Clinical Neurology and Neurosurgery 151 (2016) 92–95

Contents lists available at ScienceDirect

Clinical Neurology and Neurosurgery

journal homepage: www.elsevier.com/locate/clineuro

Prevention of infection by antibiotic-impregnated shunts after pediatric hydrocephalus treatment: A single center, retrospective study in China

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ARTICLE INFO

Article history:
Received 30 June 2016
Received in revised form 9 October 2016
Accepted 12 October 2016
Available online 17 October 2016

Keywords:
Child
Hydrocephalus
Shunt
Infection
Antibiotic-impregnated shunts

ABSTRACT

Objective: To investigate infection prevention by antibiotic-impregnated shunts (AIS) relative to conventional ones after pediatric hydrocephalus treatment.
Methods: This single center, retrospective analysis comprised 807 consecutive pediatric cases of hydrocephalus shunting performed by the same neurosurgeon between January 2001 and February 2013. Conventional and AIS catheters were used in 303 and 504 cases, respectively. Study outcomes were infection rates at 6 months (primary), and at 1 month and between 1 and 6 months (secondary). An infant (<1 year) subgroup was also analyzed.
Results: The AIS relative to the conventional catheter group had significantly lower infection rates at 6 months (1.98% [10/504] vs. 5.95% [18/303], two-tailed p = 0.0046; central nervous system: 60% and 55.56%; abdominal: 20% and 27.77%; wound: 20% and 16.67%, respectively) and 1 month (0.19% [1/504] vs. 2.65% [8/303], p = 0.0023, respectively), but statistically similar rates between 1 and 6 months (1.79% [9/504] vs. 3.30% [10/303], p = 0.2296, respectively). In the infant subgroup, AIS application was also associated with reduction in shunt infection (1.49% [7/470] vs. 3.76% [10/266], p = 0.0489, respectively).
Conclusion: AIS as compared to conventional catheter use appears to lower infection risk at 6 months, mainly during the first month, after hydrocephalus therapy in children.

1. Introduction

Hydrocephalus, one of the most common pediatric neurological diseases, is most often treated with shunt surgery. Infection, which remains a common complication and the main cause of postsurgical disability and mortality, develops in 0.3%–12.9% of patients [1,12], usually within 6 months after shunt implantation. Antibiotic-impregnated shunt (AIS) catheters with in vitro antimicrobial activity for up to 2 months were introduced to minimize postoperative infection, however, reported clinical results have been inconsistent [14,15]. The present retrospective analysis of data gathered at our hospital over 12 years therefore compared infection rates at the highest risk window of up to 6 months follow-up between 504 and 303 children with hydrocephalus who underwent treatment with AIS and conventional shunt catheters, respectively.

2. Materials and methods

2.1. General information

The study protocol was approved by the Institutional Review Board of Shanghai Children's Medical Center, and adheres to the principles set forth in the US Code of Federal Regulations, Title 45, Part 46, Protection of Human Subjects, revised January 15, 2009 and the World Medical Association Declaration of Helsinki. All patient's parents provided written informed consent before the procedures.

Between January 2001 and February 2013, 807 consecutive children with hydrocephalus were treated with shunt surgery performed by the same neurosurgeon at the Department of Neurosurgery of Shanghai Children's Medical Center affiliated to Shanghai Jiaotong University School of Medicine. Shunt valve choice was decided mainly based on the family's economic status and on hydrocephalus severity and in consultation between the patient's family and the surgeon: 303 cases received conventional catheters (from Aesculap and Johnson & Johnson), and 504 cases received AIS (Johnson & Johnson AIS catheters, and including Johnson & John-

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http://dx.doi.org/10.1016/j.clineuro.2016.10.009
0303-8467/

son or Aesculap valves). The follow-up period extended to at least 6 months.

2.2. Surgical procedure and treatment

One day before surgery, children were bathed and their hair washed, and 30 min before surgery, 50 mg/kg body weight of a second-generation cephalosporin was administered intravenously; macrolides or penicillins were used in those allergic to cephalosporins. Children's hair was shaved off under surgical field, and they were placed in the supine position, with head tilted and neck and shoulder padded. The posterior horn of the left lateral ventricle at the occipital lobe was punctured. For children with non-symmetric expansion of one lateral ventricle, the expanded side was punctured. Before use, the shunt was rinsed and soaked in antibiotic solution, the shunt valve was placed at the subcutaneous pedicle of the postauricular flap, and the remote catheter was led though a small incision below the xiphoid using a subcutaneous tunneler sheath. After surgery, antibiotics that had been used before surgery were administered routinely for 3 days, and the patient was discharged 7 days later after suture removal.

2.3. Assessment of shunt infection

All parents were advised to bring back their children to the same hospital for any complications and follow-up. Children were diagnosed with shunt infection if they developed: 1. symptoms of acute bacterial meningitis or abdominal infection, such as fever, vomiting, lethargy, abdominal distension, abdominal pain, loss of appetite, and difficulty feeding; 2. signs of local infection in the shunt catheter region, such as skin irritation and ulceration; and/or 3. at least one of the following cerebrospinal fluid (CSF) findings: routine CSF white blood cell (WBC) count $>20 \times 10^6$/L or red blood cell (RBC)-to-WBC ratio <500/1; decreased CSF glucose concentration and increased protein concentration; and positive CSF bacterial cultures.

2.4. Statistical analysis

Continuous data are expressed as mean ± standard deviation and were compared using the Student's *t*-test, while categorical data are expressed as number and percentage and were compared using the chi-square test (SPSS v22, IBM, USA). A two-tailed p value < 0.05 was considered statistically significant.

3. Results

Mean age was 17.1 months (range 3 months-4 years), and 13.7 months (range, 1 month-3.2 years) for AIS and conventional shunt catheter groups, respectively. Most of the cases (736/807) were infants younger than 1 year old. Overall, of the 807 children with hydrocephalus who underwent shunt surgery, 28 (3.47%) developed shunt infection during 6-month follow-up. Clinical data of infected cases were included in Tables 1 and 2. Infection rate was significantly lower in the AIS than conventional shunt catheter group at 6 months (1.98% [10/504] vs. 5.95% [18/303]; p < 0.0001), which also was the case at 1 month (0.19% [1/504] vs. 2.65% [8/303]; p = 0.0014); however, infection rates were statistically similar between 1 and 6 months (1.79% [9/504] vs. 3.30% [10/303]; p = 0.2296) follow-up. Age distribution was similar (ranges, 3–48 and 2–38 months) but weight was lower (6.06 ± 1.84% vs. 9.34 + 4.18%, p = 0.004) among children who developed infections (central nervous system: 60% and 55.56%; abdominal: 20% and 27.77%; wound: 20% and 16.67%, respectively) in the AIS group as compared to the conventional catheter group. In the subgroup of infants(<1 year), AIS application was also associated with reduction in shunt infection (1.49% [7/470] vs. 3.76% [10/266], p = 0.0489, respectively).

4. Discussion

In this single center retrospective analysis of children with hydrocephalus, AIS relative to conventional catheter use for shunt surgery was associated with significantly lower rates of infection throughout 6 months follow-up, which was mainly determined by significantly lower rates at 1 month follow-up.

Even after five decades of experience treating hydrocephalus with shunt surgery, postsurgical shunt infection remains a major complication that not only seriously affects survival and quality of life but also represents a heavy economic burden for the patient's family. The overall 6-month infection rate of 3.47% in the present study is consistent with published experience which averages around 11%, and can reach as high as 15–25% in infants younger than 6 months [1]. Beyond age, shunt infection rate can be influenced by the child's physical condition, presence of skin problems, and surgical techniques, time, complications including hemorrhage, and number of staff present, among others [2]. In the present study, the age and infection location distributions were similar among children who developed infections in the two groups studied, and all procedures were performed by the same neurosurgeon.

Most bacterial shunt infections arise from normal skin flora, most commonly coagulase-negative staphylococci (*Staphylococcus epidermidis* and *aureus*), and Gram-negative bacteria (*E. coli*), which enter the shunt catheter or cerebrospinal fluid compartment at the time of catheter insertion or through contamination during the surgical procedure. The bacteria colonize the catheter's inner wall or surface and produce an extracellular mucus biofilm that acts as a protective barrier against the body's immune defenses and antibiotics. Over decades, several measures have been implemented to prevent shunt infection. Rigorous surgical disinfection and an optimized operating room environment reduced shunt infection rate to 1% or less [3]. Wide use of intravenous antibiotics was also advocated; however, prophylactic antibiotic use remains controversial. For instance, second generation cephalosporins have limited effect on infection prevention because they cannot cross the blood-brain barrier and achieve an effective concentration in the CSF compartment.

Most shunts are infected intraoperatively, with infection manifesting within one year in over 90% of patients, most within 6 months. Another approach to prevent and treat shunt infection therefore involves use of antibacterial materials on shunts to kill bacteria ideally within one month. Izci et al. [4] employed silver coated catheters in patients with shunt infection and significantly increased CSF protein level; three months later, CSF bacterial cultures were negative and the protein level had dramatically decreased. Currently, shunt catheters impregnated with antibiotics are the most widely used shunt catheters; those in the present study were impregnated with rifampicin and clindamycin which are effective against the most common pathogenic staphylococci. In vitro experiments have shown that AIS catheters can kill all bacteria within 48–52 h with pharmacological effect maintained for 2 months [5,6]. Even if the effect disappeared earlier chance of infection is not increased indicating that the bactericidal effect of AIS catheters is stronger than their inhibitory effect [7].

Despite the strong bactericidal effect of AIS catheters, clinical study results are inconsistent. In a review of 353 cases of children undergoing shunt surgery, Sciubba et al. [8] reported a 2.4 fold lower infection rate for AIS than conventional catheters (1.4% vs. 12%, respectively). A British multicenter, retrospective study