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Changing Patterns of Causative Organisms of Neonatal Septicaemia at the Lagos University Teaching Hospital

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Summary

Iroha EO, Egri-Okwaji MTC, Kesah CN, Odugbemi TO. Changing Patterns of Causative Organisms of Neonatal Septicaemia at the Lagos University Teaching Hospital. *Nigerian Journal of Paediatrics* **1998; 25:** A prospective study of neonatal septicaemia at the newborn unit of Lagos University Teaching Hospital over a ten-month period has revealed an overall rate of 35 per 1000 live births. The commonest causative organism was *Klebsiella pneumoniae*, being responsible for 45 percent of the isolates, a finding that was at variance with that of a study carried out in the same institution over 20 years earlier which showed that *E coli* was the commonest organism. *Staphylococcus aureus* and coagulase negative staphylococcus were second and third with 12 percent and nine percent, respectively. *Klebsiella pneumoniae* was resistant to the commonly used and readily available antibiotics such as gentamicin; conversely, all strains of the organism were sensitive to ofloxacin. While further tests are being carried out on the safety of ofloxacin in neonatal practice, we suggest that, as recommended by others, a combination of cloxacillin and amikacin or tobramycin should be the initial therapy in neonatal septicaemia, while awaiting results of bacterial cultures.

Introduction

BACTERIAL infections continue to be an important cause of morbidity and mortality during the neonatal period and could run a rapid and disastrous course, unless promptly diagnosed and treated.[1-3] The manifestations of infection in this age group are often subtle, making early diagnosis difficult.[4] [5] Moreover, the patterns of bacterial infections vary not only from place to place but from time to time. The changing patterns if undetected, can lead to the use of ineffective antibiotics with adverse outcome.[6 7] In most cases, the choice of antibiotics has to be made before the aetiological agents are identified and antibiotic sensitivity studies performed. There is therefore, the need for a regular bacteriological surveillance of neonatal units so as to be aware of the common pathogens that are involved in neonatal septicaemia and the susceptibility of these pathogens to commonly used antibiotics. To our knowledge, no prospective study along this line, has been carried out in the neonatal unit of the Lagos University Teaching Hospital (LUTH) in the past 10 years. The present study was therefore, undertaken in order to identify causative bacterial agents in neonatal septicaemia, as well as determine the antibiotic sensitivity patterns of such pathogens.

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Patients and Methods

Four hundred and ninety four babies, aged 0-28 days were admitted to the inborn neonatal intensive care unit of the LUTH, over a 10-month period (February-November, 1995); 251 of the 494

who presented with or developed features of sepsis were investigated for infection, using the criteria of Silverman and Homan.[5]

Venous blood was drawn once, from a peripheral vein of all such babies after preparation of the skin and before commencement of antibiotics. The blood was aseptically introduced into aerobic and anaerobic culture media at the patient's bed side. Brain heart infusion broth (*Difco*), supplemented with sodium polane thiosulphonate (*Liquoid*), in concentration of 0.05 percent was used for aerobic culture of blood, whereas thioglycholate brewers medium broth (oxoid) was used for anaerobic blood culture. The blood culture specimens were processed according to standard methods in the bacteriology laboratory.[8] Inoculated blood culture media were discarded as negative if there was no growth after continuous incubation for up to 7-10 days, subcultures being made each day. All Gram negative bacilli isolated were identified using API 20E and AQ1 20E (*Analytic Profile Index System, Biometrieux 69280, Mercy L'Etoile, France*). All other bacterial isolates were identified by standard techniques.[9] Sensitivity test was performed on Mueller-Hinton agar by the disk diffusion method.[10] Gram positive Abdiscs code NZ22P and Gram negative Abdisk Ciode NZZIN (*Abteh Biologicals Ltd, Liverpool*) were used for testing Gram positive and Gram negative organisms, respectively. Single discs of ofloxacin (10ug), ceftazidime (30ug), cefuroxime (30ug) and *Augmentin* (30ug) were also included. The diameter of growth inhibition zone was measured in millimeter (mm) using calibrated ruler. The result was interpreted as susceptible, intermediate and resistant as recommended. [11] Standard organisms used included *Escherichia coli* ATCC 25922, *Escherichia coli* ATCC 35218 and *Pseudomonas aeruginosa* ATCC 27853; they were obtained from *Smithkline Beecham Laboratory, Paris, France.*

Initial treatment of suspected cases of sepsis which was based on clinical judgement, consisted of a combination of intravenous (i.v.) gentamicin and i.v. cloxacillin given in appropriate dosages. The response to antibiotic therapy was carefully monitored and therapy was altered if antibiotic sensitivity results indicated otherwise, or in the event of poor clinical response. The clinical details, course and results of laboratory investigations were recorded on a proforma. Statistical analysis where relevant, was by means of the chi-squared test.

Results

Of the 251 neonates screened for sepsis, 32 (12.7%) had positive blood cultures, with 33 isolates. Table 1 shows the pattern of organisms isolated. *Klebsiella pneumoniae* was the commonest bacterial pathogen, being 15 (45 percent) of the overall isolates followed by *Staphylococcus aureus* 4 (12.1 percent) and coagulase negative staphylococcus 3 (9.1 percent). The frequency of the other isolates is shown in Table 1. There was a preponderance of Gram negative organisms 24 (73 percent) over Gram positive ones 8 (24 percent). Fourteen patients presented with early onset sepsis while 18 had sepsis after 48 hours of birth.

Table 1
Causative Organisms in Neonatal Septicaemia

Organisms	*No of Isolates*		*Total No of Isolates*
	Early onset (n = 14)	*Late onset (n = 19)*	*(n = 33)*
Klebsiella pneumoniae	9(64)	6 (32)	15 (45)
Staphylococcus aureus	1(7)	3 (16)	4 (12)
Coagulase negative staphylococcus	2(14)	1 (5)	3(9)
Enterococcus faecalis	1(7)	1 (5)	2 (6)
Acinetobacter calcoaticus var anitratus	1(7)	1 (5)	2 (6)
Pseudomonas aeruginosa	0(0)	2 (11)	2 (6)
Pseudomonas cepacia	0(0)	1 (5)	1 (3)
Flavimonas aryzihabitans	0(0)	1 (5)	1 (3)
Salmonella arizonae	0(0)	1 (5)	1 (3)
Providencia rettgeri	0(0)	1 (5)	1 (3)
Aeromonas subria	0(0)	1 (5)	1 (3)

Figures in parentheses represent percent of total

Results of the sensitivities of the major organisms isolated to various antimicrobials are contained in Table II. All the 13 isolates of *Klebsiella pneumoniae* were 100 percent sensitive to ofloxacin while 10 (67 percent), six (40 percent), five (33 percent) and four (27 percent) were sensitive to ceftriazone, streptomycin, ceftazidime, gentamicin, and *Augumentin*, respectively; conversely, there was 100 percent resistance to ampicillin and cotrimoxazole. The other gram negative bacilli isolated were mostly susceptible to ofloxacin,

ceftazidime, and gentamicin and grossly resistant to ceftriaxone, *Augmentin*, ampicillin and cotrimoxazole. All the staphylococcus strains were sensitive to ofloxacin, *Augmentin*, cefuroxime, and cloxacillin, but were resistant to ampicillin and penicillin G.

Table II

Susceptibility of some Bacterial Isolates to Antimicrobial Agents

Agents	*Number of Susceptible Isolates*			
	K pneumoniae (n=15	*Ps Aer n=2*	*Staph aureus (n=4)*	*Coag neg Staph (n=3)*
Ofloxacin	15(100)	2(100)	4(100)	3 (100)
Ceftriaxone	10(67)	0 (0)	1 (25)	2 (67)
Streptomycin	6 (40)	0 (0)	1 (25)	2 (67)
Ceftazidime	5 (33)	1 (50)	2 (50)	1 (33)
Gentamicin	4 (27)	2 (100)	2 (50)	3 (100)
Augmentin	4 (27)	0 (0)	4 (100)	3 (100)
Cefuroxime	2 (13)	1 (50)	4 (100)	3 (100)
Ampicillin	0 (0)	0 (0)	0 (0)	0 (0)
Cotrimoxazole	0 (0)	0 (0)	-	-
Cloxacillin	-	-	4 (100)	3 (100)
Erythromycin	-	-	2 (50)	1 (33)
Chloramphenicol	-	-	1 (25)	2 (67)
Penicillin G	-	-	0 (0)	0 (0)

Figures in parentheses represent percent of total
K = Klebsiella Ps Aer = *Pseudomonas aeruginosa*
Staph = Staphylococcus Coag neg = Coagulase negative

During the ten-month study period, there were 917 lives births at LUTH; this number comprised 195 preterm and 722 term neonates. Seven hundred of these were delivered by booked mothers while 217 were delivered by unbooked mothers. The overall prevalence rate of sepsis in the inborn unit of the Lagos University Teaching Hospital during the period was thus 35 per 1000 live births. Further analysis showed that the rate was 92 per 1000 preterm births, 19 per 1000 term births, 20 per 1000 booked deliveries and 83 per 1000 unbooked deliveries. The 32 neonates with septicaemia comprised 23 of the 481 male neonates and nine of 436 females; this difference in the sex incidence was significant ($P<0.05$).

There were 28 deaths in the unit during the 10 months study period; ten of these died of septicaemia. Thus, 31 percent (10/32) of the septic neonates died while sepsis accounted for 35.8 percent (10/28) of the deaths during the study period. The mortality of 44 percent in the pretem babies was significantly higher ($P<0.05$) than that of 14 percent among the term neonates. Similarly, early onset sepsis was associated with 64 percent (9/14) mortality in contrast to one of 5.5 percent (1/18) in those with late onset sepsis. The difference in mortality was significant ($P<0.05$).

Discussion

The prevalence of septicaemia in the newborn during the period of this study was 35 per 1000 live births, a very high rate when compared with those reported from other centres. [12 13] The finding that neonatal septicaemia accounted for 36 percent of all neonatal deaths in the unit during the study period, is similar to those of other studies within the region, [7 14] and underscores the importance of neonatal sepsis as a cause of newborn mortality in our centre. The commonest pathogens isolated in this study were the Gram negative organisms which were responsible for 73 percent of cases, with *Klebsiella pneumoniae* being the predominant pathogen. This is at variance with the results reported from the same unit about 20 years ago when *E coli* was the predominant gram negative organism, but is similar to more recent studies from other newborn units in this region. [15 16] Other important pathogens isolated in the present series include *Staphylococcus aureus*, coagulase negative staphylococcus and *Pseudomonas aeruginosa*. The failure to isolate Group B streptococcus in this study confirms the observation previously made by other workers that the organism is not a common cause of neonatal septicaemia in Nigeria. [15 17] This is in contrast to the situation in Europe and North America where the organism plays an important role. [13 17]

The striking feature of the antimicrobial susceptibility profile of the isolates in the present study is the high rate of *in vitro* resistance of *Klebsiella pneumoniae*, the most commonly isolated organism, to gentamicin and the third generation cephalosporins. Amongst the cephalosporins tested, ceftazidime had the highest *in vitro* activity whilst cefuroxime was the least active against *Klebsiella pneumoniae*. The staphylococcus was 100 percent sensitive to cloxacillin and gentamicin, while ofloxacin was effective against all isolates. The emergence of multi-drug resistant Klebsiella spp

in our unit has created problems in the choice of initial antibiotic therapy for neonatal sepsis while awaiting blood culture results. Prior to this study, our choice had been a combination of cloxacillin and gentamicin. With this disturbing trend of resistance however, there is a need to review the use of gentamicin as one of the initial drugs. If there had been no reservations in the use of the quinolone group of antibiotics in the newborn, one would have recommended ofloxacin as an antibiotic of choice in all cases of neonatal septicaemia. Despite the reservations, a successful short-term use of the drug in severe neonatal sepsis was recently reported from Ibadan.[18] In view of the apparent potency of the quinolone group of antibiotics in combating the emerging resistant organisms in sepsis, there is an urgent need to carry out pharmakokinetic studies on them in order to determine conclusively, their safety or otherwise, in paediatric practice. The synthetic aminoglycosides namely, amikacin and tobramycin have been shown to have antibacterial activities similar to gentamicin and have been recommended as alternative drugs for use in situations where there is gentamicin resistance.[19] It may therefore, be justifiable to recommend amikacin and tobramycin as substitutes for gentamicin in the initial 'blind' therapy of neonatal septicaemia, while awaiting antimicrobial susceptibility results.

The high rate of bacterial infections in the newborn, the emergence of resistant bacteria and the poor outcome emphasize the need for frequent review of antibiotics used in neonatal sepsis and the adoption of preventive measures to minimise infections in the newborn.

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