

Short Communication

Antimicrobial Susceptibility of Isolates from Neonatal Septicemia

Nalini Agnihotri, Neelam Kaistha and Varsha Gupta*

Department of Microbiology, Government Medical College Hospital, Chandigarh 160 031, India

(Received March 12, 2004. Accepted July 13, 2004)

SUMMARY: A retrospective study of bacterial isolates from cases of neonatal septicemia was undertaken over a period of 5 years (July 1998 - June 2003) at the Government Medical College Hospital, Chandigarh, India. The study was carried out to determine the bacterial profile, the antimicrobial susceptibility of the isolates, and the change in trends over the study period. A total of 3,064 blood samples for blood culture were obtained, out of which 588 were positive for bacterial isolates. Most of the cases detected by blood culture occurred in the first week of life (64.4%). Gram-negative bacilli (58.5%) predominated over Gram-positive cocci (41.5%). *Staphylococcus aureus* was found to be the most common isolate (35.0%). The incidence of Gram-positive and Gram-negative organisms changed little over the 5 year span. However, a constant and significant rise in the incidence of *Acinetobacter* spp. was observed between the first to fifth year of the study period. Amikacin was found to be the most effective drug against Gram-negative bacteria. For *S. aureus* and *Pseudomonas aeruginosa*, overall resistance percentages of 5 years show that netilmicin and ciprofloxacin, respectively, were the most effective drugs.

Septicemia in neonates refers to generalized bacterial infection documented by a positive blood culture in the first 4 weeks of life and is one of the four leading causes of neonatal mortality in India (1). Prior to the antibiotic era, the mortality from septicemia was 90%, but it declined to 24-58% after antibiotics came into use (2). This retrospective study was undertaken to evaluate major aerobic bacterial isolates from neonatal septicemia cases in our hospital, to determine their antibiograms, and to identify the change in trends over the last 5 years.

During a 5 year period from July 1998 to June 2003, a total of 3,064 blood samples for culture were obtained from neonates having a clinical picture suggestive of septicemia/bacteremia. All the blood samples for culture were collected before instituting antibiotic therapy. The processing of blood samples for culture and isolate identification was done by standard methods (3). The antibiotic susceptibility was determined by the Stokes disc diffusion method as per the NCCLS recommendations (4). Mueller-Hinton agar and antibiotics were purchased from Himedia India, Ltd. (Mumbai, India). The concentrations of the various antibiotics were as follows (in μg): amoxycillin (30), erythromycin (5), cephalixin (30), netilmicin (10), ciprofloxacin (5), gentamicin (10), amikacin (30), cefotaxime (30), ceftriaxone (30), piperacillin (75), carbenicillin (100), tobramycin (10), ceftazidime (30). The plates were incubated at 37°C and read after overnight incubation.

Out of 3,064 suspected cases of septicemia, 588 (19.2%) were positive for bacterial isolates. The incidence of Gram-negative and Gram-positive organisms was 58.5% and 41.5%, respectively. There were 379 (64.5%) isolates from early onset (age ≤ 1 week) septicemia cases, while 209 (35.5%) were from late onset (age > 1 week) illness. The percentage of isolates from culture positive neonates is shown in Table 1. The antibiotic resistant patterns for *Staphylococcus aureus*, Gram-negative bacilli, and non-fermenters are shown in Table 2.

There was a constant and significant increase in the incidence of *Acinetobacter* spp. (from 2.6 to 14.1%) during the first to fifth year of the study period. Netilmicin was found to be the most effective drug against *S. aureus*. Most of the isolates of *S. aureus* and Gram-negative isolates of the family *Enterobacteriaceae* were resistant to ampicillin/amoxycillin. Amikacin was found to be the most effective drug against Gram-negative isolates but resistance to it increased over 5 years. However, among the aminoglycosides, resistance to amikacin was less frequent than that to gentamicin. Ciprofloxacin was found to be the most effective drug against non-fermenters (Table 2).

Neonatal septicemia remains a major clinical problem in neonatology, with high morbidity and mortality rates. In India, the current neonatal mortality rate is 43.4 per thousand live births (5). In the present study, positive cultures were obtained in 19.19% of the suspected cases of septicemia, which is in conformity with earlier reports (2,6). However, negative cultures do not rule out the possibility of neonatal sepsis. While some of these neonatal septicemia patients may be picked up by hemotological and pathological findings both in fatal and non-fatal cases (6), a number of them could also be due to infection by anaerobic pathogens (7). Though Gram-negative organisms (58.5%) predominated over Gram-positive cocci (41.5%), but the predominant organism was *S. aureus* (35.3%), which is in agreement with earlier studies (2,6). The next most predominant organism was *Klebsiella pneumoniae* (18.37%), which has also been shown to be one of the three most common isolates in neonatal septicemia (2).

Early onset disease presents as a fulminant, multisystem illness during the first 5-7 days of life; late onset disease is most commonly recognized after the first week of life. In the present study, *S. aureus* remained the most common isolate, causing both early and late onset disease, followed by *K. pneumoniae*, which is in accordance with earlier studies reporting a lack of significant difference between the bacteriology of early and late onset septicemia (8). In the present study, an increase in the incidence of *Acinetobacter* was observed over 5 years. The role of *Acinetobacter* as a potential pathogen in neonatal septicemia has also been stressed by others (9).

*Corresponding author: Mailing address: Department of Microbiology, Government Medical College Hospital, Chandigarh 160 031, India. Tel: +91-172-2665253-59 ext 1061, Fax: +91-172-2609360, 2608488, E-mail: varshagupta_99@yahoo.com

Table 1. Number of microbial isolates from culture positive neonates

Isolates	Frequency of isolation (%)	Early onset disease (n = 379)	Late onset disease (n = 209)
<i>Staphylococcus aureus</i>	206 (35.0)	150	56
<i>Klebsiella</i> spp. (100 <i>K. pneumoniae</i> + 8 <i>K. oxytoca</i>)	108 (18.4)	64	44
<i>Escherichia coli</i>	64 (10.9)	40	24
<i>Acinetobacter</i> spp.	61 (10.4)	20	41
<i>Pseudomonas aeruginosa</i>	51 (8.7)	20	31
<i>Enterobacter</i> spp.	46 (7.8)	24	22
<i>Enterococcus faecalis</i>	30 (5.1)	18	12
Others (<i>Proteus</i> spp., CONS, <i>Streptococcus pyogenes</i>)	22 (3.7)	15	7

Table 2. Resistant percentages of *Staphylococcus aureus*, Gram-negative bacilli (GNB), and non-fermenters to various antibiotics in 5 years

Antibiotics	Resistant percentages of Isolates															
	<i>S. aureus</i>					GNB					Non-fermenters					
	Years	I	II	III	IV	V	I	II	III	IV	V	I	II	III	IV	V
	No. of isolates	30	31	43	59	43	30	53	39	47	59	15	20	16	26	35
Amoxycillin		57.8	43.4	42.8	70.8	90.0	80.0	84.3	72.7	100.0	61.5	–	–	–	–	–
Erythromycin		18.1	20.0	33.3	35.2	27.2	–	–	–	–	–	–	–	–	–	–
Cephalexin		23.5	10.0	15.3	36.6	20.0	–	–	–	–	–	–	–	–	–	–
Netilmicin		4.5	0	3.7	16.6	–	–	–	–	–	–	–	–	–	–	–
Ciprofloxacin		5.0	3.7	5.8	6.7	12.5	12.5	15.3	18.9	60.0	51.1	0	11.1	0	30.4	50.0
Gentamicin		–	–	–	–	–	21.4	32.6	45.4	40.6	47.0	–	–	33.3	42.8	40.0
Amikacin		–	–	–	–	–	7.1	5.4	10.0	26.0	20.0	0	29.4	27.2	21.7	18.1
Cefotaxime		–	–	–	–	–	19.2	22.2	21.7	58.5	55.5	–	–	–	–	–
Ceftriaxone		–	–	–	–	–	19.1	30.0	44.4	56.8	51.4	–	–	–	–	–
Piperacillin		–	–	–	–	–	–	–	–	–	–	16.6	33.3	–	0	50.0
Carbenicillin		–	–	–	–	–	–	–	–	–	–	22.2	50.0	0	25.0	45.4
Tobramycin		–	–	–	–	–	–	–	–	–	–	–	50.0	0	20.0	50.0
Ceftazidime		–	–	–	–	–	–	–	–	–	–	33.3	20.0	25.0	66.6	64.2

Neonatal septicemia is a life-threatening emergency, and rapid treatment with antibiotics is essential for a favorable outcome. Classical initial (empiric) treatment of neonatal sepsis and meningitis consists of ampicillin and an aminoglycoside. With the advent of the third-generation cephalosporins, however, the empiric antimicrobial approach for neonatal sepsis has changed in many centers. In the present study, *S. aureus* and Gram-negative isolates were frequently found to be resistant to amoxycillin/ampicillin, thus indicating that the use of these drugs alone may be ineffective. Netilmicin was found to be the drug of choice against *S. aureus*. Amikacin was found to be the most effective drug against Gram-negative isolates, but resistance to this drug increased over the 5 year study period. Ciprofloxacin was found to be the most effective drug against non-fermenters. Quinolones have also been found to be effective by others in the treatment of multidrug resistant Gram-negative infections in various patients, including premature and extremely low birth weight infants (10). Thus, our study suggests that aminoglycosides, third generation cephalosporins and quinolones are the most suitable drugs for the treatment of neonatal septicemia as per in vitro susceptibility results.

REFERENCES

1. Singh, M. (1991): Perinatal and neonatal mortality in a hospital. *Indian J. Med Res.*, 94, 1-5.
2. Kaushik, S. L., Parmar, V. R., Grover, N., Grover, P. S. and Kaushik, R. (1998): Neonatal sepsis in hospital born babies. *J. Commun. Dis.*, 30, 147-152.
3. Collee, J. G., Fraser, A. G., Marmion, B. P. and Simmons, A. (ed.) (1996): Mackie and McCartney Practical Medical Microbiology. p. 113-129. 14th ed. Churchill Livingstone, Edinburgh.
4. National Committee for Clinical Laboratory Standards (2000): Performance standards for antimicrobial susceptibility testing. 8th Information Supplement M2A7. Vol. 20, No. 1-2, National Committee for Clinical Laboratory Standards, Villanova, Pa.
5. Ramji, S. (2001): The national family health survey (1998-99). Childhood mortality. *Indian Pediatr.*, 38, 263-266.
6. Somu, M., Shetty, M. V., George, M., Subramanian, I. and Raju, B. V. (1976): A critical analysis of septicaemia of infancy. *Indian Pediatr.*, 13, 443-450.
7. Chow, A. W., Leake, R. D. and Terry, Y. (1974): The significance of anaerobes in neonatal bacteremia: Analysis of 23 cases and review of literature. *Pediatrics*, 54, 736-745.
8. Bhakoo, O. N., (1980): Neonatal bacterial infection at Chandigarh- A decade of experience. *Indian J. Pediatr.*, 47, 419-424.

9. Christo, G. G., Shenoy, V., Mathlai, J., Shivananda, P. G. and Venkatesh, A. (1993): *Acinetobacter* species in neonates. Indian J. Pediatr., 30, 1413-1416.
10. Khaneja, M., Naprawa, J., Kumar, A. and Piecuch, S. (1999): Successful treatment of late onset infection due to resistant *Klebsiella pneumoniae* in an extremely low birth weight infant using ciprofloxacin. J. Perinatol., 19, 311-314.