Original Article

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Frequency of Postoperative Infections in Cerebrospinal Fluid Shunts Performed with or Without Topical Vancomycin at a Tertiary Care Hospital

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Abstract

Introduction: The aim of the study was to compare the frequency of postoperative infection in cerebrospinal fluid shunts performed with and without topical vancomycin at a tertiary care hospital.

Material & Methods: An Observational Cohort Study was conducted from 10th October, 2020 to 9th April, 2021 at Pakistan Institute of Medical Sciences, Islamabad, Pakistan. Total 74 patients of both genders with ages in the range of 1-5 years undergoing cerebrospinal fluid shunts were selected. Patients were divided into two groups (Group A and Group B). Patients with meningitis and ventriculitis before the shunt surgery were excluded. Patients in both the groups received cefotaxime 50 mg/kg body weight intravenously within 60 minutes prior to skin incision and underwent standard cerebrospinal fluid shunt procedure. In the study group (Group B), 10 mg of vancomycin was diluted in 8 ml of normal saline and was divided into two halves. One half was injected in the reservoir of the cerebral shunt and the second half was infiltrated subcutaneously around the reservoir and peritoneal catheter. Standard postoperative care was provided to all the patients. Postoperatively, all the patients received intravenous cefotaxime 50 mg/kg body weight repeated 8 hourly for 72 hours. They were monitored for any signs of infection and shunt infection was labelled.

Results: Majority of the patients 54 (72.97%) were between 1 to 3 years of age with overall mean age of 2.43 ± 1.28 years. In this study, frequency of postoperative infection was observed to be significantly lower in patients undergoing shunting with versus without topical vancomycin (2.70% vs 29.73%).

Conclusion: This study concluded that the frequency of postoperative infection is found to be significantly lower in patients undergoing cerebrospinal fluid shunting with versus without topical vancomycin.

Keywords: Hydrocephalus, Ventriculoperitoneal Shunt, Vancomycin, Infection.

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Introduction

Hydrocephalus is a pathological accumulation of cerebrospinal fluid within the ventricular system of the brain which leads to raised intracranial pressure and compression on brain parenchyma. It is a common paediatric neurosurgical problem. Hydrocephalus is of various types namely obstructive or non-communicating and non-obstructive or communicating. It may be congenital or acquired and primary or secondary. There are various methods of treatment for hydrocephalus. The most commonly used treatment is placement of ventriculoperitoneal shunt.[1]

Cerebrospinal fluid formation occurs at a rate of 450 ml/day or 0.3 ml/min. Upto 80% of cerebrospinal fluid is produced from choroid plexus of lateral, third and fourth ventricles, 20% is produced by the brain parenchyma and ventricular ependyma.[2] Ventricular system is formed by cavities connected in series within the brain and filled with cerebrospinal fluid.

There are four ventricles: two lateral ventricles in cerebrum, third ventricle in diencephalon and fourth ventricle between cerebellum and pons. The lateral ventricles are connected with third ventricle and third with the fourth ventricle through cerebral aqueduct, fourth ventricle is connected with spinal canal and subarachnoid space that surrounds brain.[3]

Cerebral shunts are commonly used to treat hydrocephalus, the swelling of the brain due to excess buildup of cerebrospinal fluid (CSF). If left unchecked, the cerebrospinal fluid can build up leading to an increase in intracranial pressure (ICP) which can lead to intracranial hematoma, cerebral edema, crushed brain tissue or herniation.[4] The cerebral shunt can be used to alleviate or prevent these problems in patients who suffer from hydrocephalus. Shunts can come in a variety of forms but most of them consist of a valve housing connected to a catheter, the end of which is usually placed in the peritoneal cavity. The main differences between shunts are usually in the materials used to construct them, the types of valve used, and whether the valve is programmable or not.[5]

Ventriculoperitoneal (VP) shunting is one of the most common neurosurgical procedures performed to treat patients with hydrocephalus, which is a disorder related to an abnormal accumulation of cerebrospinal fluid (CSF) in the brain. The operation involves diverting CSF from the ventricles of the brain to the peritoneal cavity of the abdomen by catheter implantation.[6] Despite the introduction of new shunt materials and insertion techniques, CSF shunts have a higher risk of failure than most currently approved medical devices.[7,8] In paediatric surgical series, shunt failures occur in 14% of patients just within the first month after shunt placement,8 and 40 to 50% of shunts will fail within the first year. Adults also experience a relatively high (29%) shunt failure rate within the first year.[9]
Postoperative infection also remains a serious concern where the reported frequency of infection varies from as low as 7.6% to as high as 40.0% in two recent local studies.[10,11] Infection of a ventriculoperitoneal shunt is related to notable morbidities like mental, motor, and psychological retardation and convulsive state.[7] Shunt infections are largely due to skin flora colonization of the shunt device at surgery, as 90% of infections are caused by Staphylococcus species, and most infections occur within the first few days after surgery.[11,12] An infection usually requires shunt revision leading to prolonged hospitalization which is accompanied by very high extra costs and most importantly, it may have deleterious neurological effects.[12,13] Therefore, measures which can prevent or at least reduce the burden of postoperative shunt infection are hot focus of research.

Van et al. (2018) in a Canadian study reported that the frequency of infection was significantly lower in patients undergoing CSF shunt with topical vancomycin as compared to controls (3.0% vs 6.8%; p=0.023).[14] Similar, significant difference in the frequency of postoperative infection has also been reported by an Egyptian study where Moussa et al. (2016) observed it to be significantly lower in patients undergoing shunting with versus without topical vancomycin (5.0% vs 30.0%; p-value=0.034).[15]

As reviewed above, the reported frequency of postoperative infection after cerebrospinal fluid shunting is quite high in local population11 and in the light of this evidence, topical instillation of vancomycin in patients undergoing CSF shunts can considerably reduce the load of postoperative infection with its associated morbidity and economic burden.[14,15] However, the existing evidence is limited to only 2 above mentioned studies. Owing to limited published research evidence and lack of local such published material, need for the present study is felt with a hope that if the study reveals significantly lower frequency of postoperative infection after topical vancomycin, it will help in the better management of patients undergoing shunt surgery in future practice.

Materials & Methods

Study Design: Observational Cohort Study.
Setting: Department of Neurosurgery at Pakistan Institute of Medical Sciences (PIMS), Islamabad, Pakistan.
Duration of Study: 10th October 2020 to 9th April 2021.
Sample Size: Sample size of 74 cases (37 cases in each group) is calculated with 80% power of test and 5% level of significance while taking expected frequency of postoperative infection to be 5.0% with and 30.0% without topical vancomycin in patients undergoing CSF shunt procedure.
Sampling Technique: Non-probability, Consecutive sampling.
Sample Selection:
a. Inclusion Criteria:
●Children of both genders with ages in the range of 1-5 years undergoing VP shunt.
●Children where written informed consent is given by the parents for inclusion in the study.
b. Exclusion Criteria:
●Children with meningitis (neck stiffness, fever ≥100oF, CSF leukocyte count ≥10/μL) and ventriculitis (fever ≥101oF, CSF leukocyte count ≥10/μL) before the shunt surgery.
●Patients undergoing revision shunt surgery (as per history and clinical record).

Data Collection Procedure: After approval from the Hospital's Ethical Review Board, 74 children undergoing CSF shunting at elective lists of Pakistan Institute of Medical Sciences, Islamabad and who fulfilled the above criteria were included in this study. Their parents were counseled and explained the details of the study. Written informed consent and detailed history was taken from parents of each patient. These patients were then divided into following two groups:
●Group A: Standard Approach (n=37)
●Group B: Standard Approach + Topical Vancomycin (n=37)

Patients in both the groups received cefotaxime 50 mg/kg body weight intravenously within 60 minutes prior to skin incision and underwent standard cerebrospinal fluid shunt procedure. In the study group (Group B), 10 mg of vancomycin was diluted in 8 ml of normal saline and was divided into two halves. Using a 28-gauge needle with a length of 8 mm, one half was injected in the reservoir of the cerebral shunt and the second half was infiltrated subcutaneously around the reservoir and the peritoneal catheter (divided in equal portions to be injected every 5 cm of the subcutaneous path of the peritoneal catheter). Standard postoperative care was provided to all the patients. Postoperatively all the patients received inj. cefotaxime 50 mg/kg body weight repeated 8 hourly for 72 hours. During postoperative

hospital stay, patients were monitored for any sign of infection and shunt infection was labelled if any. Patient's demographic details along with presence or absence of postoperative infection was recorded in the attached proforma. All the surgeries were performed by a single team of neurosurgery and all the pre and postoperative care as well as patient's evaluation was done by a single surgeon (first author himself) to eliminate bias. Confounding variables were controlled by exclusion.

Data Analysis Procedure: All the collected data was entered and analysed through SPSS version [17].

1. Numerical variables; age was presented by mean ±SD.
2. Categorical variables; gender and postoperative infection were presented by frequency and percentage. Frequency of postoperative infection was compared between the two groups using Chi-square test taking p≤0.05 as significant.
3. Data was stratified for age and gender to address effect modifiers. Post stratification chi-square test was applied taking p≤0.05 as significant.

Results

Age range in this study was from 1 to 5 years with a mean age of 2.43 ± 1.28 years. The mean age of patients in group A was 2.38 ± 1.21 years and in group B was 2.49 ± 1.30 years. Majority of the patients 54 (72.97%) were between 1 to 3 years of age as shown in Table-I. Gender distribution for both groups is shown in Table-II.

In this study, the frequency of postoperative infection has been observed to be significantly lower in patients undergoing shunting with topical vancomycin versus without topical vancomycin (2.70% vs 29.73%; p-value=0.002) as shown in Figure-I.

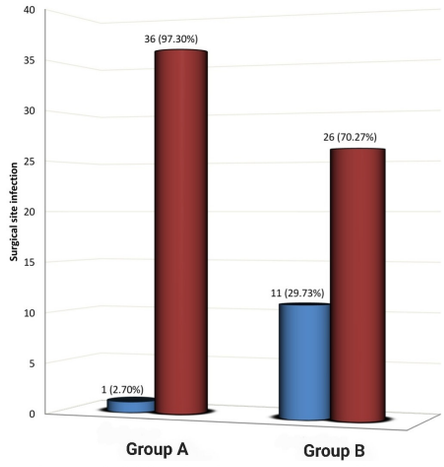
Stratification of post-operative infection according to age and gender is shown in Table-III & IV respectively.

Table-I: Age distribution for both groups (n=74).

Age (years)	Group A (n=37)		Group B (n=37)		Total (n=74)	
	No. of patients	%age	No. of patients	%age	No. of patients	%age
1-3	28	75.68	26	70.27	54	72.97
4-5	09	23.32	11	29.73	20	27.03
Mean ± SD	2.38 ± 1.21		2.49 ±1.30		2.43 ± 1.28	

Table-II: Gender distribution for both groups (n=74).

Gender	Group A (n=37)		Group B (n=37)		Total (n=74)	
	No. of patients	%age	No. of patients	%age	No. of patients	%age
Male	19	51.35	17	45.95	36	48.65
Female	18	48.65	20	54.05	38	51.35



P-value = 0.002 which is statistically significant

Figure-I: Comparison of the frequency of postoperative infection between ventriculoperitoneal shunts performed with and without topical vancomycin.

Table III: Stratification of postoperative infection according to age.

Age patients (years)	Group A (n=37)		Group B (n=37)		P-value
	post-operative infection		post-operative infection		
	Yes	No	Yes	No	
1-3	10	18	01	25	0.004
4-5	01	08	00	11	0.257

Table IV: Stratification of postoperative infection according to gender.

Gender	Group A (n=37)		Group B (n=37)		P-value
	post-operative infection		post-operative infection		
	Yes	No	Yes	No	
Male	08	11	00	17	0.002
Female	03	15	01	19	0.242

Discussion

The treatment of hydrocephalus consists of inserting a cerebrospinal fluid (CSF) shunt to the peritoneal or pleural cavities or to the atrium of the heart in the majority of cases. This insertion of foreign body materials may be accompanied by many potential problems, of which shunt infection is a major one. The average shunt infection rate is about 5-15%, although lower and higher rates are reported.16-23 Shunt infections are largely due to skin flora colonization of the shunt device at surgery, as 90% of infections are caused by Staphylococcus species, and most infections occur within the first few months after surgery.24 The impact of a shunt infection is very high. An infection usually leads to shunt explantation and subsequent re-insertion of a new shunt, leading to prolonged hospitalization of weeks, which is accompanied by very high extra costs, and most

importantly, it may have deleterious neurological effects. Many efforts have been made to reduce the shunt infection rate. Preoperative intravenous (IV) prophylactic antibiotics are administered routinely and this is a mainstay of prevention.[25] Many different measures appear to contribute to reducing the shunt infection rate, although evidence for each separate measure is minimal or non-existent.[26] Combining all these measures into an institutional shunt infection prevention protocol is the most effective means of preventing shunt infections.[20] The latest development is the use of antibiotic-impregnated catheters (AIC), with the prolonged release of two different antibiotics. Several meta-analyses have shown that AIC significantly reduces the shunt infection rate.[16-28] The use of AIC comes with significant extra costs and there are some concerns that it may increase the development of antibiotic resistance.

This study compares the frequency of postoperative infection between cerebrospinal fluid shunts performed with versus without topical vancomycin. In this study, the frequency of postoperative infection has been observed to be significantly lower in patients undergoing shunting with versus without topical vancomycin (2.70% vs 29.73%; p-value=0.002). Van et al. (2018) in a Canadian study reported that the frequency of infection was significantly lower in patients undergoing CSF shunt with topical vancomycin as compared to controls (3.0% vs 6.8%; p=0.023).[14]

Vancomycin is widely used intrathecally for treating shunt-related infections.29 However, it is only sporadically used for preventing infection, both intravenously and intrathecally. Ragel et al. initiated the use of both gentamicin and vancomycin intrathecally for preventing infection and reduced the shunt infection rate from 5.4% to 0.4%.30 Moussa and Mohamed used a similar antibiotic regimen in a small, prospective, randomized trial of children aged <1 year, but applied the antibiotics differently. Gentamicin and vancomycin were injected at the end of surgery into the ventricular reservoir and through the skin around the shunt hardware every 5 cm along the hardware, and in one group of patients, repeated after a week. They thus significantly reduced the shunt infection rate (from 30% to 2.5%).[15]

A meta-analysis by Klimo et al. showed that the application of IV antibiotics has more or less become an internationally accepted standard with a moderate degree of clinical certainty that it lowers the shunt infection rate,31,32 although the number of antibiotics used varies widely. There appears to be consensus that IV antibiotics should be given 15-30 minutes prior to skin incision, but whether antibiotics should be continued for one or more days after surgery is subject to wide practice variation. KR et al33 found a good effect on 4 shunt infection patients by intraventricular antibiotics therapy. Swayne R et al34 also reported a good result by using intraventricular antibiotics in VP shunt infection patients who had gram positive cocci in CSF culture.

The choice of antibiotics has been a very difficult problem and different doctors have different choices. Most doctors select antibiotics according to the sensitivity of the drugs, but not every VP shunt infection patient has a satisfactory result of bacteria susceptibility test. So, empiric antibiotics are very important. Due to blood brain barrier, a variety of antibiotics for curing the infection of the central nervous system are restricted. 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.[35] But Nau R et al and Yenis Gutierrez-Murgas et al[36,37] found pH gradient between the CSF and blood, drug configuration, drug solubility, protein binding ability, the extent of meningeal inflammation, metabolic and structural characteristics of biofilms which may make these infections less susceptible to antibiotic treatment. One approach to reducing shunt-related CSF infection is to use antibiotic-impregnated shunt (AIS) catheters instead of a standard shunt (SS). AIS catheters have been available for more than a decade, and contain 0.054% rifampin and 0.15% clindamycin, shown to effectively prevent colonization.[38-40]

Conclusion

This study concluded that the frequency of postoperative infection is found to be significantly lower in patients undergoing CSF shunting with versus without topical vancomycin. So, we recommend that shunting with topical vancomycin should be used routinely in patients undergoing CSF shunt procedure in order to reduce the postoperative infections.

List of Abbreviations: CSF: Cerebrospinal fluid, ICP: Intracranial pressure, VP: Ventriculoperitoneal, IV: Intravenous, AIC: Antibiotic-impregnated catheters, AIS: Antibiotic-impregnated shunt, SS: Standard shunt

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