

Continue Lumbar Drainage for Intracranial Pressure Control of HIV-Associated Cryptococcal Meningitis Patients from Low to Middle Income Area/Country

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Abstract

Background: The aim of this pilot study was to compare the intracranial pressure (ICP) control between the continuous lumbar drainage (CLD) and repeated lumbar puncture (LP) on the patients with HIV-associated Cryptococcal Meningitis (CM).

Methods: From January 2017 to January 2019, a total of forty patients with HIV-associated CM patients were randomized and allotted into CLD or repeated LP groups, respectively. During the first two weeks of the treatment, either CLD or LP were used to control the ICP pressure except the routine antifungal therapy was given following the consensus and guidelines of CM. The ICP pressure, protein concentration and cell count from CSF were assayed and compared between the two groups.

Result: All the patients were survived. At the day 14 post treatment, a drop in ICP was observed among patients and clinical symptoms were relieved. The ICP of CLD group was significantly lower than those of LP group ($P < 0.05$). The protein concentration and cell count from CSF of CLD group were significantly less than LP group ($P < 0.05$).

Conclusions: CLD is a simple, safe or the first-choice control of intracranial hypertension in the patients with HIV associate cryptococcal meningitis. Especially, for patients were treated in primary and/or secondary hospitals located at the low-middle income areas/country.

Keywords: HIV-associated; cryptococcal meningitis; continuous lumbar drainage; low-middle income; cerebral spinal fluid; intracranial pressure

Abbreviations: HIV: Human Immunodeficiency Virus; CM: Cryptococcal Meningitis; ICP: Intracranial Pressure; CLD: Continuous Lumbar Drainage; LP: Lumbar Puncture; CSF: Cerebral Spinal Fluid; ART: Antiretroviral Therapy

Introduction

Cryptococcal meningitis (CM) is the most important causes of death among the human immunodeficiency virus associated (HIV-associated) patients in worldwide [1]. The mortality rate is up to 30% even in developed countries [2]. Mortality from cryptococcal meningitis in resource-limited settings is approximately 70% [3]. Survivor of CM often developed major irreversible neurological impairments like blindness and deafness. Besides the standard antifungal and antiretroviral therapy (ART), the management of

elevated of intracranial pressure (ICP) plays a very important role in reducing the mortality and morbidity of HIV-associated CM patients, especially in the first two weeks post treatment. Along with medication, invasive therapeutic approaches are necessary for managing of the intracranial hypertension in CM patients. Presently, repeated lumbar puncture, drainage of cerebrospinal fluid (CSF) and Ventriculoperitoneal shunting (VP) are the main invasive methods used to reduce the ICP. If the patient is from a

lower to middle income area and/or country and is hospitalized in the primary and secondary care hospital, the option for the ICP control will focus on continuous lumbar drainage (CLD) and repeated lumbar puncture (LP) rather than VP operation. A pilot prospective study was conducted to compare the CLD and LP within the first two weeks of onset of CM.

Materials and Methods

From Jan 2017 to Dec 2019, a total of forty patients diagnosed with HIV-associated CM were recruited into this prospective study. The written informed consent was obtained from each patient. This study was approved by Ethical Committee of the First Affiliated Hospital and infectious disease hospital of Guangxi Medical University and has been performed in accordance with the Declaration of Helsinki. The patients were randomized and divided into the CLD group and repeated lumbar puncture (LP) group as control. All the data obtained from the two groups are listed in Table 1. The treatments followed the recommended guidelines from IDSA 2010 [4] and Chinese medical association [5]. The treatment includes primary therapy (induction and consolidation steps) and maintenance therapy. The repeated LP was performed at the day 0, 2, 5, 7, 9, 12 and 14 post the onset of treatment. The procedure of CLD is as following:

- Patient was in lateral recumbent position under close monitoring.
- A soft and sterile catheter (18 gauge) of lumbar drainage was placed through the lumbar vertebral L4-5 interspace.

Table 1: Clinical features of forty HIV-associated CM.

| | CLD(n=20) | LP(n=20) | p value |
|----------------------------------|---------------|---------------|---------|
| Sex | | | |
| Male | 16 | 15 | 0.705 |
| Female | 4 | 5 | |
| Age(years) | 40.65±11.59 | 41.15±9.73 | 0.883 |
| Complete Cell Count | | | |
| RBC(×10 ¹² /L) | 3.96±0.69 | 3.94±0.57 | 0.911 |
| Hemoglobin(g/L) | 106.75±19.08 | 105.6±10.97 | 0.817 |
| WBC(×10 ⁹ /L) | 5.26±1.68 | 5.27±1.44 | 0.983 |
| Neutrophil (×10 ⁹ /L) | 4.05±1.59 | 4.06±0.72 | 0.977 |
| Lymphocyte(×10 ⁹ /L) | 0.69±0.30 | 0.689±0.30 | 0.924 |
| N/L | 6.81±3.20 | 6.99±3.30 | 0.864 |
| CD4(cells/mL) | 29.08±17.84 | 29.1±16.83 | 0.995 |
| CD8(cells/mL) | 318.55±151.80 | 319.03±165.78 | 0.992 |
| CD4/CD8 | 0.10±0.06 | 0.10±0.05 | 0.937 |
| CSF | | | |
| ICP (cmH ₂ O) | 260±87.07 | 247±51.50 | 0.56 |
| Cell count(X10 ⁶ /L) | 91.59±51.24 | 98.94±33.31 | 0.594 |

| | | | |
|------------------|---------------|---------------|-------|
| Protein(mg/L) | 707.29±368.19 | 713.88±369.57 | 0.955 |
| Glucose(mmol/L) | 2.54±0.87 | 2.64±0.73 | 0.69 |
| Chloride(mmol/L) | 119.59±6.36 | 118.87±5.68 | 0.709 |

CLD: Continuous Lumbar Drainage, LP: Lumbar Puncture, RBC: Red Blood Cells, WBC: White Blood Cells, CSF: Cerebrospinal Fluid, ICP: Intracranial Pressure.

Total 3 4 cm long catheter tube was inserted and fixed. Another side of tube was cap and attached to a container for collecting CSF. The drainage level was kept at the same as the patient's bed. The drainage speed was adjusted to 10- 20 ml per hour and the maximal daily drainage of CSF volume was under 400 ml. The drain was kept in place for up to two weeks. The ICP was monitored and recorded every 10 min during first 6 hours of procedure and every hour in first 72 hours. Then interval of observation was 2 hours within first 7 days and 3 hours between day 8 to 14. All the patients and their vital signs were monitored closely. The clinical outcomes and adverse effects were evaluated and monitored daily. The routine CSF assays were done, and results are expressed in Table 2. These assays include the pressure of CSF; cell counts and classification; the levels of protein, glucose, and chloride from CSF. Results are listed in Table 2.

Table 2: Routine examination of CSF post 14 days of treatment.

| Variables | CLD | LP | p value |
|---------------------------------|--------------|-------------|---------|
| ICP (cmH ₂ O) | 163.73±46.6 | 214.5±75.5 | 0.024 |
| CSF | | | |
| Cell count(X10 ⁶ /L) | 21.5±14.31 | 39.45±31.96 | 0.0274 |
| Protein(mg/L) | 521.2±201.04 | 651.2±188.5 | 0.0415 |
| Glucose(mmol/L) | 2.74±1.67 | 2.75±2.36 | 0.9877 |
| Chloride(mmol/L) | 125.03±6.26 | 125.03±8.13 | 1 |

Statistical analysis

Values are expressed as mean± SD. The P value <0.05 was considered statistically significant. Statistical analysis was performed by using a statistical software package (IBM® SPSS® Statistics, Version 19.0).

Results

All the patients survived by the end of day 14 post treatment either using CLD or LP. The catheter was changed after 14 days. No sign of sepsis or infections signs were observed at the site of puncture. As Table 2 demonstrated the CSF assay results. The ICP levels dropped in both methods, either CLD or LP. CLD group showed a significantly lower ICP values than LP group (P<0.05). The levels of protein and total cell counts from CSF has a significantly difference between the CLD group and LP group (P<0.05). However, the glucose and chloride values in CSF of both groups showed marginal differences (P>0.05).

Discussion

For HIV infected patients, the CM is one of the most common complication due to the patient's immunodeficiency. The management of intracranial hypertension of these patients at the early stage of treatment are the critical to reduce the mortality of CM. Several guidelines for use of antifungal therapy on these patients, in low-income and middle-income counties are available [6]. One of the bigger challengers for clinicians is to control the ICP and reduce the symptoms as well its side effects. So far, besides the drug administration for the control of ICP, lumbar puncture (LP) and surgical shunt operation are two commends to control ICP and relief the symptoms for patients in worldwide [7]. Surgical shunt operation still needs the availability of highly trained surgeon and professional personnel. This surgical procedure is mostly conducted in the tertiary level hospitals. The demand of expensive equipment and the cost for the patients from the lower-middle income families remain a burden to the country. Obviously, for most patients with HIV associated CM, the primary and initial treatment was started at the primary and secondary level hospitals. Therefore, choice of either CLD or repeated LP to control ICP is priority decision taken by the physicians at these healthcare centers. Repeated LP during the first 1-2 weeks after onset of CM may cause the cerebral hernia and these procedures and interventions are very painful and stressful for the patients. From our preliminary pilot study, data shows that CLD is a more efficient method to reduce ICP. The levels of cell count and protein from CLD group were significantly lower than those of LP group. The possible reason may be related to better effectiveness of CDL to reduce the accumulation of CSF and enhanced elimination of cryptococcus from center nervous system. After controlling the ICP levels, the symptoms and signs of CM patients were relieved. In general, CLD is a safe and efficacious procedures in most patients [8,9].

Conclusions

From our pilot prospective study results indicated that the continuous lumbar drainage may be first choice to control ICP of HIV associated CM patients who are from lower to middle income area/country and initially treated at the primary and secondary hospitals, especially during the first crucial two weeks. Our preliminary study is first available to compare CLD and LP and a large multiple hospital study will be pursued in our area soon.

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Conflict of interest

The authors declare that there are no conflicts of interest regarding the publication of current paper.

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