

Study of Predictors of Cerebrospinal Fluid Shunt Infections In Infants And Children At Tertiary Hospital.

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Abstract

Purpose: To determine risk factors like etiologies, age at insertion, causative pathogens of CSF shunt infections and their antimicrobial susceptibility pattern, treatment modality, reinfections, and clinical outcomes in these patients.

Material and Methods: Present study was conducted in patient’s underage of 12 years undergoing cerebrospinal fluid shunt procedures. The CSF shunt fluid, EVD, shunt tube tip specimens were collected by the clinician by aseptic precautions in sterile container. The organisms isolated were subjected to antimicrobial susceptibility.

Results: In the present study, a total of 90 patients who had undergone Ventriculoperitoneal shunt were analyzed. Maximum cases were of congenital malformations (MMC and aqueduct stenosis) 61 (67.78%), followed by tuberculous meningitis 24 (26.6%). 20 shunt infections occurred in 90 patients establishing an infection rate of 22.22%. VP shunt infections occurred at a median 86.25

days after insertion. Shunt infections were observed more in males 15 (75%) than females 5 (25%). Most common organisms isolated were *Acinetobacter Baumannii* 3 (30%) followed by *Enterococcus faecalis* 2 (20%) followed by one isolate each of *Enterobacter aerogenes*, *Pseudomonas aeruginosa*, and Methicillin resistant *Staphylococcus aureus* (MRSA).

Conclusion: Age at shunt placement, etiology, signs and symptoms, cell count, presence of pus cells and organisms in

Gram stain, culture positive and the interval between the age at shunt placement and onset of infection were the most important predictors of shunt infections.

Keywords: Cerebrospinal fluid, Ventriculoperitoneal shunt, hydrocephalus, *Acinetobacter Baumannii*

Key Message: Early and prompt intervention of shunt infections can prevent shunt failure, reinfection, long-term neurological outcome and can reduce mortality.

Introduction

Cerebrospinal fluid (CSF) shunt has been the treatment of choice for hydrocephalus. CSF shunting procedures provide a rapid means of normalizing intracranial pressure and can prevent neuronal damage as well as other detrimental sequelae.^[1]

Hydrocephalus can be caused by congenital malformations like aqueduct stenosis, neural tube defects or can be acquired by various causes meningitis, trauma, and tumors.^[2] Despite the advent of modern neurosurgical techniques, new anti-biotics, and modern imaging techniques, infection after ventriculoperitoneal (VP) shunt insertion and/or ventriculostomy is still a serious issue.^[3] Shunt infection rates range from 20 to 40%.^[1]

Shunt infection risk factors are associated with surgeon experience level, patient age at the time of initial shunt placement, etiology of hydrocephalus, the presence of previous infection, patient skin colonization, surgical technique used.^[4] The main causative agents of shunt infections are Gram positive like *Staphylococcus epidermidis* (52.8 to 88.9%), *Staphylococcus aureus* (12 to 40%) also *Streptococcus* Group B and *Enterococcus* species. Gram-negative bacilli (9 to 22%) like *Enterobacter* species, *Klebsiella pneumoniae* and *Pseudomonas aeruginosa*.^[5,6,7]

Carbapenem resistant isolates and MRSA are increasing across the globe and making difficult to treat shunt infections. Inadequate or inappropriate treatment can cause reinfection of shunt. Hence, early diagnosis and effective treatment is compulsory to reduce morbidity and mortality.^[3]

The present study was undertaken to study incidence, clinical features relevant to CSF shunt infection, risk factors like etiologies, age at insertion, causative pathogens of CSF shunt infections and their antimicrobial

susceptibility pattern, treatment modality, reinfections, and clinical outcomes in these patients.

Material and methods

Present study was a prospective, observational study was conducted in Department of microbiology, XXX medical college & hospital. Duration of present study was one year (from Jan 2017 to Dec 2017). Ethical committee approval was obtained.

Inclusion criteria

1. Patients' under age of twelve years undergoing cerebrospinal fluid shunt procedures.
2. Patient giving consent of study.

Exclusion criteria

1. Children on corticosteroid, immunosuppressive and antimetabolite therapy.
2. Children with haematological disorder.

Study protocol was explained in language best understood to patient's parents. Details of patients undergoing cerebrospinal fluid shunt surgery such as demographic findings, predisposing medical conditions, clinical sign and symptoms, age at insertion of shunt, shunt infections, other laboratory parameters, antibiotics used for perioperative prophylaxis, treatment modality including type and duration of antibiotics, follow up and outcome was noted. The various risk factors associated with VP shunt infections were analysed.

The CSF shunt fluid, EVD, shunt tube tip specimens were collected by the clinician by aseptic precautions in sterile container. The specimens were immediately transported to the laboratory and processed as per standard laboratory techniques.

Gross findings as volume of CSF, gross appearance of CSF was noted. Smear for Gram Stain was prepared using 1-2 drops of the sediment/specimen on a glass slide. Two loopfuls of fluid / sediment on Sheep Blood agar (SBA), Sheep chocolate agar (SCA) and

MacConkey agar (MA). SBA and SCA were incubated in candle jar at 37° Celsius for 24 hours, for MA incubated aerobically at 37 degree for 24 hours. Specimen / sediment was inoculated in Trypticase soy broth (TSB) and thioglycolate broth. Subculture of the TSB is done after 4 hours and 24 hours on MA, SBA and SCA.

Media was examined for macroscopic evidence of growth after overnight incubation. If no visible growth is observed on the culture media, media was reincubated and examined after 24 hours. Thioglycolate broth was examined for turbidity every day for seven days. If broth is turbid then subculture done on SBA, SCA and MA. If no turbidity in broth is observed, then broth is discarded after seven days of incubation.

Isolated organisms were identified using Gram stain characteristics, colony characteristics and biochemical reactions as per standard microbiology techniques. From the primary culture plate bacterial suspension was prepared in trypticase soya broth till turbidity matched with 0.5 McFarland standard (0.5×10^8 CFU/ ml).

The organisms isolated were subjected to antimicrobial susceptibility using the Kirby-Bauer disc diffusion method on Muller Hinton agar and Muller Hinton Blood agar as per standard microbiological techniques. Results obtained were interpreted as per Clinical and Laboratory Standards Institute (CLSI) guidelines 2017.^[9]

Results were expressed as mean and standard deviation for continuous data and frequency as number and percentage. Unpaired t test was used to compare mean levels between two groups. Categorical data was analyzed by Chi square test. p value of less than 0.05 was considered as statistically significant.

Results

In the present prospective study, a total of ninety patients who had undergone Ventriculoperitoneal (VP) shunt were analyzed. Maximum patients belonged to age group

0 to 1 month 29 (32.23) followed by 1 month to \leq 6 months 17 (18.89%). Maximum patients 72 (80%) were under the age of 2 years. Mean age 18 months with standard deviation of 8.6 months. Out of the total 90 cases 53 (59%) were males and 37 (41%) were females. Of the 90 cases maximum cases were of congenital malformations (MMC and aqueduct stenosis) 61 (67.78%), followed by tuberculous meningitis 24 (26.6%). So congenital malformations were the commonest etiologies for shunt surgery in this study.

According to the criteria defined by CDC / NHSN¹⁰, 20 shunt infections occurred in 90 patients establishing an infection rate of 22.22%. VP shunt infections occurred at a median 86.25 days after insertion. Out of the twenty infections 9 (45%) infections occurred within 1 month. 15 (75%) infections occurred within 6 months of shunt insertion of which 9 were culture positive indicative of definite infections. Of the 20 infected patients most, common age group was of > 1 year to ≤ 2 years 08 (40%) followed by 0 to ≤ 1 month 5 (25%) and > 1 month to ≤ 6 months. 04 (20%). Mean 16.5 months and Standard deviation 15.9 months. All infected patients were younger than 2 years old 18 (90%) except two patients who were of age 3 years and 5 years. Shunt infections were observed more in males 15 (75%) than females 5 (25%). Commonest underlying condition amongst all the infected cases were congenital malformations (MMC + aqueduct stenosis) 13 (65%) followed by tuberculous meningitis 6 (30%) and head injury 01(5%). Fever (45%) and neurological signs 80% (vomiting, irritability, anterior fontanelle bulging) were the consistent findings among infected patients

In 5 infected patients cell count was increased and mean 10.82. In 5 infected patients' protein was increased and mean 27.17. In 5 infected patients' sugar was decreased and mean 40.

Pus cells and organisms were seen on CSF shunt fluid Gram stain 5 (25%) of the infected cases.

Out of 20 infected patients 10 (50%) were culture positive. According to Overturf's 11 diagnostic criteria for ventriculoperitoneal shunt infections, 10 culture positive cases were definite shunt infections and other 10 culture negative were cases of probable shunt infections.^[11]

Most common organisms isolated were *Acinetobacter Baumannii* 3 (30%) followed by *Enterococcus faecalis* 2 (20%) followed by one isolate each of *Enterobacter aerogenes*, *Pseudomonas aeruginosa*, and Methicillin resistant *Staphylococcus aureus* (MRSA) as shown in table I.

Amongst *Acinetobacter Baumannii* two were resistant to baseline drugs and carbapenems, which were sensitive to colistin and tigecycline. One isolate of *Klebsiella pneumoniae* also showed carbapenem resistance which was sensitive to colistin as shown in table II.

Enterococcus faecalis was the commonest isolate. All Gram-positive isolates were sensitive to vancomycin and linezolid shown in table III. The patient infected with MRSA isolate succumbed to infection.

In 07 patients' conservative management was done. In 02 patients underwent shunt exteriorization followed by revision of shunt. Other 10 patients were managed by complete shunt replacement. So in 12 (60%) patients complete revision of shunt was done. One patient with MRSA infection succumbed to the infection. In our prospective analysis of 90 shunt operations, 22 patients were lost in follow up. 48 patients had well-functioning shunt. 20 had shunt infections out of which 07 (35%) were managed conservatively and 12 (60%) had complete shunt replacement shown in table IV. One patient succumbed to the infection.

Age at shunt placement, aetiology, signs and symptoms,

cell count, presence of pus cells and organisms in Gram stain, culture positive and the interval between the age at shunt placement and onset of infection were the most important predictors of shunt infections shown in table V.

Discussion

Hydrocephalus is a common neurosurgical disease that develops via a variety of etiologies, including congenital anomaly, intracranial hemorrhage, infections, and tumour.^[12] Although CSF shunts contributed to the significant improvement of the management and outcome of hydrocephalus, the shunt has several complications, including infections, which is a major threat to pediatric patients.^[13]

Many factors have been reported to be associated with increased risk of infections including the age of patient, etiologies of hydrocephalus, type of shunt implanted, surgeons experience, presence of previous shunt infection, patient skin colonization and surgical technique used.^[6] So special consideration should be paid concerning the patients preoperative condition. The incidence of infection following VP shunt placement is reported to be around 20 to 40%.^[12] Of the 90 patients who underwent shunt surgery males 53 (59%) were more than females 37 (41%). Male preponderance was also observed in study by Agarwal et al (68%),^[2] and Simon et al (56%)^[14]. A total of 72 VP shunts (80%) were inserted in patients less than 2 years age group with mean age of 18 months. Similar results were reported by Pan et al.,^[15] i.e., 20.7 months.

Hydrocephalus was the most common clinical condition. Most common etiologies for these patients included congenital malformations like meningocele 52 (57.78%) and aqueduct stenosis 09 (10%) comprising of 67.78%. Ahmed et al.,^[16] also reported congenital malformation (64%) as a commonest cause of hydrocephalus. Hydrocephalus secondary to tuberculous

meningitis were seen in 24 (26.67%), similar findings were observed by Pan et al.,^[15] (25.54%).

Present study demonstrated that infections occurred in 20 (22.22%) out of the 90 patients who underwent VP shunt insertion. This result is similar to the studies by Bokhary et al^[17], Braga et al^[5]. However, studies by Mancao et al^[18], McGirt et al^[4], Lee et al^[19] showed lower infection rate.

In our study children under the age of 2 years old 18 (90%) showed more risk (RR=2.25) of acquiring infections. Only two patients were infected more than 2 years of age. Braga et al^[5] inferred that greater susceptibility of shunt infections in children is due to relative deficiency in their immune response against bacteria.

Patients with congenital malformation and TBM showed increased risk of developing infections. Braga et al^[5] showed increased infection rate in MMC cases. Also, study by Clemmensen et al^[20] reported that relative risk of having an infection is significantly higher in MMC. Patients with neurological signs had more risk of getting infections as found in our study was statistically significant. Also, patient with fever symptoms had increased risk (RR= 1.286) of getting infections. The study by Mancao et al.,^[18] also reported fever (62%) and neurological signs (68.9%) were consistent findings in shunt infected cases. Other signs and symptoms observed were feeding changes and abdominal signs.

10 (11.11%) cases were culture positive which is statistically significant. According to Overturf's 11 diagnostic criteria for ventriculoperitoneal shunt infection 11.11% were definite shunt infections and other 11.11% were cases of probable shunt infections.^[11] Pan et al.,^[15] and Wang et al.,^[3] also reported definite shunt infection rate of 16.21% and 9.3% respectively.

In the present study 10 organisms were isolated out of which 6 (60%) were Gram negative and 4 (40%) were Gram positive. Acinetobacter Baumannii 03 (30%) was the most common isolated organism. Bisno et al.,^[6] also showed 20% Acinetobacter species in shunt infections. In other studies, Gram-positive microorganisms are found to predominate in the shunt infections where Coagulase negative staphylococcus are common cause of shunt infections as they are the skin commensal and infants resident skin flora keeps on changing. In the study by Mancao et al.,^[18] showed 79.5% of Gram positive and 10.2% Gram negative organisms.

Acinetobacter Baumannii 03 (50%) was the most common isolated Gram-negative organism of which two were resistant to baseline drugs and carbapenems. These carbapenem resistant isolates were sensitive to colistin and tigecycline. In the study by Demoz et al.,^[21] reported baseline and carbapenem resistant Acinetobacter Baumannii from shunt fluid which was only sensitive to ampicillin-sulbactam and colistin, similar to our study.

Out of 20 infected cases, 12 (60%) patients who had shunt failure were reshunted during initial 5 years of age which was statistically significant. There was 9 times risk of revision of shunt in infected cases (RR=9.75). Nine (75%) out of 12 cases were under the age of 2 years. Similar findings were by reported by Yilmaz et al (75.9%).^[8] The shunt related mortality in our study was 1.11%. In the study by Agarwal N et al.,^[2] mortality was 4.17%.

Understanding the risk factors for recurrent shunt infections (RSI) has been gaining importance in clinical studies and determining these risk factors could have a substantial impact on how shunt infections are treated. The recent literature indicates that the overall rate of RSI ranges from 14.6% to as high as 51.7%.^[8]

The present study had a limitation such as institution based, small number of cases since the results may vary with a larger sample size.

Conclusion

This study on CSF shunt infections suggests that age at shunt placement, etiology, signs and symptoms, cell count, presence of pus cells and organisms in Gram stain, culture positive and the interval between the age at shunt placement and onset of infection were the most important predictors of shunt infections. Early and prompt intervention of shunt infections can prevent shunt failure, reinfection, long-term neurological outcome and can reduce mortality.

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