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MONOTHERAPY VERSUS COMBINATION IN TREATMENT OF FEBRILE NEUTROPENIA

Pediatrics

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ABSTRACT

Introduction: Childhood cancers are associated with several complications either disease or treatment related.Febrile neutropenia is one of them and is associated with significant mortality and morbidity. The outcome of cancers. may be changed due to dose reduction, delays in chemotherapy which occur as a result of FN.

Objective: To assess the efficacy of mono versus combination therapy in management of FN in childhood cancer patients being treated at a tertiary care hospital.

Materials and methods: Randomized control trial using random number table. All children diagnosed with malignancy and receiving treatment at Goa medical college and presenting with febrile neutropenia over a period of twelve months were enrolled.Endpoint was taken as patient becoming afebrile for more than 24 hours.Stastistical analysis was performed using SPSS and significance was set at p value of < 0.05 for the group of antibiotics used.

Results and conclusions: Monotherapy with Ceftazidime was found to have higher success rate as compared to combination therapy with cefotaxim plus amikacin. However it was not statistically significant.

KEYWORDS

Febrile Neutropenia;absolute Neutrophil Count,malignancy

Materials and methods:

Study location: Department of Pediatrics, Goa Medical College, Bambolim

Study design: Prospective Randomised control trial

Study duration: Period of 12 months from July 2011 to July 2012

Patients with febrile neutropenia were randomly allotted into two groups by simple randomisation technique by table of Random numbers into A) cefotaxim + amikacin and B) ceftazidime monotherapy Following blood investigations were sent before starting the antibiotics: Complete Blood Count(CBC) , Blood Culture/ Sensitivity (Bld C/s) , urine Routine/Microscopy (UrineR/M), urine culture/Sensitivity (UrineC/S). Depending upon the nature of symptoms specific tests were carried out like chest X-ray, Abdominal Ultrasonography (USG), Stool routine microscopy or culture sensitivity (optional tests)

Depending upon the group to which the patient was randomised to, antibiotics were started in the following doses.

Cefotaxim- 150mg/kg/day divided TDS as infusion
Amikacin – 15mg/kg/day divided TDS as an infusion
Ceftazidime – 150mg/kg/day divided TDS as an infusion

In both the above groups G-CSF was given in a dose of 5microgram/kg subcutaneously and continued until ANC was >1000. Paracetamol was given orally in a dose of 15mg/kg/dose if Fever >100degree F. and active chemotherapy was withheld. After 48 hrs of initiation of antibiotics laboratory investigation were repeated i.e. complete blood count and blood c/s as well as urine r/m and urine c/s. Patients were evaluated for subjective, objective and laboratory criteria for outcome of treatment.

End points of the study were:

A) Fever subsided and ANC>1000- success- continue same group of antibiotics
B) Fever subsided and ANC< 1000- success- continue same group of antibiotics and continue G-CSF
C) Fever did not subside and ANC<1000- failure- change group of antibiotics to 2nd line (Vancomycin plus Amikacin
D) Fever did not subside but ANC>1000- failure- change group of antibiotics to 2nd line.(Vancomycin plus amikacin)

Statistical methods;

Statistical analysis was performed using SPSS software. Chi square tests were used to measure the degree of association between the variables. Statistical significance was set at a p value of <0.05 for the group of antibiotics used.

When comparing two groups of antibiotics Ceftazidime had a success rate of 62% wherein 15 out of 24 cases were successfully treated and a failure rate of 37% wherein 9 out of 24 cases required the initiation of 2nd line treatment. On the other hand combination therapy of cefotaxim+amikacin had a success rate of 46% i.e 12 out of 26 cases were successfully treated 14 out of 26 cases had to be treated with 2nd line antibiotics with a failure rate of 56% (p value 0.085 which was not significant). Similarly comparison of antibiotics was also done in 2 different phases of chemotherapy treatment wherein In the intensive phase ceftazidime had success rate of 75% with 6 out of 8 cases showed improvement while in the maintenance phase it has increased to 87% 14 out of 16 cases responded to the monotherapy treatment. On the other hand combination of cefotaxim+amikacin had a success Rate of 60% (9 out of 15 cases) responded to the combination therapy in the intensive phase and 90% in the maintenance phase.(10 out of 11 cases) (p value of 0.085).

Table1: Comparison Of Success Rates In The Two Groups

	Ceftazidime	Cefotaxim+amikacin
Success	15(62%)	12(46%)
Failure	9(38%)	14(53%)

Table2: Comparison Of Success Rates In Different Phases Of Treatment

	Intensive		Maintenance	
	Success	Failure	Success	Failure
CEFTAZIDIME	6	2	14	2
CEFOTAXIM + AMIKACIN	9	6	10	1

Discussion:

While comparing two groups of antibiotics our study found that ceftazidime had a higher success rate as compared to cefotaxim plus amikacin combination however it was not statistically significant.

According to a study conducted by Pizzo et al, NEJM, 1986, RCT comparing ceftazidime monotherapy with combination of cephalothin and Gentamicin and carbenicillin, they found similar results where monotherapy was as good as combination therapy.

In our study we also studied duration of neutropenia and the use of G-CSF in treatment of neutropenia. Mean duration was found to be 4.72 days for the treatment of neutropenia. It decreased the number of days of receiving antibiotics shortened the duration of neutropenia. Simiilarly In a study conducted by Janice L. Gabrilove et al, N Engl J Med 1988, use of G-CSF significantly reduced the no of days of neutropenia and use of antibiotics.

The major drawback of our study was the small sample size and the short duration of the study. Also it was carried out at a single centre which may alter the results of the study.

CONCLUSION

This study shows no significant difference in therapeutic efficacy between the two groups i.e. ceftazidime monotherapy and combination of cefotaxim+amikacin. The cost of treatment was significantly less for ceftazidime monotherapy as compared to combination therapy. No significant life threatening complications were noted in any of the groups. Success rate of ceftazidime was higher but not statistically significant.

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