Original Article

Infections of ventriculoperitoneal shunt and a simple effective treatment

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Received September 24, 2015; Accepted December 17, 2015; Epub February 15, 2016; Published February 29, 2016

Abstract: Objective: Sensitive antibiotic combine with shunt valve injection is a new, simple and effective method to treatment for VP shunt infection. Methods: We retrospectively reviewed 15 consecutive patients who were diagnosed intracranial infection after VP shunt and received our new treatment between Feb 2010 and Feb 2013. We have a 2-5 years follow-up to evaluate prognosis and security. Results: All 15 patients were cured and discharged, 14 cases save their shunt device completely, and just 1 case removed the shunt device as repeated episodes of infection. No recurrence of infection by follow-up for 2-5 years. Conclusions: Sensitive antibiotic combine with shunt valve injection was a safely, easily, economically and effectively treatment for intracranial infection after ventricle peritoneal and it also can save the ventricle peritoneal shunt device.

Keywords: VP shunt infection, CSF, shunt valve injection

Introduction

Hydrocephalus is one of the most common diseases in neurosurgery and neurology, as the pathological increase in CSF volume and caused by cerebral tumor, brain injury, infection or subarachnoid hemorrhage. Ventriculoperitoneal Shunt is one of the most common treatments for hydrocephalus [1]. Patwardhan et al [2] reported that approximately 40000 patients accepted CSF shunt annually and it cost billions of dollars every year to cure hydrocephalus in the United States. Even though VP shunt can improve the prognosis and neurological function, it is also reduced the mortality and morbidity of hydrocephalus. But, VP shunt have a high failure rate as it’s complications are large. So Vinchon et al [3] reported that more than 50% patients undergo multiple shunt revisions after the first VP shunt during their lifetime. Among the shunt complications, shunt infection is one of the most frequent occurrence and serious complication of VP shunt [4-6]. A lot of research shows the incidence and risk factors may lead to shunt infection such as experience of the neurosurgeon, age at shunt insertion, cause of hydrocephalus, etiology and so on [5-8].

The treatment strategies of VP shunt infection have many different kinds just as: (1) give systematically antibiotics alone or combined with intrathecal medications; (2) remove of the total shunt material with insertion of an external drainage, intravenous antibiotics for 2 weeks [6, 9]; (3) externalization of the peritoneal catheter with replacement of the shunt when the CSF is sterile [9]. As a large of literature reported VP shunt infection had a high rate of cure with removal of shunt material with insertion of an external drainage, and replacement of the shunt after the CSF was clear with normal protein, glucose, WBCs, red blood cells. Even this way had a higher success rate over 95% [10], but it would lead to an increasing of perioperative morbidity and mortality, a longer period of hospitalization, a higher medial cost. Or is there another treatment can replace removal the shunt materials to cure VP shunt infection? In this series, we report our treatment experiences of VP shunt infection in a single institution during last 5 years.
Methods and materials

Patient's population

Between Feb 2010 and Feb 2013, 282 new hydrocephalus patients aged 18 years to 69 years received VP shunt in the Department of Neurosurgery 101 PLA Hospital, Jiansu, China, and VP shunt infection occurred in 15 (5.3%) patients. The clinical features are shown in Table 1. All of 15 patients, five patients were female and ten patients were male, 6 patients had post-traumatic hydrocephalus, 5 patients had hydrocephalus after intracranial aneurysm-induced hemorrhage, 2 patients were poor glioma-induced chronic hydrocephalus and 2 were congenital hydrocephalus. The mean duration from shunt operation to shunt infection was 28 days (range: 7 to 63 days). The clinical features were fever, poor feeding, depressed consciousness and neck rigidity, etc.

Diagnosis of VP shunt infection

The diagnosis of shunt infection was did not hard. CSF, urine and blood samples were taken if VP shunt infection was suspected. The criteria of VP shunt infection as follows: (1) fever, headache, nausea, and occurred neurological symptoms, meningeal irritation, abdominal symptoms and shunt malfunction; (2) CSF routine examination show CSF leukocytes more than 50 per cubic millimeter and with abnormal color; (3) CSF culture or smear had a positive result (the same pathogen from at least two consecutive CSF samples to avoid contamination). The diagnosis of VP shunt infection was defined with the meeting fulfill both criteria (1) and (2) or solely with criteria (3). In this study, Six patients (40%) had a positive CSF culture at least twice from lumbar puncture and shunt valve puncture (two cases was Staphylococcus epidermidis, three cases was Staphylococcus aureus and one case was Enterobacter cloacae), another nine patients had a negative culture but both fulfill criteria (1) and (2).

Treatment of VP shunt infection

Most literature reported that the VP shunt materials was total removal in an emergency as shunt infection was defined, and it also was a standard protocol [2, 5, 6, 9, 11, 12]. As VP shunt materials was expensive and removal operation had a high risk of bacterial infection disseminated. Both 15 cases used a same type of shunt system (Codman Hakin non-programmable shunt). When VP shunt infection was defined, firstly, vancomycin was system used in vein (0.9 NaCl 100 ml + vancomycin 0.5 g iv, tid); secondly and most importantly was shunt valve injections with vancomycin or

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<th>Cause</th>
<th>Type</th>
<th>Time (day)</th>
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</table>

Cause: reason to hydrocephalus; Type: type of hydrocephalus; Time: the time of shunt operation to infection; Revision: shunt materials revise (pressure revise and partial revise). Staph.e: Staphylococcus epidermidis; Staph.a: Staphylococcus aureus; Enterob: Enterobacter cloacae.
VP shunt infection

Discussion

Among VP shunt complications, shunt infection remains the most significant complications of VP shunt operation, and it also cause the shunt operation failure and is the majority reason of morbidity, mortality and neurological disability. In additions, VP shunt infection will greatly increase the length and cost of hospitalization. If remove VP shunt materials, the cost and length of hospitalization must be greater. In the United States, the mean hospital cost per shunt infection was close $50000 [13]. In our study, 14 of 15 cases who received our treatment just had favorable outcomes and with an acceptable hospitalization cost (¥85000±21000), while the cost of standard treatment was higher (¥154000±24000) and unacceptable for most ordinary households in China. The cost between two groups had significantly statistical difference (P=0.004). Also the hospital stay of new treatment group less than standard treatment group (P=0.004). So, our new method can greatly reduce the cost of hospital, and avoid wasting the medicine resources.

Curative criterion

(1) Temperature was normal than 7 days and no meningeal irritation; (2) Blood routine examination showed a normal WBC and procalcitonin (PCT); (3) CSF routine examination showed that WBC <10/mL, with normal protein and glucose; (4) CSF culture had a negative result at least 3 times.

Ethics statement

This study is approved by the Ethic Committee of Anhui Medical University (Approval Number: AMU-EXLL201001), and the signed informed consent was obtained.

Results

Outcome and follow-up

All of 15 cases were cured and discharged with a favorable outcome, just one case removed the total VP shunt materials as our treatment had no effect after one week with high fever, positive CSF culture, high WBC in CSF. All other patients still retained the total VP shunt materials and no complications occurred. All patients did not experience treatment-related complications at the time of hospitalization. All 14 patients who did not removed the shunt materials had a good shunt effect by CT reexamination. All patients received 2-5 years follow-up without VP shunt infection recurrence and none of them suffered CSF oozes from shunt valve. Of these 15 patients, just 3 patients had VP shunt revisions as poor shunt effect, others were good after CT reexamination.

Cost and hospital stays

All of 15 cases received 3 weeks systemic antibiotics by intravenous and 2 weeks intraventricular antibiotics treatment by shunt valve inject antibiotics. The mean hospital stays was 39 days, less than other patients who had removed the shunt materials (P=0.004). The mean hospital cost of the 14 cases who received our treatment just 85000 RMB, however, the mean hospital cost of standard treatment was about 154000 RMB (the data from our department, 9 patients who received standard treatment between 2009 and 2010) (shown in Table 3).

Table 2. Specific method of VP shunt valve injection

<table>
<thead>
<tr>
<th>Group</th>
<th>N</th>
<th>Antibiotics</th>
<th>Concentration</th>
<th>Dose</th>
<th>Frequent</th>
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<tr>
<td>Severe</td>
<td>9</td>
<td>Vancomycin</td>
<td>100 ml NaCl+0.5 g</td>
<td>5 ml</td>
<td>tid</td>
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<tr>
<td>CSSS</td>
<td></td>
<td>Cefoperazone Sodium and Sulbactam Sodium</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>No-severe</td>
<td>6</td>
<td>Vancomycin</td>
<td>250 ml NaCl+0.5 g</td>
<td>5 ml</td>
<td>bid</td>
</tr>
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<td></td>
<td></td>
<td>Cefoperazone Sodium and Sulbactam Sodium</td>
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</tbody>
</table>

Severe: severe infection (WBC >1000/ul in CSF); No-severe: no-severe infection (WBC <1000/ul in CSF); CSSS: Cefoperazone Sodium and Sulbactam Sodium.

Cefoperazone Sodium and Sulbactam Sodium. The specific method was as follows: (1). We defined the location of shunt valve by B Ultrasonic; (2). The concentration and dose of antibiotics in Table 2; (3). The antibiotics were changed based on the blood or CSF culture results, if necessary; (4). If this treatment had no improvement or efficacy on patients after one week, then the VP shunt materials must be removal as traditional treatment method.

The risks factors of VP shunt infection

In this study, we retrospectively 15 cases who occurred VP shunt infection of a total 282 VP shunt procedures, resulting in an infection rate of 5.3% per procedure. Most reported in recent literature indicates that overall rate of VP shunt...
VP shunt infection

Table 3. The effect of two groups

<table>
<thead>
<tr>
<th>Group</th>
<th>Hospital Stay (mean ± SD) (day)</th>
<th>Hospital Cost (mean ± SD) (ten thousand)</th>
<th>Revision rate (%)</th>
<th>Cure rate (%)</th>
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<tr>
<td>New treatment</td>
<td>39.1±8.1</td>
<td>8.5±2.1</td>
<td>20% (3/15)</td>
<td>93.3% (14/15)</td>
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<tr>
<td>Standard treatment</td>
<td>55.1±11.2</td>
<td>15.4±2.4</td>
<td>22.2% (2/9)</td>
<td>100% (9/9)</td>
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<tr>
<td>P value</td>
<td>0.004</td>
<td>0.000</td>
<td>0.429</td>
<td>0.897</td>
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Independent samples test was used for continuous variable. A chi-squared test, rank sum test or Fisher exact was used for categorical variable.

Infection rate ranges from 5.9%–51.7% [6, 7, 14-16]. There are many reasons maybe lead to shunt infection after VP shunt operation in literature. Matthieu Vinchon [6] found age at shunt insertion, cause of hydrocephalus, antecedents and surgeon was the risk factors to VP shunt infection. The same results also were confirmed in a study contained 1183 shunt failures in 839 pediatric patients with hydrocephalus [17]. Stone JJ [18] also found the shunt infection rate is proportional to age by cohort study. Some literature reported that it was most important to prevent shunt infection that used antibiotics or not before operation. Bayston [19] and Stevens [20] found that it can significantly reduce the shunt infection rate after operation by used prophylaxis antibiotics before operation. Also some literature reported that topical antibiotics can reduce the postoperative VP shunt infection [21], but there was no randomized control trial study to evaluate the effect of this treatment.

Treatment plan

As the blood-brain barrier (BBB) was the main obstacles in drug therapy [22], so just used systemic antibiotics alone and incomplete removed the shunt materials had an unacceptable high failure rate [23]. And no randomized controlled trial to confirm the different effect of shunt infection about immediate shunt removal and shunt presence. May be no other better therapies but shunt materials removal on treatment shunt infection in most literature. Most protocol for shunt infection based on the guidelines recommended by the Center for Disease Control [11]. The shunt materials was totally removed and inserted an external drainage, intravenous antibiotic therapy was the standard protocol, after shunt infection was cured, then the new shunt inserted. Some literature reported that a higher success rates for shunt infection if the shunt materials was removed totally and an external ventricular drainage catheter was inserted [17, 24-26]. The pathogen hidden in the shunt valve and shunt tube can lead to infection repeat and antibiotic reached and work hardly, it may be the reason of shunt system removal. But the therapies were too expensive, lavish and risky what is said above. In this study, we tried a new and simple therapy to treatment VP shunt infection and had a perfect effective by a long-term follow-up. 14 (93.3%) of 15 cases were cured successful without removal of the shunt system. And just one severe infection patient was failure by our therapy and removed the shunt system after one week. The new treatment plan was better than standard therapy with lower hospital cost, shorter hospital stay and safer treatments. By injected antibiotic from shunt valve, then the antibiotic can spread over the whole shunt tube and the antibiotics also can enter ventricular CSF and abdomen directly, which will benefit to removal all the pathogens completely. Several cases report found that intraventricular antibiotic alone therapy VP shunt infection also had a good results in literature [23, 27]. Forward KR et al [23] found a good effect on 4 shunt infection patients by intraventricular antibiotics therapy. Swayne R et al [27] also reported a good result by using intraventricular antibiotics in VP shunt infection patients who had gram positive cocci in CSF culture. In our study, just one patient whose CSF culture was Enterobacter cloacae gave up the new treatment and removal of the shunt system after one week as no clinical improvement. Other 14 patients were successful cured and no reinfection after 2-5 years follow-up. These 14 patients all had a good shunt effect before discharged.

Pathogenic and the choice of antibiotics

The positive rate of CSF culture was very low. In our study, just 6 patients (40%) found microor-
organisms in CSF samples, so it was not enough to according to the sensitivity of the drugs to treat VP shunt infection. As so, it was very important to study the distribution of VP shunt infectious bacterium spectrum. Recently, review of the literature reports that the main pathogen was Gram-positive organisms [28]. In our study, just 1 (Enterobacter cloacae) of 6 case was Gram-negative organism, other organisms contains 2 Staphylococcus aureus and 3 Staphylococcus epidermidis, a result consistent with that of other study [28, 29]. All our isolates were part of normal skin flora except Enterobacter cloacae, also that the main mechanism of shunt infection was contamination of bacterial of skin flora.

The choice of antibiotics may be a very difficult problem and different doctors had different choices. Most doctors select antibiotics according to the sensitivity of the drugs, but not every VP shunt infection patients all had a satisfactory result of bacteria susceptibility test. So, Empiric antibiotics were very important. There exiting BBB problem, a variety of antibiotics for curing the infection of nerve center system are restricted. How to select the effective antibiotics to treatment infection? The Infectious Diseases Society of America recommended vancomycin for Empiric antibiotics for broad spectrum coverage of staphylococci and other gram-positive organism, and ceftazidime, cefepime or meropenem to provide coverage against gram-negative bacteria [30, 32]. But Nau R et al and Yenis Gutierrez-Murgas et al [31, 32] found pH gradient between the CSF and blood, drug configuration, drug solubility, protein binding ability, the extent of meningal inflammation, metabolic and structural characteristics of biofilms maybe make these infections less susceptible to antibiotic treatment. In our study, all of 15 shunt infection patients accepted vancomycin (systematic medication and valve injection) for empiric antibiotic at first. 9 severe infection patients (contains one enterobacter cloacae patient) accepted vancomycin, sulbactam and cefopacrzone (two drugs also used for systematic treatment and valve injection), other 6 patients accepted vancomycin alone for vein and valve injection. Treatment duration was 2-3 weeks according to patient’s concrete condition. Both of all 15 patients had a good outcome and no neurological dysfunction and no reinfections. Same antibiotics therapy for VP shunt infections was addressed in several reports and had a good outcome [6, 9]. P Castro et al [33] also reported a case of ventriculoperitoneal shunt infection treated successfully with linezolid without implant removal.

Conclusion

Our study shows that valve injection antibiotics combined with systemic medication may be a simple, safety and effective way to treatment for VP shunt infection. It can significantly reduce the hospitalization and hospital stay largely. Our study limited by a small sample size and lack of a randomized controlled trial, even it had a distinct advantage than traditional treatment in our department. But, a larger multicenter randomized controlled trial study is required to evaluate the effectiveness of this treatment to cure VP shunt infection.

Disclosure of conflict of interest

None.

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References

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