SPECTRUM OF MICROBIAL ISOLATES FROM BLOOD CULTURE IN FEBRILE NEUTROPENIA

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Summary

Infection remains an important cause of morbidity and mortality in neutropenic hosts after chemotherapy or due to bone marrow failure. In the face of worldwide changes in the incidence and spectrum of bacteraemia, we evaluated 47 febrile neutropenic patients in the haematology department of BSMMU during the period of October 2009 to October 2010. The overall rate of blood culture positivity was 17% (8/47) which is similar to most of the recent study in the western world, but the bacterial spectrum is different from that in developed world [1,2,3,4].

Key words

Febrile neutropenia; bacteraemia; blood culture

Introduction

Blood stream infection is the most commonly documented infection and one of the most serious complications in patients with haematological malignancies and profound neutropenia undergoing chemotherapy and stem cell transplantation [5]. The high mortality resulting from neutropenic fever is partly related to microorganisms which are resistant to broad-spectrum antibiotics and are emerging in many centres [6]. It is a common practice in Bangladesh to initiate a prophylactic antibiotic in most of the neutropenic patients or who likely to develop neutropenia after initiation of chemotherapy; but no established local guideline or recommendation is available here for such use of antibiotic.

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Sometimes, the empiric use of antibiotic may have some unfavorable consequences of excessive treatment, such as insufficient microbiological diagnosis, more adverse drug reactions, and emergence of bacterial resistance. It is sometimes possible to identify the cause(s) of fever and thus avoiding unnecessary antibiotic [7]. Studies performed in the 1970s documented a 20–60% incidence of bacteraemia in the febrile neutropenic host, but it sharply decreased in the recent years [1]. To explore this issue, the results of blood cultures obtained from patients with neutropenic fever are being reevaluated in different countries. Therefore, it is rational to evaluate the incidence of positive blood cultures and the microbial spectrum to determine the cause of neutropenic sepsis which in turn will lead to evaluate the rationality of use of empiric antibiotic therapy, and thus will help to develop a local guideline for the use of empiric antibiotic therapy in febrile neutropenia.

Materials and methods

This study was done between October 2009 and October 2010 in the Department of Haematology in the Bangabandhu Sheikh Mujib Medical University (BSMMU) Hospital. This was a cross sectional observational study based on naturally occurring infections in the neutropenic patients and was done after having permission by the institutional ethical committee. Non random convenience sampling technique was used. Forty seven (47) patients voluntarily participated in this study. Patients who had (1) absolute neutrophil count <1000/mm^3 and (2) fever defined as an oral temperature of 38˚C or more maintained for one hour, or 38.3˚C on one occasion with or without on antibiotic were eligible for the study. Patients were excluded who did not give consent or did not have adequate medical records. Venous blood was collected from each patient for culture at the time of inclusion in the study but follow-up culture was not done. One, two or three samples of 10 ml blood each were taken from each patient depending upon their level of consent. The first and second samples were collected from the existing indwelling vascular device and used for aerobic and anaerobic culture respectively. The third sample was collected at the same time by direct phlebotomy from a different anatomical site for a second aerobic culture.

Thus, 40 patients were tested with 2 samples and 7 patients were tested with 1 sample for aerobic culture. Anaerobic cultures were done in 39 cases with single sample for each and not done in 8 cases. BacT/Alert FAN culture media were used for both aerobic and anaerobic conditions. The microbiological methods including species identification were done by the microbiologist in the department of microbiology of the National Medical College, Dhaka. Relevent data were recorded in standard questionare. The association of the occurrence of bacteraemia with their spectrum with the diseases and neutropenic severity were analyzed using the α^2 test with a two-tailed analysis. All statistical analyses were performed with use of SPSS software, version 12.0 for Windows (SPSS). *P* values less than or equal to 0.05 were considered significant.

Results

The mean age of the patients was 34.6 years (range 14 to 65 years); 68.1% (32/47) patients were male and 31.9% (15/47) were female. Underlying diseases were acute myeloid leukaemia in 68.1% (32/47) patients, acute lymphoblastic leukaemia in 17.0% (8/47) patients, aplastic anemia in 12.8% (6/47) patients, and non-Hodgkin's lymphoma in 2.1% (1/47) patient. (Table I)

17.0% (8/47) patients yielded positive aerobic cultures results and none yielded strict anaerobes. 87.5% (7/8) of the positive results were seen in patients with acute myeloid leukaemia, 12.5% (1/8) in patient with acute lymphoblastic leukaemia and none in patients with aplastic anemia or non-Hodgkin's lymphoma. It shows no relationship between disease and the rate of blood culture positivity (p=0.555). (Table II)

All of the patients with positive blood cultures were observed to have very severe neutropenia i.e. 0.2 X 10^9/L (p=0.014). (Table III)

There was no significant increase in the culture growth when two samples were taken compared to when one sample (p=0.378); the *Staph. aureus* was seen in one of the two aerobic samples. (Table IV)

The most common pathogen was *E. coli* seen in 50% (4/8) patients. *Staph. aureus, Pseudomonas*, *Candida* and *Stenotrophomonas maltophilia* were equally found as 12.5% (1/8). The *Candia* was found in one patient with acute lymphoblastic leukaemia and the other 87.5% (7/8) isolates were found in cases of acute myeloid leukaemia (p=0.092). (Table V)

Table I : Particulars of the patients

Total number of patients		47 (100)
Age	Mean	34.6 years
	Range	14 to 65 years
Sex	Male	32 (68.1)
	Female	15 (31.9)
	M:F	2.13
Diseases	Acute myeloid leukemia	32 (68.1)
	Acute lymphoblastic leukemia	8 (17.0)
	Aplastic anemia	6 (12.8)
	Non-Hodgkin's lymphoma	1 (2.1)

Figures in the parentheses indicate percentage

Table II : Culture Result according to Disease *(p=0.555)*

Name of the Diseases	No Growth	Growth	Total
Acute Myeloid Leukaemia	25 (78.1)	7 (21.9)	32 (100.0)
Acute Lymphoblastic Leukaemia	7 (87.5)	1 (12.5)	8 (100.0)
Aplastic Anemia	6 (100.0)	0 (0)	6 (100.0)
Non-Hodgkin's Lymphoma	1 (100.0)	0 (0)	1 (100.0)
Total	39 (83.0)	8 (17.0)	47 (100.0)

Figures in the parentheses indicate percentage

Table III : Absolute Neutrophil Count During Blood Culture *(p=0.014)*

Absolute Neutrophil Count	No Growth	Growth	Total
0-200/Cumm	17 (68.0)	8 (32.0)	25 (100.0)
201-500/Cumm	10 (100.00	0 (0.0)	10 (100.0)
501-1000	12 (100.0)	0 (0.0)	12 (100.0)
Total	39 (83.0)	8 (17.0)	47 (100.0)

Figures in the parentheses indicate percentage

Table IV : Relation between Number of Culture and Growth *(P=0.378)*

	No Growth	Growth	Total
Single Sample	5 (71.4)	2 (28.6)	7 (100.0)
Two Samples	34 (85.0)	6 (15.0)	40 (100.0)
Total	39 (83.0)	8 (17.0)	47 (100.0)

Figures in the parentheses indicate percentage

Table V : Spectrum of microbial isolates (n=8)

Organisms	Number
E. coli	4 (50)
Staph. Aureus	1 (12.5)
Pseudomonas	1 (12.5)
Stenotrophomonas maltophilia	1 (12.5)
Candida	1 (12.5)
Total	8 (100)

Figures in the parentheses indicate percentage

Discussion

The overall rate of growth in blood cultures in 47 febrile neutropenic patients in our study was 17.0% (8/47). It was 11-38% in the several studies of SCOPE project, 12% (303/2520) in the study by Margit Hummel, 11% (16/145) in the study by JS Serody et al and 19% (29/153) in the study by Esa Rintala [1,2,3,4]. Therefore, the rate of positive blood culture in the neutropenic host is still highly variable and the result of our study is not different from the recently published above studies. All of the positive blood culture results were observed in patients with very severe neutropenia i.e. <0.2 X 10^9/L (p=0.014). This result coincides with the study by Bodey GP et al [8]. The mean durations of neutropenia were not analyzed due to lack of logistic support. The most common pathogens in our study were *Escherichia coli* accounting for a prevalence of 50% (4/8). Other pathogens were found equally in 12.5% (1/8) of patients. No strict anaerobes were found. This spectrum is quite different from the developed world where the incidence of blood stream infection by gram positive organisms, particularly coagulase negative Staphylococcus, is gradually increasing up to 76% of all blood stream infections in 2000 seen under SCOPE project [1,2,3,4]. A number of factors may have contributed to this changing pattern. These are :

(1) widespread empiric antibiotic therapy especially fluoroquinolones and third/fourth generation cephalosporins resulting in selection pressure for gram-positive bacteria;

(2) the use of more intensive chemotherapy with more severe oral mucositis causing a frequent portal of entry for gram-positive organisms;

(3) increased use of long-term venous access devices; and,

(4) local infection control practices impacting upon the number of infections and spectrum of causative organisms [9].

The explanation regarding result of this study is limited by smaller scale study. However, less use of quinolone prophylaxis or central venous catheter and strong dictation to the patients about their personal hygiene including daily soap bath to reduce the bacterial load particularly skin commensal may explain such less prevalence of gram positive bacteraemia. The risk factors for the occurrence of bacteraemia during neutropenic fever need larger study with adequate logistic support.

Conclusion and recommendation

The epidemiological data obtained in this study shows the frequency of pathogens is still different from that in the developed world where a shift from Gram-negative to Gram-positive organisms is seen in the recent years [2]. This confirms that blood culture is still useful in the management of febrile neutropenia, particularly in the selected cases. Smaller scale study, lack of data about daily blood culture and actual duration of neutropenia, lack of a standard for use of empiric antibiotic and G-CSF etc. were the limitations of the study. In the face of the geographical difference, the changing spectrum with emerging multidrug-resistant organisms and the increasingly difficult use of antibiotic in these highly compromised patients, larger prospective studies are needed as a continuous process to see the local bacterial spectrum with their antimicrobial sensitivity; thereby, we can make a local guideline for the use of empiric antibiotic in the febrile neutropenic patients.

Disclosure

All the authors declared no competing interest.

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