Dynamic curve analysis of indicators related to lumbar cistern drainage for postoperative meningitis

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Abstract

Background

Lumbar cisterna drainage (LCD) is widely used in neurosurgery as an effective treatment for postoperative meningitis, vasospasm of subarachnoid hemorrhage and ventricular system hemorrhage, and for reducing intracranial pressure in patients with severe craniocerebral trauma. The purpose of this work was two-fold: to analyze the dynamic curve of cerebrospinal fluid (CSF) related indices in cases of postoperative meningitis after selective craniotomy and to provide reference data for the clinical treatment with LCD.

Methods

We conducted a retrospective study of LCD placement in patients who underwent either supratentorial craniotomy (n=23) or subtentorial craniotomy (m=28). Primary outcomes measured included pre-intervention and post-intervention dynamic changes of body temperature, and CSF biochemical parameters (white blood cell (WBC) count, polykaryocyte percentage, protein, glucose and chloride) over the course of 13 days of catheter placement. We also assessed the bivariate correlation between WBC count changes, polykaryocyte percentage, body temperature and daily CSF drainage volume. Finally, we analyzed the effect of average daily drainage volume, antibiotic choice, and surgical site on the WBC count change curves.

Results

After LCD, a trend of increased WBC count was observed on the first day of drainage, followed by an overall decrease in WBC count. There was a statistically significant (P<0.05) difference between the WBC count before drainage and the WBC count on the fourth day of drainage. Polykaryocyte percentage decreased initially and then increased progressively each day after drainage. There was a negative correlation between the change curve of the WBC count and the curve of daily drainage volume (r = -0.56). When the daily drainage volume was 250-300 ml/d, the change curve pattern of the WBC count was consistent with the overall trend of the WBC count, and there was no significant difference in the curve of the WBC count between different surgical sites (P > 0.05).

Conclusions
LCD is an effective method for the treatment of postoperative meningitis. The WBC count can decrease significantly by the fourth day after drainage, and placement of the LCD for six to seven days is ideal. An average drainage volume of 250-300 ml/d is safe and effective.

Background
Lumbar cistern drainage (LCD) is widely used in neurosurgery as an effective way to treat postoperative meningitis [1], vasospasm of subarachnoid hemorrhage [2, 3], ventricular system hemorrhage [4] and reduction of intracranial pressure in patients with severe craniocerebral trauma [5]. Of note, meningitis after neurosurgical craniotomy is a common complication that affects the prognosis and length of stay of patients [6]. Although LCD can be used in a variety of clinical cases, there are risks and potential complications, such as infection, given that the process is invasive and requires placement of a drainage tube for a certain period. The white blood cell (WBC) count in cerebrospinal fluid (CSF) and the daily drainage volume of CSF should be observed clinically in order to guide decisions in catheter removal. However, with respect to LCD placement, there is a dearth of information available on how drainage time relates to the change trend of CSF-related indicators, and how these indicators correlate with one another during the interventional treatment process. Therefore, this study retrospectively analyzed 51 cases of LCD due to postoperative meningitis and plotted the dynamic change curves of body temperature, WBC count, polykaryocyte percentage, protein, glucose and chloride over a period of 13 days. The bivariate correlation between WBC count, polykaryocyte percentage, body temperature and daily CSF drainage volume was assessed. Lastly, to provide reference data for the application of LCD in clinical practice, the effect of daily drainage volumes, antibiotic choice and surgical sites on the WBC count change curve was investigated.

Materials And Methods
Cases and inclusion criteria
The inclusion criteria of cases in this study were: 1) elective craniotomy; 2) elevated postoperative body temperature which remained above 37.5°C, with at least one of the following clinical symptoms: headache, neck stiffness, cranial nerve irritation symptoms, or disturbance of consciousness; 3) LCD was performed, and 4) in CSF during drainage, WBC count was greater than $500 \times 10^6$/L. In all, 51
patients in Shengjing Hospital of China Medical University met the above criteria between January 2012 and December 2019. Patient demographics included 23 males, 28 females, 23 cases of supratentorial surgery and 28 cases of subtentorial surgery (Table 1). This study was approved by the ethics committee of the Shengjing Hospital of China Medical University. Informed consent was obtained from all patients.

Research process
For all 51 cases, body temperature and routine CSF biochemical indicators, including WBC count, polykaryocyte percentage, protein, glucose and chloride, were recorded daily prior to catheter placement and for a period of 13 days after catheter placement. A bivariate correlation analysis was performed on the daily CSF drainage change curve, body temperature change curve, WBC change curve and polykaryocyte percentage change curve. Finally, according to the average daily drainage volume of each case, the differences in WBC change curves and drainage time between different drainage volumes were analyzed. According to the types of antibiotics used in the drainage process, the WBC change curve, drainage time and differences in the daily drainage volume between different antibiotics were analyzed. The differences in drainage time, daily drainage volume, body temperature curve, white blood cell change curve and polykaryocyte percentage change curve for various surgical sites were also analyzed (Figure 1).

Statistical analysis
Data were analyzed using SPSS17.0 software for statistical calculation. A t-test was used to determine the statistical differences between body temperature, WBC count, polykaryocyte percentage, protein, glucose and chloride at different time points. The same method was adopted to calculate statistical differences in drainage time and daily drainage volume between different groups. Lastly, the bivariate correlation between daily CSF drainage volume, body temperature, WBC and polykaryocyte percentage were analyzed. P<0.05 was considered statistically significant.

Results
General change trend of routine CSF biochemical tests
The change trend of body temperature after LCD was as follows: body temperature first decreased,
increased and then decreased. Body temperature on the second day after drainage was significantly different from body temperature before drainage \((P < 0.001)\). Body temperature began to increase on the sixth day after drainage and reached the highest point on the ninth day after drainage, after which it began to decrease (Figure 2A). The WBC count on the first day after drainage was significantly higher than WBC count before drainage \((P<0.001)\), and then began to show an overall downward trend. By day 4, the WBC count was significantly lower than the WBC count before drainage \((P=0.004<0.01)\) (Figure 2B). The change trend of the polykaryocyte percentage was similar to that of body temperature; it began to decrease significantly on the third day after drainage \((P=0.004<0.01)\) (Figure 2C). The time node was synchronized with the change of WBC. Of note, protein was above the normal range during drainage (Figure 2D), the change of glucose was within the normal range during drainage (Figure 2E) and the change of chloride was essentially below the normal range during drainage (Figure 2F). These trends were overall consistent with the characteristics of meningitis.

**Correlation analysis of daily CSF drainage with body temperature and WBC**

Correlation analysis demonstrated a negative correlation between daily CSF drainage and body temperature \((r = -0.14)\), and there was no statistical difference between the two trends \((P=0.65 > 0.05)\) (Figure 3A, 3B). There was also a negative correlation between daily CSF drainage and WBC count \((r = -0.56)\), with a statistical difference between the two trends \((P=0.046 < 0.05)\) (Figure 3C, 3D). There was a negative correlation between daily CSF flow and polykaryocyte percentage \((r = -0.29)\), with no statistical difference between the two trends \((P=0.34 > 0.05)\) (Figure 3E, 3F). Lastly, there was a positive correlation between WBC count and polykaryocyte percentage \((r = 0.696)\), and the change trend of the two was statistically different \((P=0.006 < 0.01)\) (Figure 3G, 3H).

*When the daily CSF drainage volume was 250-300 ml, the WBC change curve was most consistent with the overall WBC change curve*

Based on the observed average daily CSF drainage volumes, the patients were divided into five groups: 100-150 ml/d \((n=11, 21.6\%)\), 150-200 ml/d \((n=19, 37.3\%)\), 200-250 ml/d \((n=9, 17.6\%)\), 250-300 ml/d \((n=8, 15.7\%)\) and greater than 300 ml/d \((n=4, 7.8\%)\). The WBC change curves of the five
groups all increased on the first day after drainage, and then presented an overall trend of decline. Among them, the WBC of the 250-300ml/d group decreased the most significantly on the fourth day after drainage ($P=0.006<0.01$), and the subsequent fluctuation was smaller, which was most consistent with the overall WBC curve when compared with the other subgroups (Figure 4A). In addition, there was no significant difference in drainage time between the five groups (Figure 4B), indicating that although the WBC trend for the 200-250 ml/d group was most consistent with the overall WBC change curve, more daily flow did not shorten duration of LCD placement.

The type of antibiotic affects the WBC change curve

Patients were divided into four groups according to the types of antibiotics used during drainage, as follows: cephalosporin treatment group (more than 3 generations of cephalosporin) (n=16, 31.4%), meropenem treatment group (n=10, 19.6%), linezolid treatment group (n=7, 13.7%) and multiple antibiotic treatment group (n=18, 35.3%). The WBC count change curve of the meropenem group and the multiple antibiotic group was consistent with the overall curve, while the cephalosporin group and linezolid group showed some fluctuations. The decrease of WBC on the fourth day of drainage was the most significant in the meropenem treatment group ($P=0.011<0.05$) (Figure 4C). In addition, the drainage time between the meropenem treatment group and the cephalosporin treatment group was relatively short, and there was a statistical difference in the drainage time between the cephalosporin treatment group and the linezolid treatment group ($P=0.012 < 0.05$) and the multiple antibiotic treatment group ($P=0.021 < 0.05$) (Figure 4D). There was no significant statistical difference in the daily drainage volumes of the four groups ($P>0.05$) (Figure 4E).

Differences in body temperature and WBC curve in different surgical sites

Based on the surgical site, patients were divided into two groups: the supratentorial craniotomy group (n=23, 45.1%) and the subtentorial craniotomy group (n=28, 54.9%). A statistical difference was observed in the drainage time between the two groups ($P=0.012<0.05$), with a longer drainage time in the supratentorial craniotomy group, and no significant statistical difference was observed in the daily drainage volume between the two groups ($P>0.05$) (Figure 5A). The trends of body temperature, WBC and polykaryocyte percentage were similar in the two groups. However, according to the trend
of body temperature changes of the two groups, the overall body temperature of the supratentorial surgery group was higher than that of the subtentorial surgery group. When comparing body temperature at each time point before and 5 days after drainage, there were statistically significant differences in body temperature between the two groups (Figure 5B), suggesting that symptoms of postoperative meningitis may vary in different surgical sites and that symptoms of hyperthermia are more common in the supratentorial surgery group. Overall, the differences in WBC count (Figure 5C) and polykaryocyte percentage (Figure 5D) at each time point between the two groups were not particularly significant.

Discussion

**LCD retention time of 6 to 7 days may be ideal**

In this retrospective study of 51 patients undergoing LCD placement, we found an average drainage duration of 7 days, with the overall body temperature curve showing a trend of decrease, increase and then decrease, in which body temperature dropped to the nadir on the sixth day after drainage and reached an average of 37.3°C. In addition, the WBC count curve changed significantly from day four after drainage, when the average leucocyte count was $840 \times 10^6$/L, after which it decreased to $440 \times 10^6$/L on day six, considered the minimum WBC count required for enrollment. Similarly, the polykaryocyte percentage dropped to the nadir of 42.1%, followed by an upward trend for body temperature, WBC count and polykaryocyte percentage.

LCD is an effective treatment for postoperative meningitis. However, prolonged indwelling of drainage tubes *in vivo* may increase the risk of drainage tube-related infections. One study [7] demonstrated that the infection rate associated with LCD is 31.28% between three and seven days of drainage, but when LCD exceeds seven days, the infection rate rises to 63.33%. In addition, another study [8] showed that between four and nine days is the peak period of infection associated with LCD. The WBC count change curve seen in our study showed a small increase after day seven and a more significant increase in the polykaryocyte percentage. It is suggested that the duration of drainage at any time is prolonged and the risk of infection associated with drainage tubes is increasing. Therefore, the rational management of CSF drainage tube affects the development of postoperative meningitis [9].
Exploration of daily CSF drainage volume

The daily CSF volume during LCD is a clinical index that needs to be measured and observed closely. The first study using an external lumbar drainage system was reported by Voursh in 1963 [10]. Although the technique of LCD is relatively safe and effective, it also has certain risks and fatal complications, such as headache with low cranial pressure and even cerebral hernia [11, 12]. The occurrence of cerebral hernia is related to the rate of drainage. The rate of CSF production in normal adults is 20 ml/h, indicating that about 480ml CSF is produced every day.

Setting the drainage volume in the lumbar cisterna drainage process is very important. However, as far as we know, there are no recommendations on the average daily CSF drainage volume. In our study, the average total drainage volume was 1428 ml, the average daily drainage volume was 207 ml and the average CSF replacement was about three times. Of the 51 patients, two patients presented with headache symptoms of low cranial pressure during LCD, and the average daily drainage volume of the two patients was 380 ml and 404ml, respectively. The risk of low cranial pressure was higher (50%) when the average drainage volume was above 300 ml/d. In addition, there was a negative correlation between the daily drainage volume and the WBC count. The average daily drainage volume on the first day was 149 ml, after which it increased to 221 ml/d and remained above the baseline of 200 ml/d thereafter. With the accumulation of drainage volume, the WBC count showed a decreasing trend. Of the four groups of daily drainage, the most significant change in the WBC was noted when the daily drainage volume of CSF was between 250 and 300 ml since the average WBC count was $2619 \times 10^6$/L before drainage and subsequently decreased to $655 \times 10^6$/L on day four of drainage. When the daily CSF drainage was maintained between 200 and 300ml, patients did not show symptoms of headache with low cranial pressure. This was consistent with the control of CSF drainage of 10 ml/h by Nanidis N et al. [13]. Therefore, in order to achieve the goal of reducing the WBC count of CSF more quickly, it is relatively safe and effective to maintain the average daily drainage volume at 250-300ml.

Selection of antibiotics during LCD

Postoperative meningitis after craniotomy is a common complication of neurosurgery and affects the
prognosis of surgical patients. Some malignant tumors and tumors of the ventricular system are prone to cause postoperative intracranial infection [14,15]. Bacterial meningitis is more common in infection [16]. In our study, 51 patients were treated with at least one antibiotic during drainage. Among them, the WBC count change curve of the meropenem treatment group showed the most significant decrease in the WBC count at day four of drainage, and the drainage time of the LCD was shorter in the cephalosporin treatment group and the meropenem treatment group, suggesting that the infection rate of gram-negative bacilli may be higher in our cases. However, in all 51 cases, multiple CSF bacterial cultures were negative and the pathogen of infection could not be identified, which is also a limitation of this study. In our experience, the use of antibiotics during LCD can, on the one hand, treat meningitis and, on the other hand, reduce the risk of catheter-related infections. In addition, we found that there were notable differences in the clinical manifestations of postoperative meningitis among patients with different surgical sites. Patients who underwent supratentorial surgery tended to have a higher degree of fever, while patients who underwent subtentorial surgery had more symptoms of meningeal irritation, which required clinical screening. Conclusion
The study investigated parameters surrounding CSF change parameters when using LCD as an effective method to treat postoperative meningitis. We included 51 patients in this retrospective study and assessed the correlation and statistical significance of multiple parameters over a study duration of 13 days. The WBC count on day four after drainage showed a significant decrease compared with the WBC count before drainage. These results indicate that LCD retention time of six to seven days is ideal based on body temperature, WBC count and polykaryocyte percentage, and prolonged retention time may increase the risk associated with the drainage tube. Patients were treated with at least one antibiotic during the LCD process, and results suggest a possible prevalence of gram-negative bacilli given trends from antibiotic correlation studies. Declarations

**Consent for publication**

All authors consent to the publication of this manuscript.
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Competing interests

The authors declare that they have no competing interests.

Author contributions

All authors were involved in the study design, interpretation of the results, and the reviewing and approval of the manuscript, and in the decision to submit the article for publication. All authors also confirm accountability for the accuracy and integrity of the work.

Ethics approval and consent to participate

Informed consent from each patient was carried out before the research. The use of the research protocol was approved by the Ethics and the Human Research Review Committee of Shengjing Hospital of China Medical University.

Availability of data and materials

To get the raw data, please send an email to authors. (conglin_medicine@163.com)

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Tables

Table 1. The demographic of the cases
| Case number | Sex       | Age (Years) | Surgical site                      | Duration for lumbar drainage (Days) | Total drainage (mL) |
|-------------|-----------|-------------|------------------------------------|-------------------------------------|---------------------|
| 1           | Female    | 34          | Right frontotemporal lobe          | 10                                  | 1320                |
| 2           | Male      | 48          | Right lateral ventricle           | 10                                  | 2055                |
| 3           | Female    | 70          | Right cerebellopontine angle      | 11                                  | 2640                |
| 4           | Male      | 37          | Left frontal lobe                 | 13                                  | 2510                |
| 5           | Female    | 63          | Trigeminal nerve                  | 6                                   | 890                 |
| 6           | Male      | 29          | Left temporal lobe                | 7                                   | 1060                |
| 7           | Male      | 43          | Left cerebellopontine angle       | 8                                   | 1090                |
| 8           | Male      | 53          | Cerebellum                        | 8                                   | 980                 |
| 9           | Male      | 45          | Left temporal lobe                | 4                                   | 630                 |
| 10          | Male      | 61          | Trigeminal nerve                  | 5                                   | 1380                |
| 11          | Female    | 53          | Facial nerve                      | 6                                   | 1130                |
| 12          | Female    | 67          | Facial nerve                      | 3                                   | 405                 |
| 13          | Male      | 66          | Trigeminal nerve                  | 5                                   | 1245                |
| 14          | Female    | 59          | Left cerebellopontine angle       | 7                                   | 832                 |
| 15          | Female    | 69          | Right frontal lobe                | 7                                   | 1795                |
| 16          | Male      | 51          | Right cerebellopontine angle      | 5                                   | 1420                |
| 17          | Male      | 38          | Facial nerve                      | 7                                   | 1287                |
| 18          | Male      | 29          | Right frontal lobe                | 6                                   | 1450                |
| 19          | Female    | 60          | Left temporal lobe                | 3                                   | 550                 |
| 20          | Female    | 61          | Trigeminal nerve                  | 5                                   | 875                 |
| 21          | Male      | 54          | Facial nerve                      | 4                                   | 650                 |
| 22          | Female    | 20          | Hypothalamus                      | 6                                   | 845                 |
| 23          | Male      | 61          | Right cerebellopontine angle      | 4                                   | 730                 |
| 24          | Male      | 59          | Brain stem                        | 7                                   | 2040                |
| 25          | Female    | 54          | Left cerebellopontine angle       | 9                                   | 1350                |
| 26          | Male      | 43          | Right temporal lobe               | 6                                   | 1530                |
| 27          | Male      | 23          | Right temporal lobe               | 7                                   | 1130                |
| 28          | Female    | 47          | Multiple supratentorial lesions    | 11                                  | 2750                |
| 29          | Female    | 47          | Left cerebellopontine angle       | 5                                   | 910                 |
| 30          | Female    | 55          | Facial nerve                      | 5                                   | 1600                |
| 31          | Male      | 39          | Left frontal lobe                 | 7                                   | 2020                |
| 32          | Female    | 64          | Right middle cranial fossa base   | 5                                   | 1160                |
| 33          | Female    | 41          | Right frontal lobe                | 12                                  | 3565                |
| 34          | Female    | 60          | Left cerebellopontine angle       | 7                                   | 920                 |
| 35          | Female    | 51          | Right temporal lobe               | 8                                   | 1190                |
| 36          | Female    | 44          | Right temporal lobe               | 9                                   | 1880                |
| 37          | Female    | 46          | Right temporal lobe               | 7                                   | 1380                |
| 38          | Female    | 18          | Left cerebellopontine angle       | 8                                   | 1590                |
| 39          | Female    | 52          | Trigeminal nerve                  | 6                                   | 865                 |
| 40          | Male      | 41          | Left frontotemporal lobe          | 10                                  | 2020                |
| 41          | Male      | 27          | Right occipital lobe              | 7                                   | 1560                |
| 42          | Male      | 27          | Saddle area                       | 9                                   | 1755                |
| 43          | Female    | 63          | Trigeminal nerve                  | 4                                   | 635                 |
| 44          | Female    | 65          | Trigeminal nerve                  | 5                                   | 920                 |
| 45          | Female    | 43          | Right cerebellopontine angle      | 8                                   | 1720                |
| 46          | Male      | 51          | Right temporal lobe               | 7                                   | 872                 |
| 47          | Male      | 29          | Left temporal lobe                | 8                                   | 1570                |
| 48          | Male      | 39          | Facial nerve                      | 7                                   | 1222                |
| 49          | Female    | 59          | Trigeminal nerve                  | 6                                   | 2150                |
| 50          | Female    | 50          | Cerebellum                        | 9                                   | 3640                |
| 51          | Female    | 26          | Cerebellum                        | 3                                   | 1140                |

Figures
The research framework for this study.
Changes of body temperature and CSF biochemical parameters before and after LCD. A. Body temperature; B. WBC count; C. Polykaryocyte percentage; D. Protein; E. Glucose; F. Chloride. n.s.: no statistical significance; *: P<0.05; **: P<0.01; ***: P<0.001. Data were represented as mean ± s.e.m.
Correlation analysis. A. The change curve of body temperature and the change curve of daily CSF drainage volume; B. Correlation analysis of body temperature and daily CSF
drainage volume; C. The change curve of WBC count and the change curve of daily CSF drainage volume; D. Correlation analysis of WBC count and daily CSF drainage volume; E. The change curve of polykaryocyte percentage and the change curve of daily CSF drainage volume; F. Correlation analysis of polykaryocyte percentage and daily CSF drainage volume; G. The change curve of WBC count and the change curve of polykaryocyte percentage; H. Correlation analysis of WBC count and polykaryocyte percentage. Data were represented as mean ± s.e.m.
Figure 4

A. The WBC count change curves of different daily CSF drainage volumes; B. Comparison of the retention time of LCD among the different daily CSF drainage volumes; C. WBC change curves of different antibiotics; D. Comparison of the retention time of LCD among the different antibiotics; E. Comparison of daily CSF drainage flows of different antibiotics. n.s.: no statistical significance; *: P<0.05. Data were represented as mean ± s.e.m.
A. Comparison of the retention time and daily CSF drainage volume between supratentorial surgery and subtentorial surgery; B. Comparison of body temperature change curves between supratentorial surgery and subtentorial surgery; C. Comparison of WBC count change curves between supratentorial surgery and subtentorial surgery; D. Comparison of polykaryocyte percentage change curves between supratentorial surgery and subtentorial surgery. n.s.: no statistical significance; *: P<0.05; **: P<0.01; ***: P<0.001. Data were represented as mean ± s.e.m.