613
Migraine	11 (3.7)	5 (7.4)	6 (2.6)	
Tension headache	3 (1.0)	0 (0.0)	3 (1.3)	
Cluster headache	0 (0.0)	0 (0.0)	0 (0.0)	
Associates symptom				
Nausea	166 (55.7)	42 (61.8)	124 (53.9)	0.194
Vomiting	100 (33.6)	29 (42.6)	71 (30.9)	0.056
Photophobia	2 (0.7)	1 (1.5)	1 (0.4)	0.400
Hearing impairment	4 (1.3)	2 (2.9)	2 (0.9)	0.220
Tinnitus	65 (21.8)	8 (11.8)	24 (10.4)	0.723
Vertigo	1 (0.3)	0 (0.0)	1 (0.4)	>0.999
Diplopia	1 (0.3)	0 (0.0)	1 (0.4)	>0.999
headache (days)	10.0 (9.0–30.0)	15.0 (9.0–30.0)	10.0 (9.0–30.0)	0.579
Headache (NRS)	7.0 (5.0–9.0)	7.0 (4.0–9.0)	7.0 (5.0–8.0)	0.790

Data are expressed as mean ± standard deviation, median (IQR) or number (%). Delayed responders, patients who were delivered epidural blood patch more than three times; Immediate responders, patients who were delivered epidural blood patch two or less times. CAD = Coronary arterial disease; CVA = Cerebrovascular accident; HIVD = Herniated intervertebral disc; NRS = Numeric rating scale

Neuroimaging

Among brain MRI findings in our patients, the most common abnormalities were an pachymeningeal enhancement (n = 161 [54.0%]) (Table 2). None of the brain MRI signs differed between the immediate and delayed responders. Delayed responder had slightly higher engorgement of venous structures than immediate responder, however, there was no significant difference (29 [42.6%] vs. 72 [31.3%], P = 0.095).

In cicternography finding in our patients, the most level of cerebrospinal fluid leakage was thoracic level (n = 138 [46.3%]). Cerebrospinal leakage was confirmed at cervical, thoracic and lumbar (n = 131 [44.0%], 138 [46.3%], and 30 [10.0%], respectively). Cerebrospinal leakage was undetermined at 33 patients (11.1%). Multiple leakage was founded at 160 patients (53.7%). Cerebrospinal opening pressure was 4.8 (0.0–8.0) mmHg. Early bladder activity was founded 59 patients (19.8%). Those factor shows no significant differences between two groups.

Table 2. Brain MRI, cisternography, cerebrospinal opening pressure, and early bladder activity in spontaneous intracranial hypotension patients undergone epidural blood patch

	Total patients (n = 298)	Delayed responders (n = 68)	Immediate responders (n = 230)	*P* value
Brain MRI signs				
Pachymeningeal enhancement	161 (54.0)	35 (51.5)	126 (54.8)	0.542
Engorgement of venous structures	101 (33.9)	29 (42.6)	72 (31.3)	0.095
Brain sagging	40 (13.4)	7 (10.3)	33 (14.3)	0.367
Pituitary hyperemia	32 (10.7)	7 (10.3)	25 (10.9)	0.864
Midline shift	5 (1.7)	0 (0.0)	5 (2.2)	0.592
Midbrain-pons angle (degree)	55.3 ± 10.0	55.0 ± 8.8	55.3 ± 10.4	0.800
Vein of Galen-SSA (degree)	63.4 (46.6–74.1)	64.1 (43.0–74.6)	63.1 (47.5–73.5)	0.934
Multiple leakage	160 (53.7)	43 (63.2)	117 (50.9)	0.159
COP(mmHg)	4.8 (0.0–8.0)	4.5 (0.0–7.5)	5.0 (0.0–8.2)	0.580
Early bladder activity	59 (19.8)	17 (25.0)	42 (18.3)	0.369

Data are expressed as mean ± standard deviation, median (IQR) or number (%). Delayed responders, patients who were delivered epidural blood patch more than three times; Immediate responders, patients who were delivered epidural blood patch two or less times. SSA = Straight sinus angle; CPO = Cerebrospinal opening pressure

Number, volume, and site of epidural blood patch

In this study group, the maximum number of EBP delivering was 4 times. In delayed responders, epidural blood patch was performed by 3 (3–4). In immediate responders, epidural blood patch was performed by 1 (1–2) (Table 3).

The mean volume of injected epidural blood was 15.0 mL (12.0–15.0). There was no significant difference of injected epidural blood volume between delayed responders and immediate responders (15.0 [12.0–17.8] vs. 15.0 [12.0–15.0], P = 0.717). Also, there was no significant differences at delivering site epidural blood patch in both responders.

Table 3. Number, volume, site of epidural blood patch, and hospitalization duration after epidural blood patch in spontaneous intracranial hypotension patients undergone epidural blood patch

	Total patients (n = 298)	Delayed responders (n = 68)	Immediate responders (n = 230)	*P* value
Number of EBP	2 (1–2)	3 (3–4)	1 (1–2)	<0.001
EBP volume (ml)	15.0 (12.0–15.0)	15.0 (12.0–17.8)	15.0 (12.0–15.0)	0.717
EBP site				0.062
Cervical	131 (44.0)	21 (30.9)	109 (47.4)	
Thoracic	138 (46.3)	40 (58.8)	98 (42.6)	
Lumbar	30 (10.0)	7 (10.3)	23 (10.0)	

Data are expressed as mean ± standard deviation, median (IQR) or number (%). Delayed responders, patients who were delivered epidural blood patch more than three times; Immediate responders, patients who were delivered epidural blood patch two or less times. EBP = Epidural blood patch

Laboratory data

Table 4 depicts laboratory data, including data on prothrombin time, neutrophil, lymphocyte, platelet distribution time width, Neutrophil to lymphocyte ratio, and platelet to lymphocyte ratio were significantly different between poor responder and good responder.

Prothrombin time (INR) was significantly higher in delayed responders compared to immediate responder, but considered clinically in normal value with trivial difference (1.0 ± 0.1 vs. 0.99 ± 0.1, P < 0.001). Platelet distribution width was significantly less in delayed responder group than immediate responders (11.1 (10.2–12.0) vs. 11.4 (10.7–12.7), P = 0.046) Neutrophil was less and lymphocyte was more in delayed responders than immediate responder (57.8 ± 13.2% vs. 63.0 ± 11.5%, P = 0.002; 33.4 ± 10.7% vs. 28.5 ± 9.9%, P = 0.001). Consequently, delayed responders had less

neutrophil to lymphocyte ratio compared with immediate responders (1.8 [1.2–2.5] vs. 2.2 [1.6–3.5], P = 0.002). In addition, delayed responder also had less platelet to lymphocyte ratio (117.0 (83.4–145.4) vs. 131.3 (104.0–160.9), P = 0.010). Platelet to neutrophil ratio was marginally higher in delayed responders than immediate responder, but statistically not significant (68.1 (44.4–87.6) vs. 58.2 (43.1–77.6), P = 0.072)

Table 4. Laboratory data in spontaneous intracranial hypotension patients undergone epidural blood patch

	Total patients (n = 298)	Delayed responders (n = 68)	Immediate responders (n = 230)	*P* value
Hemoglobin (g/dL)	13.6 ± 1.6	13.8 ± 1.3	13.6 ± 1.7	0.430
Hematocrit (%)	40.3 ± 4.0	40.6 ± 3.6	40.2 ± 4.2	0.386
Platelet	241.2 ± 55.6	238.8 ± 48.8	241.9 ± 57.5	0.694
Prothrombin time (INR)	1.0 ± 0.1	1.0 ± 0.1	0.99 ± 0.1	<0.001
Platelet distribution width (%)	11.3 (10.6–12.5)	11.1 (10.2–12.0)	11.4 (10.7–12.7)	0.046
APTT (sec)	27.5 (26.0–29.1)	27.7 (26.2–29.0)	27.4 (26.0–29.1)	0.429
White blood cell (cells/mm^3)	6600 (5400–8100)	6500 (5100–8000)	6600 (5500–8200)	0.357
Neutrophil (%)	61.8 ± 12.1	57.8 ± 13.2	63.0 ± 11.5	0.002
Lymphocyte (%)	29.6 ± 10.3	33.4 ± 10.7	28.5 ± 9.9	0.001
Monocyte (%)	6.2 (4.9 –7.4)	6.6 (5.1–7.6)	6.1 (7.4–4.9)	0.237
Eosinophil (%)	1.4 (0.6–2.4)	1.4 (0.6–2.5)	1.4 (0.6–2.4)	0.923
Basophil (%)	0.3 (0.2–0.5)	0.3 (0.2–0.5)	0.37 (0.2–0.5)	0.904
ANC (cells/μL)	3925.0 (3000.0–5552.5)	3820.0 (2735.0–5262.5)	4020.0 (3040.0–5632.5)	0.266
ESR (mm/hr)	9.0 (4.0–18.0)	7.5 (3.3–15.8)	10.0 (4.0–18.0)	0.209
C-reactive protein (mg/L)	0.1 (0.1–0.1)	0.1 (0.1–0.1)	0.1 (0.1–0.2)	0.215
NLR (%)	2.1 (1.5–3.2)	1.8 (1.2–2.5)	2.2 (1.6–3.5)	0.002
PLR (%)	129.2 (100.5–158.5)	117.0 (83.4–145.4)	131.3 (104.0–160.9)	0.010
PNR (%)	60.8 (43.3–81.5)	68.1 (44.4–87.6)	58.2 (43.1–77.6)	0.072

Data are expressed as mean ± standard deviation, or median (IQR). Delayed responders, patients who were delivered epidural blood patch more than three times; Immediate responders, patients who were delivered epidural blood patch two or less times. APTT = Activated partial thromboplastin time; ANC = Absolut neutrophil count; ESR = Erythrocyte sedimentation rate; NLR = Neutrophil to lymphocyte ratio; PLR = Platelet to lymphocyte ratio; PNR = Platelet to neutrophil ratio

Hospitalization period

An average of hospitalization period after blood patch of total subjects were 7 ± 6 days. The delayed responders had longer hospitalization period after blood patch than the immediate responders (12 ± 7 vs. 5 ± 4 days, P <0.001).

Univariate and multivariate logistic regression analysis

The univariate logistic regression analysis showed that neutrophil to lymphocyte ratio, and platelet to lymphocyte ratio were significantly associated with delayed response in the patients with spontaneous intracranial hypotension undergone epidural blood patch (Table 5). In taking consideration of the biological plausibility, clinical importance, multicollinearity, and statistical difference, that neutrophil to lymphocyte ratio, platelet to lymphocyte ratio, epidural blood patch at cervical region, and bain engorgement of venous structures were analyzed in a multivariate logistic regression analysis. We confirmed that there was no multicollinearity between the variables. The multivariate logistic regression analysis showed that neutrophil to lymphocyte ratio (odd ratio = 0.710, P = 0.006) were independent factors significantly associated with a delayed response of epidural blood patch in the patient with spontaneous intracranial hypotension (Table 5).

Table 5. Logistic regression analysis of factors associated with a poor response after epidural blood patch.

Variables	Univariate				Multivariate			
	Coefficient	OR	95% CI	*P* value	Coefficient	OR	95% CI	*P* value
Neutrophil to lymphocyte ratio (%)	-0.350	0.705	0.556–0.894	0.004	-0.329	0.720	0.565–0.917	0.008
Platelet to lymphocyte ratio (%)	-0.008	0.992	0.986–0.998	0.015	-0.004	0.996	0.989-1.004	0.370
Epidural blood patch site								
Cervical		1				1		
Thoracic	-0.457	0.633	0.241–1.664	0.354	0.156	0.479	0.174–1.323	0.156
Lumbar	0.293	1.341	0.533–3.474	0.533	0.918	1.052	0.401–2.761	0.918
Brain engorgement of venous structures	0.477	1.611	0.919–2.826	0.096	0.518	1.679	0.931–3.028	0.085

DISCUSSION

In this study, we analyzed many related factors in EBP. In demographic comparison, there was no difference and no related factors found. There was no association in EBP site or vein blood volume between clinical outcomes. In laboratory data, the NLR is revealed statistically associated as elevated NLR with favor outcome. The overall outcome of EBP in this study over all subjects was well treated without complication regardless of any factors.

Intracranial hypotension often does not need any aggressive treatment because it recovered spontaneously.[22,23] When it fails to bring symptom relieving in conservative management, a EBP could be considered as a first line interventional treatment if there is an explicit CSF leakage or not.[7,24] Although, this interventional management shows favor results in previous study,[23] the response of each EBP is unpredictable or insufficient in single attempt.[12] To overcome this, a repetitive EBP is an accepting concept however it has anecdotal aspect.[25] In this study, we believe to predict its response ahead of attempting EBP there should be some beneficial field for example; to estimate a hospitalized day, to avoid unnecessary EBP attempting or to enhance its favor outcome.

In this study, we also analyzed response of EBP and composition of EBP. To the best of our knowledge, there is paucity of research related the optimal EBP in treating SIH. Hence, we raised several standards in this study. Firstly, our definition of immediate responder is a group of the subjects who had symptom reliving in 2 or less times attempting EBP. There are two reasons. When we refer to previous study a complete symptom resolution was obtained in 77% of patients after one (57%) or two (20%) EBPs.[12] Moreover based on radiologic finding, there are one hundred and sixty(53.7%) subjects had suspected least two different leakage sites and 33(11.1%) subjects failed to determine accurate leakage site. For these two reasons we presumed there need more than two separate EBP attempting. Secondly, universal protocol which related how to assess the outcome of EBP in SIH is not concrete yet. In this study, we set 72 hours observational term to evaluate the outcome and to decide the delivering an additional EBP. Referring to the other previous study, the mean blood volume of each EBP is various.[23] In this study, we set the target vein blood volume for epidural administration to 20ml. However, the great part of the subjects were not able to fulfil the target volume (20ml) because their discomfort during blood administration. The average blood volume was 15ml for each EBP but this value does not mean any optimum blood volume of EBP.

In this study, we revealed the NLR is the associated factor to EBP outcome. The neutrophil to lymphocyte ratio (NLR) is now surmising laboratory data which represents a subclinical inflammation and refer to other previous study over elevated NLR, it could be considered as a potential laboratory data which may represents prognostic value.[26,27] Consequently in this study, we revealed the elevated NLR associated with a favor EBP outcome in SIH. Besides, referring to another previous study

over acute pulmonary embolism or ischemic stroke relating with elevated NLR, they show it might be related to their clinical outcome and could be utilized as a prognostic factor.[28,29] Similarly, we interpret this our result might has a prognostic clinical meaning. Nonetheless the pathophysiologic understanding about NLR is not transparent in this study level, however our estimation is a subclinical inflammation might affect or exert upon platelet function.[30] Some lines of other study, they showed the platelet may have an important role in EBP outcome through the platelet rich plasma(PRP) EBP for treating the unsuccessful to conventional EBP case.[30] In the light of this platelet role in EBP, we cautiously conjecture an elevated NLR represents a subclinical inflammation which enhance the aggregation of platelet as like the condition of pulmonary embolism.[29]

For the secondary outcome, we investigated the difference of average hospitalization period of two groups. Apparently, the immediate response group showed shorter hospitalization period than delayed response group. A poor response to initial EBP required any additional EBP delivering and the longer hospitalization period in delayed responder could be taken as a natural disease course. It is a careful conjecture, however a SIH patient with an elevated NLR may need longer hospitalization period when compare to who does not elevated, thus. Also, this might help to plan a SIH treatment and to estimate required supply, effectively.

There are few limitations in this study. Firstly, the NRL value in those two group; values in the immediate responders and the delayed responders could be considered in a normal range.[31] Despite of there is no definite normal value over NLR which generally accepted until now, a relatively elevated NLR value revealed as an associated factor of EBP in SIH. In this study level, those values are difficult to define as an abnormally elevated NLR. For this reason, we only carefully estimate a relatively elevated NLR associated to EBP in SIH results.

Secondly, our estimation upon elevated NLR and enhanced platelet aggregation is remained in hypothetical. Recently, Platelets are recognized for a potent immune modulators and has role in a host's defense against infection.[30,32] In this study, there is very limited data to support our hypothesis. Some clinical laboratory data which related to platelet aggregation function might be useful to prove our hypothesis; e.g. a bleeding time or a platelet function test might be helpful to support our theorical estimation. Our opinion is to investigate co-relation between subclinical inflammation and platelet aggregation function in further study, that would be helpful to claim our hypothesis.

Lastly, we carefully concern upon the limitation of retrospective collected data. There was an absence of regulated protocol for blood sampling ahead of delivering EBP. In most of subject's vein blood samples were collected in few days ahead of EBP delivering. The vein blood for EBP and for sampling was not collected in identical moment. The value might be altered or distorted when we

investigate in a delicately designed control study. To overcome this shortness, we enrolled plenty number of subjects in this study.

Conclusion

A relatively elevated NLR value was associated to a favor outcome of autologous EBP. However, a pathophysiologic understanding is unclear in this study level. Our analysis in this study may suggest that a blood sampling for prediction upon a EBP response in SIH treatment is recommendable.

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국문 초록

서론

자발성 두개내 저압증을 치료하기 위해 시행되는 경막외 자가혈액을 이용한 봉합술은 비교적 좋은 성적을 보이고 있다. 하지만 증상 해결을 위해 반복적으로 시행되어지는데 환자 마다 그 횟수가 다양함에도 불구하고 이를 예측할 수 있는 연구가 없다. 이러한 이유로 우리는 자발성 두개내 저압증 환자에서 시행하였던 자가혈액을 이용한 경막외 봉합술의 횟수에 따라 두군으로 나누고 차이를 분석하여 결과에 영향을 미칠 수 있는 인자에 대해 알아보기로 하였다.

연구방법

서울 아산병원에서 2001년부터 2016년까지 자발성 두개내 저압증을 입원하여 경막외 자가혈액을 이용한 봉합술을 시행하였던 환자를 대상으로 조사하였으며 321명을 대상으로 후향적으로 분석하였다.

연구결과

경막외 자가혈액을 이용한 봉합술의 횟수를 기준으로 두 군으로 분류하였다. 2회 이하의 시행에서 증상 호전을 보인 즉각적 반응 그룹 (n = 230)으로 분류하였고 3회 이상의 시행에서 반응을 보이는 지연된 반응 그룹 (n = 68)으로 분류하였다. 두 군 간의 차이는 Neutrophil to lymphocyte ratio 와 Platelet to lymphocyte ratio에서 관찰되었다. 로지스틱 회귀분석 결과 상대적으로 높은 Neutrophil to lymphocyte ratio를 보이면 지연된 반응에 포함될 위험도가 저하되었다 (상대 위험도 = 0.710, 95% 신뢰구간 0.556-0.908).

결론

높은 Neutrophil to lymphocyte ratio를 갖는 환자에서 경막외 자가혈액을 이용한 봉합술을 시행할 경우 좀더 양호한 반응을 보일 것으로 예상 가능하다.