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Efficacy of Extended Antibiotic Cover for Ventricular Drains in Preventing Infections

[1]Kavitha Raju Manjooran, [1]Princy Louis Palatty, [2]Sreehari Nirmala Ramachandran and [2]Sajesh Karunakara Menon

[1]Department of Pharmacology, Amrita School of Medicine, Amrita Institute of Medical Sciences, Amrita Vishwa Vidyapeetham, Kochi 682041, Kerala, India

[2]Department of Neurosurgery, Amrita School of Medicine, Amrita Institute of Medical Sciences, Amrita Vishwa Vidyapeetham, Kochi 682041, Kerala, India

ABSTRACT

Background and Objective: Antimicrobials are essential in preventing infections during neurosurgical interventions. The primary and secondary objectives of this study are to determine the efficacy of extended antibiotic cover for ventricular drains in preventing infections and to determine the safety profile of extended antibiotic cover for ventricular drains in preventing infections, respectively. **Materials and Methods:** This is an observational cross-sectional study conducted in a tertiary care centre in Kerala (January, 2019 to June, 2023). Patients admitted under Department of Neurosurgery undergoing external ventricular drain insertion and willing for the study are selected. They are administered intravenous ceftriaxone 2 g as extended antibiotic cover before and after procedure till the desired duration of cerebrospinal fluid drainage. Any sign of development of immediate infection is observed which is confirmed by cerebrospinal fluid culture sensitivity report and other cerebrospinal fluid parameters. The sample size obtained in this study was 33. Data was analysed using SPSS version 20.00. **Results:** The study involved 33 patients with a female preponderance (72.7%). External ventricular drain was kept for an average of 10.32±4.603 days. The cerebrospinal fluid culture and sensitivity during drain *in situ* showed no growth (87.9%) and one case of *Acinetobacter baumannii* complex (3%). The cerebrospinal fluid culture and sensitivity following drain removal showed no growth (78.8%) and one case of *Acinetobacter baumannii* complex (3%). **Conclusion:** This study showed the use of high-end beta-lactams according to the antibiotic stewardship program for their use until the drain is removed and that there is no possibility for foci of infection. The post-operative period is often uneventful in optimizing such therapeutic need-based innovation.

KEYWORDS

Ceftriaxone, neurosurgery, drainage, antimicrobial stewardship, *Acinetobacter*, cross-sectional studies

INTRODUCTION

Cerebrovascular disease constitutes 4.1% of total global disability adjusted life years and also major contributor in neurology[1]. Cerebrovascular disease includes aneurysms, stroke, vascular malformations, vertebral stenosis, intracranial stenosis etc. Incidence of subarachnoid haemorrhage in Asia in the year 2010 was 7.7 per 100 000 person-years[2]. The most common presentation is severe headache which is

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acute in onset along with nausea, vomiting, altered sensorium etc. This requires emergency management since it is associated with high morbidity and high mortality. There are various causes leading to sub arachnoid haemorrhage. Trauma accounts for the most common cause. Among the non-traumatic causes, ruptured intracranial aneurysms are the major cause. Investigations include computed tomography brain, computed tomography angiography and magnetic resonance angiography. Surgical management includes coiling, clipping, embolization, etc. One of the post-operative complications that can arise is raised intracranial pressure. External ventricular drainage is necessary to monitor and regulate cerebrospinal fluid pressure. Since, this involves an indwelling catheter for a longer period, development of cerebrospinal fluid infection can be fatal. Hence, prompt, rational use of antibiotics can aid in recovery. The antibiotic prophylaxis in neurosurgery is generally advocated to be given as a single dose of antibiotic before the procedure[3]. A study by Lucey and Myburgh[4] showed that antibiotic prophylaxis using intravenous cephalothin 1 g for 24 hrs resulted in positive cultures (45%). Extended antibiotic cover involves use of higher generation of beta-lactams for more than 48 hrs post-operatively[5].

In current study, the investigators explored the effectiveness of extended antibiotic cover more than the prescribed guidelines to offset any infection for the duration of the drain, which would otherwise carry a higher propensity for infection.

The primary objective is to determine the efficacy of extended antibiotic cover for ventricular drains in preventing infections. The secondary objective is to determine the safety profile of extended antibiotic cover for ventricular drains in preventing infections.

MATERIALS AND METHODS

This is an observational cross-sectional study conducted in a tertiary care centre in Kerala (January, 2019 to June, 2023). Patients admitted under Department of Neurosurgery undergoing external ventricular drain insertion and willing for the study are selected. They are administered intravenous ceftriaxone 2 g as extended antibiotic cover for before and after procedure till the desired duration of cerebrospinal fluid drainage. Any sign of development of immediate infection is observed which is confirmed by cerebrospinal fluid culture and sensitivity report and other cerebrospinal fluid parameters.

Sample size calculation: Based on the proportion of infection rate (11.8%) was observed in an earlier publication[6] and with 95% confidence and 20% allowable error, the minimum sample size comes to 10. Infection rate will be estimated in percentage with 95% confidence interval. Sample size obtained in this study was 33.

Inclusion criteria: Patient with

- Age >18 years
- Diagnosis of sub arachnoid haemorrhage
- External ventricular drain

Exclusion criteria: Patient with

- Bleeding or clotting disorders
- On antiplatelet or anticoagulant medications
- Already on antibiotic medication

Statistical analysis: The T-test, non-parametric test and Wilcoxon signed rank test were used. Data was analysed using SPSS version 20.00.

Ethical consideration: Institutional ethics committee approval was obtained for this study. Informed consent was obtained from all individual participants included in this study.

RESULTS

The study involved 33 patients with a female preponderance (72.7%). Duration of hospital stay is expressed in a median (Q1, Q3) of 22(16,28) days. External ventricular drain was kept for an average of 10.32±4.603 (Mean±Standard Deviation) days.

The most common comorbidity in patients with aneurysmal subarachnoid haemorrhage in this study was hypertension (57.60%), dyslipidemia (18.20%) and diabetes mellitus (15.20%).

The most common location of aneurysms in current study was anterior communicating artery (42.4%), left internal carotid artery (21.2%) and right internal carotid artery (12.1%).

The cerebrospinal fluid parameters considered in this study were cell count, glucose and protein. Table 1 represents data pertaining to cerebrospinal parameters that were analyzed with non parametric test and Wilcoxon signed rank test.

The cerebrospinal fluid culture and sensitivity during drain *in situ* showed no growth (87.9%) and one case of *Acinetobacter baumannii* complex (3%) which is shown in Fig. 1. The cerebrospinal fluid culture and sensitivity following drain removal showed no growth (78.8%) and one case of *Acinetobacter baumannii* complex (3%) which is depicted in Fig. 2.

Antibiotics given in positive growth in culture and sensitivity are given in Table 2. Follow-up cultures of these patients became negative after the administration of antibiotics as per the culture and sensitivity reports.

The Glasgow coma scale score (Mean±Standard Deviation) on admission was 14.36±1.186 and on discharge was 14.80±0.645. Analysis of Glasgow's coma scale score at admission and discharge with t-test revealed p-value of 0.126.

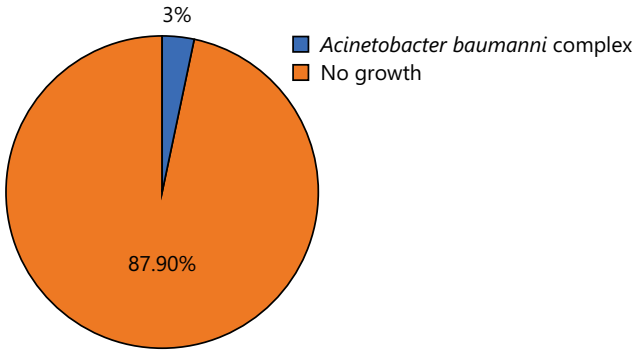

Fig. 1: Cerebrospinal fluid culture and sensitivity during drain *in situ*

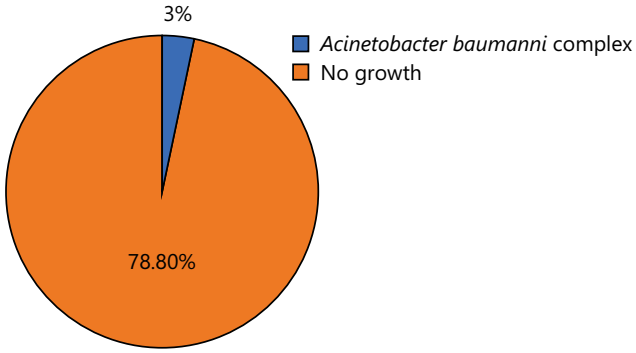

Fig. 2: Cerebrospinal fluid culture and sensitivity after drain removal

Table 1: Analysis of cerebrospinal fluid parameters

Cerebrospinal fluid parameters	Percentiles 25th	50th (Median)	75th	p-value (significant) Wilcoxon signed rank test
Cell count during drain *in situ* (cells/mm^3)	16.00	55.00	177.00	0.959
Cell count after drain removal (cells/mm^3)	5.50	13.50	42.50	
Glucose during drain *in situ* (mg/dL)	53.00	60.20	71.65	0.028
Glucose after drain removal (milligram/dL)	56.90	69.20	79.20	
Protein during drain *in situ* (mg/dL)	27.82	60.55	99.82	0.114
Protein after drain removal (mg/dL)	20.30	22.20	38.50	

Table 2: Antibiotics given for positive growth in cerebrospinal fluid culture

Cerebrospinal fluid culture and sensitivity during drain *in situ*	*Acinetobacter baumannii* complex **Antibiotics given:** • Intravenous Meropenem • Intrathecal Amikacin
Cerebrospinal fluid culture and sensitivity after drain removal	*Acinetobacter baumannii* complex **Antibiotics given:** • Intravenous Ceftriaxone • Oral Sulphamethoxazole-Trimethoprim

DISCUSSION

This study explored the effect of extended antibiotic cover, the following parameters were noted. In this study, the average age of patients reporting aneurysmal sub arachnoid haemorrhage was 58.85±12.792 years. Another study found the median age to be 22.5 years[7]. A study by Harrison *et al.*[8] found the average age when subarachnoid haemorrhage developed to be 56.8±16.8 years. It was noticed here that 72.7% were females and 27.3% were males, unlike, the study by Mehreen *et al.*[7] where females were 51% and males were 49%. The most common comorbidity in this study was hypertension (57.6%), dyslipidaemia (18.2%) and diabetes mellitus (15.2%), while, another study showed the commonest comorbidity to be seizures (28%), diabetes (24%), ventricular septal defect (4%) and remaining patients did not have any (44%)[7]. Hypertension (57.2%) followed by diabetes (6.4%) were the most common comorbidity in a study by Cai *et al.*[9]. The total duration of hospital stay was a median of 22 days. Mehreen *et al.*[7] found the median hospital stay to be 20 days in patients who developed infections. Length of hospital stay in patients with aneurysmal subarachnoid haemorrhage and external ventricular drain was more than 14 days (41.88%) in a study by Prasetyo *et al.*[10]. The drain remained in situ for a mean of 10.32±4.603 days in this study. Average number of days of external ventricular drain *in situ* was 7.3±2.2 days in another study[11]. Duration of external ventricular drain was a median of 7 days in a study by Hagel *et al.*[12]. The most common location of aneurysm in current study was anterior communicating artery (42.4%), left internal carotid artery (21.2%) followed by right internal carotid artery (12.1%). A study by Bhogal *et al.*[13] found middle cerebral artery (33%) and anterior cerebral artery and branches (32%) to be the most common origin of ruptured intracranial aneurysm followed by posterior communicating artery (24%). Göttsche *et al.*[14] found the most common location to be anterior complex (40.1%) followed by internal carotid artery (23.9%).

The median cerebrospinal fluid cell count was 55 cells/mm^3 with drain *in situ*. The median cerebrospinal fluid cell count after drain removal was 13.5 cells/mm^3. You *et al.*[15] was at the median of 100 cells/mm^3. The current study found that the median cerebrospinal fluid glucose was 60.2 mg/dL with drain *in situ* and it was 69.2 mg/dL after drain removal. The cerebrospinal fluid glucose was at the median of 59.4 mg/dL in another retrospective study conducted in patients with spontaneous sub arachnoid haemorrhage[15]. The average cerebrospinal fluid glucose level at admission was 86.8 mg/dL in another study by Ghosh *et al.*[16] in patients with aneurysmal subarachnoid haemorrhage. In this study, the median cerebrospinal fluid protein was 60.5 mg/dL with drain *in situ*, while it was 22.2 mg/dL after drain removal. The cerebrospinal fluid protein concentration was at the median of mg/dL in another study[15]. The average cerebrospinal fluid protein level at admission was 88.6 mg/dL in another study by Ghosh *et al.*[16] in patients with aneurysmal subarachnoid haemorrhage.

Positive cultures were of *Acinetobacter baumanni* complex in this study during drain *in situ* (n = 1, 3%) as well as after drain removal (n = 1, 3%). The follow-up culture and sensitivity became negative after administration of antibiotics based on sensitivity report. The common microbes isolated by Mehreen *et al.*[7] were *Klebsiella pneumoniae* (n = 3), *Pseudomonas aeruginosa* (n = 2) and *Acinetobacter baumannii* (n = 2). Antibiotic prophylaxis used was intravenous cefoperazone-sulbactam 1.5 g twice and intravenous amikacin 750 mg twice for pre-procedure and continued for 3 weeks post-procedure in their study[7]. Intravenous ceftriaxone 2 g was used in current study as an extended antibiotic cover. Although this study examined cerebrospinal fluid culture and sensitivity during drain *in situ* and after drain removal, the other study did not. Another study by Walti *et al.*[17] found coagulase-negative *Staphylococci* (63%) and *Propionibacterium acnes* (15%) to be most common sources of external ventricular drain-related infection.

Glasgow coma scale score during admission and discharge in this study was 14.36±1.186 and 14.8±0.645, respectively. Glasgow coma scale score in patients with aneurysmal sub arachnoid haemorrhage was 12.1±3.7 on admission in another study by Bae *et al.*[18]. A study by Kulkarni *et al.*[19] found the Glasgow coma score of 15 at discharge (96.3%). A *post hoc* analysis study by Lee *et al.*[20] found the mean extended Glasgow outcome scale in patients who required intracranial pressure monitoring to be 2.73±2.62.

The nature of cerebrospinal fluid samples studied was clear. No adverse drug reactions were noted for the antibiotics received by the patients in current study. The discharge period of patients was uneventful with no clinical features of any central nervous system infection. The present guidelines advocate the schedule of giving antibiotics as a single dose not exceeding 24 hrs. This study shows that for the complete resolution of a probable infection, it is preferable to have a higher generation beta-lactam for the duration of the drain *in situ* (or until the drain is removed). Risking CSF contamination is never an alternative and it would be unethical. The study was done in the absence of a comparator. This could be a possible limitation of the study. Ethical issues may arise considering the emergency nature of intervention. The recommendation from this study is to provide high-end antibiotics for the duration of the drain *in situ*.

CONCLUSION

The extended antibiotic coverage has improved the outcome in terms of low infection in cases with long-term indwelling intraventricular catheter drainage. The antibiotics used have been well tolerated without any safety concerns. The guidelines need to adopt this pertinent use of antibiotics in external ventricular drains for an extended period from a single dose before procedure to more than 48 hrs postoperatively till the desired duration of cerebrospinal fluid drainage specific to each case. Ceftriaxone has proved to be effective and safe with the advantage of being cost-effective. The probability of developing infection despite extended cover is very minimal as observed in this study. Cautious use of antibiotics for a minimalistic term would not justify the risk of infection. This study showed the use of high-end beta-lactams according to the antibiotic stewardship program for their use until the drain is removed and that there is no possibility for foci of infection. The post-operative period is often uneventful in optimizing such therapeutic need-based innovation.

SIGNIFICANCE STATEMENT

External ventricular drainage is necessary to monitor and regulate cerebrospinal fluid pressure in aneurysmal subarachnoid haemorrhage and has an indwelling catheter. The antibiotic prophylaxis in neurosurgery is generally advocated to be given as a single dose of antibiotic before the procedure. Extended antibiotic cover involves use of a higher generation of beta-lactams for more than 48 hrs post-operatively. The investigators explored the effectiveness of extended antibiotic cover more than the prescribed guidelines to offset any infection for the duration of the drain, which would otherwise carry a higher propensity for infection. The extended antibiotic coverage has improved the outcome in terms of low infection in cases with long-term indwelling intraventricular catheter drainage and has been well tolerated without any safety concerns.

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