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Antimicrobial susceptibility patterns and risk factors profile of patients with septicaemic meliodosis: Single centre experience over a period of five years

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Abstract

Aims and Objective: In this paper, we review the antimicrobial susceptibility patterns and risk factors in patients with septicaemic meliodosis, seen over a period of five years - from 2010 to 2014. *Material and methods:* We have collected all blood culture of *B. pseudomallei* positive patients, between the periods January 2010 to December 2014 for the study. Identification of *B. pseudomalleifrom* positive blood cultures was done by cultural characteristics where all isolates were serologically confirmed using polyclonal antiserum raised in rabbits. Antimicrobial susceptibility testing was done using standardized protocols. Geometric mean MIC for each antibiotic for each year was calculated and reported. *Results:* A total of 54 patients were found to have *B. pseudomallei* septicaemia during the study period, 8 in 2010, 14 in 2011, 14 in 2012, 11 in 2013 and 7 in 2014. Of them, 47 (87%) were males, while the rest 7 (13%) were females. Ages of the patients ranged from 0 to 67 years (mean - 43.22±14.778).The organism was largely susceptible to ceftazidime, doxycycline, trimethoprim-sulfamethoxazole and carbapenems. We found only a single isolate of *B. pseudomallei* which showed resistance to meropenem and doxycycline. *Conclusion:* The study results re-assured that the organism is largely susceptible to routinely used antibiotics. The collation of MIC data over 5 years in the tertiary care institution was unable to reveal an evident MIC trend for ceftazidime, doxycycline, trimethoprim-sulfamethoxazole and carbapenems.

Keywords: Septicaemic Meliodosis; *B. Pseudomallei*; Antibiotic Sensitivity; Risk Factors.

Introduction

Melioidosis, caused by *Burkholderiapseudomallei*, has been on a steady rise, with an increasing number of cases being reported from the Indian subcontinent in the previous two decades [1]. The disease is endemic in Southeast Asia and northern Australia. A soil saprophyte, *B. pseudomallei* is a non-fermenting, oxidase positive gram negative bacilli. The organism is commonly transmitted via inoculation of contaminated soil through skin abrasions. Diabetes mellitus, chronic renal impairment pulmonary disease, thalassaemia,congestive heart failure, corticosteroid therapy, malignancy, immunosuppression and prolonged alcohol intake are known risk factors for melioidosis [2] The disease can have a wide spectrum of presentations ranging from localised, disseminated to septicemic.

The most serious form of the disease is an acute septicaemic illness which is associated with a high mortality rate. A correct diagnosis and prompt

initiation of appropriate treatment is crucial for patient survival. The organism is intrinsically resistant to a large number of antimicrobial such as penicillin, first and second-generation cephalosporins, aminoglosides and macrolides. The treatment of melidiosis thus consists of an initial intensive therapy with minimum of 10-14 days when ceftazidime or meropenem or imipenem is given, with or without sulfamethoxazole-trimethoprim. In the eradication phase, the backbone of therapy is sulfamethoxazole-trimethoprim for a minimum duration of 3 months, with or without doxycycline [3].

In this paper, we review the antimicrobial susceptibility patterns and risk factors in patients with septicaemicmeliodosis, seen overa period of five years- from 2010 to 2014. We aimed 1) to study the antimicrobial susceptibility patterns of bloodstream *B. pseudomallei* isolates. 2) to analyze the MIC trend of *B. pseudomallei* isolates over a period of five years (2010-2014). 3) to study the various risk factors associated with septicaemicmeliodosis.

Materials and methods

All blood culture *B. pseudomallei* positive patients, between the periods January 2010 to December 2014, were included in the study. Blood culture testing was performedin the BacTAlert automated system (bioMe´rieux). Identification of *Burkholderiapseudomallei* from positive blood cultures, was done by cultural characteristics and biochemical methods. All isolates were serologically confirmed using polyclonal antiserum raised in rabbitsin our hospital. Antimicrobial susceptibility testing was done by determining minimum inhibitory concentration (MIC) for ceftazidime, doxycycline, trimethoprim-sulfamethoxazole, meropenem (2010 and 2011 isolates) and imipenem (2012-2014 isolates), as per Clinical and Laboratory Standards Institute (CLSI M45) guidelines. Geometric mean MIC for each antibiotic for each year was calculated as it was a more sensitive indicator of MIC changes over the years.Clinical and demographic data was obtained from the medical records of the patient.

Results

A total of 54 patients were found to have *B. pseudomallei* septicaemia during the study period, 8 in 2010, 14 in 2011, 14 in 2012, 11 in 2013 and 7 in 2014. Of them, 47 (87%) were males, while the rest 7 (13%) were females. Ages of the patients ranged from 0 to 67 years (mean±SD 43.22±14.778). The table 1 gives an account of the various predisposing factors seen in the patients.

The table 2 depicts the number of isolates susceptible, intermediate or resistant to the various antimicrobials testedin each year. Trends of geometric mean MIC of B pseudomallei isolates over 5 years is presented in Table 3.

Discussion

There were 54 blood stream isolates of *B. pseudomallei*during the five year period from 2010 to 2014. Male preponderance was seen (87%), as has been reported in other studies [1,4] which is mostly due to the outdoor nature of the work. The mean age of the patients was 43 years. Diabetes was the commonest predisposing factor seen (55.5%). This is comparable to what has been reported in other studies (37-68%) [1,5]. Tuberculosis, hypertension, chronic kidney disease and transplantation were present in minority of patients.

In this study, the organism has been largely susceptible to ceftazidime, doxycycline, trimethoprim-sulfamethoxazole and carbapenems. Hence, the patients were treated with ceftazidime with or without meropenem in the intensive phase and sulfamethoxazole-trimethoprim with doxycycline in the continuation phase. Clinical

Table 1: Predisposing factors for melioidosis

Predisposing factor	N=54	Percentage (%)
Diabetes mellitus	30	55.5
Tuberculosis	8	14.8
Hypertension	3	5.5
Chronic kidney disease	2	3.7
Transplantation	1	1.9

Table 2: Antimicrobial susceptibility testing by MIC for B pseudomallei isolates from 2010-2014 (CLSI M45)

	Ceftazidime			Imipenem/Meropenem			Doxycycline			Cotrimoxazole		
	S ≤8.0	I 16	R ≥32.0	S ≤4.0	I 8	R ≥16.0	S ≤4.0	I 8	R ≥16.0	S ≤2/38	I -	R ≥4/76
2010	8	-	-	8	-	-	8	-	-	8	-	-
2011	14	-	-	13	-	1	13	-	1	14	-	-
2012	14	-	-	14	-	-	14	-	-	14	-	-
2013	11	-	-	11	-	-	11	-	-	11	-	-
2014	7	-	-	7	-	-	7	-	-	7	-	-

Table 3: Geometric mean MIC of B pseudomallei isolates over 5 years (2010 -2014)

Year	MIC (µg/ml) Ceftazidime	Imipenem	Meropenem	Doxycycline	Cotrimoxazole
2010	1.89	-	0.67	1.53	0.88
2011	2.33	-	0.61	1.91	0.35
2012	1.46	0.57	-	1.51	0.63
2013	1.82	0.50	-	1.69	0.99
2014	3.02	0.54	-	1.37	0.92

trial evidence supports the use of ceftazidime or a carbapenem antibiotic for initial parenteral therapy, which should be administered for at least 10-14 days. This is followed by a prolonged course of oral antimicrobial therapy with trimethoprim-sulfamethoxazole with or without doxycycline [6].

We found only a single isolate of B. pseudomalleiwhich showed resistance to meropenem and doxycycline. Resistance to these drugs is very uncommon [7,8]. Beheraet al from Andhra Pradesh, India, have reported a case of disseminated septicaemicmelioidosis with ceftazidime resistance [9]. Low rates of resistance have also been reported from Malaysia [10].

We attempted to study if any MIC trends could be made out over 5 years. However, there was no consistent trend for any antibiotic. The geometric mean MICs over five years did not show any evidence of an increasing trend.

Conclusion

Melioidosis is a largely an under-recognized infection and needs a high index of suspicion for diagnosis. Prompt initiation of treatment is essential, especially in the septicaemic form of the disease. It is re-assuring to find that the organism is largely susceptible to routinely used antibiotics. The collation of MIC data over 5 years in the tertiary care institution was unable to reveal an evident MIC trend for ceftazidime, doxycycline, trimethoprim-sulfamethoxazole and carbapenems.

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