Prospective Comparative Trial of Ceftriaxone versus Ceftazidime as Prophylactic Perioperative Antimicrobials in Neurosurgery

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Background: Previous reports have suggested that both ceftriaxone and ceftazidime are effective as prophylactic perioperative antibiotics in neurosurgery. This study was designed to compare the infection rates following the use of these antibiotics as prophylactic agents during neurological surgery in our centre. In a tertiary hospital
Methods: This was a prospective study in which patients were allocated into two groups. One group received ceftriaxone (Roche-rocephine) and the other group received ceftazidime (GlaxoSmithKline – fortum). Patients were followed up for evidence of surgical site infections for up to 6 weeks after discharge. Clinical and or laboratory evidence of wound infection were used as outcome measure.
Results: There were 118 patients, 58 patients received ceftriaxone and 60 patients received ceftazidime. Infection occurred in 4 (6.9%) in the ceftriaxone group and in 9 (15%) in the ceftazidime group. The difference was not statistically significant. The infection rate following ventriculoperitoneal (VP) shunting procedure was similar (11.8%) in both groups.
Conclusion: Our study confirmed the efficacy of ceftriaxone and ceftazidime in preventing surgical site infection that may follow neurosurgical procedures, but the difference in infection rates following the use of their use was not statistically significant.

Introduction

Ceftriaxone and ceftazidime are both potent antibiotics belonging to the third generation of cephalosporins. They have broad spectrum activities against gram-positive and gram-negative microbes. Although the choice of prophylactic antibiotics for neurosurgical procedures is not fully established as several regimen have been used[1-6], the morbidity and mortality that often accompanies postoperative intracranial infections have compelled us to consider these antimicrobials as prophylactic antibiotics in our centre. In addition, we have observed higher infection rate in other previously used antimicrobial agents. Previous reports have also demonstrated the use of these agents in neurosurgical operations[7-10]. In this study we compared the infection rates in our patients who received either ceftriaxone or ceftazidime as prophylactic perioperative antibiotics.

Patients and Method

This prospective study was carried out between September 1998 and December 1999. Consecutive patients were allotted into two groups; Group I received intravenous ceftriaxone (Roche - Rocephine) 100mg/kg daily for two days while Group II received intravenous ceftazidime (GlaxoSmithKline – fortum) 50mg/kg every twelve hours for two days. The first dose of antibiotics was given at induction of anaesthesia. We also used irrigation fluid containing 40mg of Gentamycin in 500 ml of normal saline in all the patients. Patients who had evidence of intracranial or scalp infection and those on antibiotics before surgery, were excluded from the study.

Clinical and/or laboratory evidence of wound infection or intracranial infection was used as outcome measures. The patients were followed up in the ward and in the clinic for six weeks. We analyzed the presence or absence of wound infection, demographic data, diagnosis and type of surgical procedure. The statistical significance of the difference in infection rates in the two groups was determined by Chi-square. The p-value less 0.05 or less was considered as significant.

Results

There were a total of one hundred and eighteen patients. Fifty eight patients received ceftriaxone and sixty patients received ceftazidime. The age range was 1 month to 94 years with a mean age of 24.86.

Table 1. List of operations

Procedure	Frequency	%	Valid %	Cumulative %
VP Shunt	34	28.8	28.8	28.8
Repair of Encephalocoele	1	0.8	0.8	29.7
Craniotomy & Excision of Tumour	12	10.2	10.2	39.8
Suboccipital Craniectomy &Tumour Excision	6	5.1	5.1	44.9
Cranioplasty	2	1.7	1.7	46.6
Craniotomy & Lobectomy	3	2.5	2.5	49.2
Craniotomy & Clot Evacuation	3	2.5	2.5	51.7
Wound Debridement & Elevation of Fracture	12	10.2	10.2	61.9
Craniotomy & Clipping Of Aneurysm	1	0.8	0.8	62.7
Burr Hole &Drainage Of Haematoma	22	18.6	18.6	81.4
Craniotomy& Drainage Of Abscess	2	1.7	1.7	83.1
Laminectomy	5	4.2	4.2	87.3
Repair Of Myelomeningocele	10	8.5	8.5	95.8
Laminectomy & Excision Of Tumor	5	4.2	4.2	100.0
Total	**118**	**100.0**	**100.0**	

Table 2. Outcome in Patients Who Had Ceftriaxone as Prophylactic Antimicrobial

Type of Operations	Patients with Postoperative Infections	Patients without Postoperative Infections	Total
VP Shunt	2	15	17
Repair Of Encephalocele		1	1
Craniotomy & Excision Of Tumor		2	2
Wound Debridement And Elevation Of Fracture		6	6
Craniotomy&Clipping Of Aneurysm		1	1
Burr Hole & Drainage Of Haematoma		1	1
Laminectomy	1	4	5
Repair Of Myelomeningocele	1	8	9
Laminectomy & Excision Of Tumor		3	3
Total	**4**	**54**	**58**

Table 1 shows the various procedures performed during the study period. Ventriculoperitoneal (VP) shunt for hydrocephalus was the most common procedure performed with a frequency of 38 (28.8%). Only 1 patient had craniotomy and clipping of aneurysm. Table 2 shows procedures in which ceftriaxone were used in the irrigation fluid. VP shunt for hydrocephalus was the most common procedure followed by burr hole drainage of subacute and chronic subdural haematoma. Infection occurred in four procedures in this group. Two out of these were in the patients who had VP shunt. The overall infection rate was 6.9%. The infection rate in VP shunt procedures was 11.8%.

Table 3 shows the procedure in which ceftazidime was used. The pattern is similar to table 2 with VP shunt for hydrocephalus being the most common procedure followed by burr hole drainage of subacute and chronic subdural haematoma. Nine patients had infection with infection rate of 15%. Two of the 17 patients who had VP shunts had infection as in the ceftazidime group. The infection rate in VP shunt procedure was similar to the infection rate in ceftriaxone group.

Table 3. Outcome in Patients Who Had Ceftaziime as Prophylactic Antimicrobial

Type Of Operation	Patients With Postoperative Infections	Patients Without Postoperative Infection	Total
VP Shunt	2	15	17
Craniotomy And Excision of Tumor	3	7	10
Suboccipital Craniectomy And Tumour Excision	2	4	6
CRANIOPLASTY		2	2
Craniotomy and Lobectomy		3	3
Craniotomy and Clot Evacuation		1	1
Wound Debridement & Elevation of Fracture	1	5	6
Burr Hole &Drainage of Haematoma		11	11
Craniotomy& Drainage of Abscess		1	1
Repair Of Myelomeningocele	1		1
Laminectomy & Excision of Tumor		2	2
Total	**9**	**51**	**60**

Table 4. Relationship between Patients with and Without Postoperative Infections in the Two Groups.

Group	Number of patients with infection	Number of patients without infections	Total number of Patients
Ceftriaxone group	4	54	58
Ceftazidime group	9	51	60
Total	**13**	**105**	**118**

$X^2 = 1.975$, df 1; p=0.160

There were 9 patients with infection in ceftazidime group compared to 4 patients in the ceftriaxone group but this was not found to be statistically significant (Table 4).

Discussion

The study was carried out in a wide range of neurosurgical procedures. The infection rates are quite high compare to infection rate reported from other parts of the world[1,2,4,5,6,11,12]. This may be related to many factors including poor patients' personal hygiene and inadequate sterilization of the instruments, theatre gown and drapes due to imperfect sterilization techniques. These are peculiar problems of the developing world. Improvement of these various factors will certainly help to improve the infection rate in our neurosurgical procedures. Surprisingly, the infection rate following our VP shunt procedure is comparable to reports from other parts of the world[13]. This may be related to the short duration of follow up in our series or perhaps because of the greater attention to meticulous aseptic techniques during VP shunt procedure.

The overall infection rate was higher in ceftazidime group (15%) compared to ceftriaxone group (6.9%). This difference was, however, not statistically significantly. Furthermore, the infection rate in VP shunt procedure was the same in both groups with a value of 11.8%. This result is not surprising because both drugs are third generation cephalosporin with similar mechanisms of action. Their spectrum of activity is also fairly the same. In addition, the two antimicrobials have been found to be effective as prophylactic agents in neurosurgical procedures[1, 3, 7-11, 14-16]

The total cost for our regime for ceftriaxone is ₦7800 or 54 USD and ₦11500 or 82 USD for ceftazidime. If the inconvenience of double dosing, the cost of injection materials and nursing time is added to the cost, ceftazidime will be more expensive than ceftriaxone. This will suggest that ceftriaxone will be a better choice of antibiotic as prophylactic agent in our environment. During the

course of the study, we discovered that there were about eight brands of ceftriaxone in the drug market in Nigeria. The efficacy of these is difficult to ascertain using the present study because we restricted the brand used to Roche rocephin. Our study confirmed the use of ceftriaxone and ceftazidime in preventing surgical site infection in neurosurgical procedures. There was no statistical significance in the different infection rates for both antibiotics. The infection rates were similar for both antibiotics following VP shunt insertion.

References

1. Zhao JZ, Wang S, Li JS, Yang J, Zang JT, He Q, Shao LL, Dai ZX, Chao HY, Lau KC, et al. The perioperative use of ceftriaxone as infection prophylaxis in neurosurgery. Clin Neurol Neurosurg. 1995; 97(4):285-9.
2. Whitby M, Johnson BC, Atkinson RL, Stuart G. The comparative efficacy of intravenous cefotaxime and trimethoprim/sulfamethoxazole in preventing infection after neurosurgery: a prospective, randomized study. Brisbane Neurosurgical Infection Group. Br J Neurosurg. 2000; 14(1):13-8.
3. Warnke JP, Wildfeuer A, Eibel G, Pfaff G, Klammer A. Pharmacokinetics of ampicillin/sulbactam in patients undergoing spinal microneurosurgical procedures. Int J Clin Pharmacol Ther. 1998;36(5):253-7.
4. Holloway KL, Smith KW, Wilberger JE Jr, Jemsek JG, Giguere GC, Collins JJ. Antibiotic prophylaxis during clean neurosurgery: a large, multicenter study using cefuroxime. Clin Ther. 996; 18 (1):84-94.
5. Yamamoto M, Jimbo M, Ide M, Tanaka N, Umebara Y, Hagiwara S. Postoperative neurosurgical infection and antibiotic prophylaxis. Neurol Med Chir (Tokyo). 1992; 32 (2):72-9. 6 Gaillard T, Gilsbach JM. Intra-operative antibiotic prophylaxis in neurosurgery. A prospective, randomized, controlled study on cefotiam. Acta Neurochir (Wien). 1991; 113 (3-4):103-9.
6. Cacciola F, Cioffi F, Anichini P, Di Lorenzo N. Antibiotic prophylaxis in clean neurosurgery. J Chemother. 2001; 13(1):119-22.
7. Nau R, Prange HW, Kinzig M, Frank A, Dressel A, Scholz P, Kolenda H, Sorgel F. Cerebrospinal fluid ceftazidime kinetics in patients with external ventriculostomies. Antimicrob Agents Chemother. 1996 ;40(3):763-6
8. Kraus DH, Gonen M, Mener D, Brown AE, Bilsky MH, Shah JP. A standardized regimen of antibiotics prevents infectious complications in skull base surgery. Laryngoscope. 2005; 115(8):1347-57.
9. Cacciola F, Cioffi F, Anichini P, Di Lorenzo N. Antibiotic prophylaxis in clean neurosurgery. J Chemother. 2001; 13 1(1):119-22.
10. Zhu XL, Wong WK, Yeung WM, Mo P, Tsang CS, Pang KH, Po YC, Aung TH. A randomized, double-blind comparison of ampicillin/sulbactam and ceftriaxone in the prevention of surgical-site infections after neurosurgery. Clin Ther. 2001;23(8):1281-91.
11. Mastronardi L, Tatta C. Intraoperative antibiotic prophylaxis in clean spinal surgery: a retrospective analysis in a consecutive series of 973 cases. Surg Neurol. 2004;61(2):129-35
12. Sciubba DM, Stuart RM, McGirt MJ, Woodworth GF, Samdani A, Carson B, Jallo GI. Effect of antibiotic-impregnated shunt catheters in decreasing the incidence of shunt infection in the treatment of hydrocephalus. J Neurosurg. 2005; 103:131-6.
13. Eftekhar B, Ghodsi M, Nejat F, Ketabchi E, Esmaeeli B. Prophylactic administration of ceftriaxone for the prevention of meningitis after traumatic pneumocephalus: results of a clinical trial. J Neurosurg. 2004 ;101(5):757-61
14. Winkler D, Rehn H, Freckmann N, Nowak G, Herrmann HD. Clinical efficacy of perioperative antimicrobial prophylaxis in neurosurgery--a prospective randomized study involving 159 patients. Chemotherapy. 1989; 35(4):304-12.
15. Arnaboldi L. Antimicrobial prophylaxis with ceftriaxone in neurosurgical procedures. A prospective study of 100 patients undergoing shunt operations. Chemotherapy. 1996; 42(5):384-90.