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CHANGING PATTERN OF BACTERIAL ISOLATES AND ANTIMICROBIAL SUSCEPTIBILITY IN NEONATAL INFECTIONS IN KORLE BU TEACHING HOSPITAL, GHANA

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C.C. ENWERONU-LARYEA and M.J. NEWMAN

ABSTRACT

Background: Most neonatal deaths in developing countries are caused by infections, birth asphyxia and prematurity. Even though most of these deaths occur at home, newborns admitted to hospital neonatal units have a high risk of contracting fatal multi-drug resistant infections.

Objective: To compare the type of bacteria and the pattern of antimicrobial susceptibility of organisms causing neonatal infections in 2001/02 with 1991/92 in the same neonatal unit.

Design: We reviewed the hospital records of newborns admitted to the neonatal unit in 2001/02 that had positive blood cultures and compared the findings with similar work done 1991/92.

Setting: Neonatal Unit, Korle Bu Teaching Hospital, Ghana.

Results: Gram negative organisms (predominantly *Enterobacter*, *Klebsiella* and *Acinetobacter*) remained the predominant cause of neonatal infection. There was a reduction in the proportion of gram negative bacteraemia [70.9% in 1991/92 vs. 54.2% in 2001/02 ($p < 0.001$)] due to the increased prevalence of *coagulase negative staphylococcus* (31.9% in 2001/02 vs. 0% in 1991/92) as a cause of neonatal bacteraemia ten years later. In 1991/92 as 2001/02 all bacterial isolates showed less than 40% susceptibility to ampicillin. The susceptibility of *Klebsiella* and *Enterobacter* to commonly used aminoglycosides and cephalosporins had decreased from over 80% in 1991/92 to less than 35% in 2001/02.

Conclusion: Bacterial causes of neonatal infections change over time and antimicrobial resistance is a major cause for concern in neonatal units in resource-poor hospitals. Improving infection control practices and instituting systems to monitor antimicrobial use and resistance will compliment community efforts to reduce neonatal mortality.

INTRODUCTION

The World Health Organisation estimates that 98% of the four million newborn deaths that occur annually take place in developing countries (1,2). These neonatal deaths are mostly caused by infections (32%), birth asphyxia (29%) and prematurity (24%) (3). Most of these deaths occur at home; however, many newborns admitted to hospital still die from

several potentially preventable causes including multi-drug resistant infections.

Inadequate infection control practices, overcrowding and lack of effective antimicrobial stewardship in many developing countries increase the risk of multi-drug resistant nosocomial infections. In addition, microbiological services to guide the choice of antimicrobial drugs for sick newborns is usually inadequate and drug choices are often

based on suspected severity of illness, availability of drugs and affordability of the drug by parents. About 70% of hospital-acquired neonatal infections in these countries are resistant to ampicillin and gentamicin, the two most commonly used empirical antimicrobial agents (4). Newer antimicrobial agents are frequently not available or affordable, as a result infected infants have a high risk of death from treatable disease.

In our institution as in many hospitals in sub-Saharan Africa, infection is a major cause of neonatal death. While some of these infections may be acquired from the mother, the lack of basic hygienic facilities and the inappropriate use of antimicrobial drugs make these overcrowded neonatal units reservoirs of multi-drug resistant nosocomial pathogens (5). There is a pressing need to limit the emergence and spread of antimicrobial resistant bacteria, because of the high human and financial toll.

Anyebuno and Newman (6) reviewed the causes of neonatal bacteraemia and antimicrobial susceptibility in newborns admitted to our neonatal unit in 1991 and 1992. They found that the majority of the infections were caused by gram negative organisms susceptible to commonly used aminoglycosides and third generation cephalosporins. To inform institutional policy on antimicrobial drug use and the need for monitoring bacterial resistance we reviewed the pattern of change ten years later.

MATERIALS AND METHODS

We reviewed the hospital records of newborns admitted to the neonatal unit of Korle Bu Teaching Hospital Accra, Ghana from January 2001 to December 2002. The Korle Bu Teaching Hospital is the largest hospital that offers neonatal services in Accra, Ghana's capital city. Patients are referred from surrounding districts over a 50 kilometers radius and a population of five million.

The 50 bed (seven incubators and 43 bassinets) unit admits 1800 to 2000 newborns annually. It usually provides care for 70 to 80 newborns at any one time. There were no facilities for mechanical ventilation and parenteral nutrition in 2001/02 as in 1991/92.

The total staff strength of 28 nurses and seven doctors (one paediatrician, three residents and

three house officers) provided twenty four-hour care for the newborns. Nurses worked eight hourly shifts of three nurses per shift in 2001/02 and 1991/92. There were no structural changes in the neonatal unit from 1991 to 2002. The criteria for admission (sick newborns, low birth weight <1,800 grams, newborns at risk for sepsis and those with significant hyperbilirubinaemia or requiring blood transfusion) was similar during both study periods. The criteria for blood culture investigations in the newborn in 2001/02 were similar to 1991/92. The first line empirical antibiotic treatment in 1991/92 was crystalline penicillin and gentamicin while in 2001/02 ampicillin and gentamicin were used in keeping with hospital policy. There was a change in hospital policy in 2001/02 to a "cash and carry system" such that payment for laboratory services must be made before the service could be provided.

Data were collected from the hospital records of newborns with positive blood culture during the year 2001/02. The type of organism and the antimicrobial susceptibility of isolates were compared to similar data in the same neonatal unit in the year 1991/92.

Laboratory methods: The standard procedure for blood culture in 2001/02 was similar to 1991/92. Venous blood (0.5 - 1.0 ml) was collected aseptically and immediately inoculated directly into 20 ml of culture media (brain heart infusion in 1991/92 and thioglycolate broth in 2001/02) at the bedside. This was incubated at 37°C in air for seven days. The bottles were examined daily for evidence of growth. The growths were gram stained and sub-cultured onto blood agar and MacConkey agar (from Biotec in Suffolk, United Kingdom). Antibiotic sensitivity testing was done by the Kirby-Bauer (7) method against nine selected antimicrobial agents with ECO control (ATCC 25923). The antimicrobial agents tested were ampicillin (10µg), cloxacillin (5µg), gentamicin (10µg), amikacin (30µg), cefuroxime (30µg), cefotaxime (30µg), ceftriazone (30µg), chloramphenicol (30µg) and cotrimoxazole (25µg). Susceptibility of only one colony per blood sample was tested. The same method was used during the 1991/92 study.

Statistical analysis: We compared the proportion of organisms that were susceptible to each of the

commonly used antimicrobial agents between the two study periods using the z-test for proportions. A value of 0.05 or less was considered significant. The analysis was performed with SigmaStat for Windows version 3.11 (Systat Software Inc. 2004).

RESULTS

Patients: There was a 48.7% increase in newborns admitted to the neonatal unit from 2833 in 1990/91 to 4213 in 2001/02.

Bacterial isolates: *Coagulase negative staphylococcus* (CONS) was the most common isolate in 2001/02. There was no documented isolate of CONS ten years previously when *enterobacter* was the most common isolate (see Table 1). *Enterobacter* and *klebsiella* were the most common gram negative isolates in 2001/02 as in 1991/92. There was a significant reduction in the proportion of gram negative bacteraemia [70.9% in 1991/92 vs. 54.2% in 2001/02 ($p < 0.001$)] ten years later.

Antimicrobial susceptibility: Most bacteria were resistant to ampicillin and gentamicin, the first-line empirical drugs used in the neonatal unit in 2001/02. Antimicrobial susceptibility of the isolates to ampicillin in 1991/92 vs 2001/02 was 11% vs 1.9% (*Enterobacter*), 3% vs 3.8% (*Klebsiella*), 31% vs 0% (*Escherichia coli*), 9% vs 35.7% (*Acinetobacter*) and 62% vs 22% (*Streptococcus faecalis*). Even though CONS isolates were not reported in 1991/92 less than 40% of the 80 isolates in 2001/02 were susceptible to gentamicin, ampicillin and cloxacillin (30, 9.5 and 39.1%) respectively.

The susceptibility of *Staphylococcus aureus* in 1991/92 (48 isolates) vs. 2001/02 (27 isolates) respectively to gentamicin was 71% vs. 68% ($p = 0.99$), ampicillin 20% vs. 14.8% ($p = 0.8$), cloxacillin 100% vs. 51.8% ($p < 0.001$) and cefuroxime 100% vs. 70.4% ($p < 0.001$). The susceptibility of *Enterobacter* and *Klebsiella* to gentamicin, amikacin, cefuroxime and cefotaxime was significantly reduced ($p < 0.001$). The pattern of change in the antimicrobial susceptibility of gram negative organisms to aminoglycosides and cephalosporins is shown in Table 2.

Table 1

Proportion of bacterial isolates in 2001/02 and 1991/92

Bacterial isolate	2001/02 % isolates (n = 251)	1991/92 % isolates (n = 443)
<i>Enterobacter species</i>	59 23.5	131 29.6
<i>Klebsiella species</i>	31 12.3	40 9
<i>Acinetobacter species</i>	16 6.4	42 9.5
<i>Escherichia coli</i>	9 3.6	39 8.8
<i>Pseudomonas species</i>	8 3.2	23 5.2
<i>Citrobacter species</i>	8 3.2	5 1.1
<i>Salmonella species</i>	5 2.0	28 6.3
<i>Proteus species</i>	0 0	6 1.4
Total gram negative bacteria	136 54.2	314 70.8
<i>Coagulase negative staphylococcus</i>	80 31.9	0 0
<i>Staphylococcus aureus</i>	27 10.7	48 10.8
<i>Streptococcus faecalis</i>	7 2.8	64 14.4
Group B streptococcus	0 0	8 1.8
Non-group B streptococcus	1 0.4	9 2.1
Total gram positive bacteria	115 45.8	129 29.1

Table 2

Two-tailed statistical analysis of the susceptibility of gram negative bacterial isolates to commonly used aminoglycosides and cephalosporins in 1991/92 and 2001/02

Bacterial isolate	1991/92 vs. 2001/02 percentage susceptibility (number of isolates tested)							
	Amikacin		Gentamicin		Cefuroxime		Cefotaxime	
	No.	(%)	No.	(%)	No.	(%)	No.	(%)
<i>Enterobacter</i>	76*	93	121*	43	121*	80	78*	91
	48	34	53	9.4	53	17	44	18.8
<i>Klebsiella</i>	18*	95	34*	44	37*	89	19*	90
	25	20	26	7.7	26	11.5	28	10.7
<i>Acinetobacter</i>	27	86	37	62	34	59	26*	96
	14	100	14	50	15	33.3	9	44
<i>Pseudomonas</i>	22	72	21	86				
	5	80	5	40				
<i>Citrobacter</i>	3	100	2	100	2	100	2	100
	6	66.7	6	33	6	33	6	50
<i>Escherichia coli</i>	15	93	31	65	33	94	16	100
	8	75	8	25	9	66.7	7	42.9

* denotes statistical significance p-value < 0.01

DISCUSSION

We found that gram negative organisms especially *Enterobacter*, *Acinetobacter* and *Klebsiella* were still the major causes of neonatal infections. The proportion of infections caused by gram positive organisms may have significantly increased because of the increasing recognition of coagulase negative *Staphylococcus* as an important cause of neonatal bacteraemia. Most bacteria were not susceptible to ampicillin and gentamicin. Susceptibility to cephalosporins and aminoglycosides had significantly reduced in the last ten years.

Even though this is a hospital-based study, newborns were referred to the neonatal unit from all levels of healthcare facilities including home births. It would have been helpful to identify how many of these infections were acquired from the neonatal unit or the community. The "cash and carry" system of health service made this difficult as infants with suspected sepsis were started on empirical antimicrobial treatment on admission. Blood culture was usually done few days later during which they could have acquired nosocomial infections.

There was a 48.7% increase in the number of infants admitted to the unit without a corresponding improvement in infrastructure, laboratory services

or an increase in the number of health workers. This level of overcrowding makes the implementation of infection control practices difficult and thus augments the spread of multi-drug resistant nosocomial infections. The factors that promote emergence of antimicrobial drug resistance include compromised host, close proximity to infected persons, inadequate hygienic practices and high intensity of antimicrobial use. All these factors existed in our unit in 2001/02 and most likely contributed to significant reduction in the susceptibility of common bacterial isolates (*Klebsiella*, *Enterobacter*, CONS) to available antimicrobial drugs.

The "cash and carry system" of health care delivery creates great difficulties in a neonatal unit as parents are not usually available to provide money for laboratory investigations and drugs at the time an infant is admitted. As a result microbiological investigations to guide antimicrobial drug choices and duration of treatment are not always done and newborns were treated with affordable and available antimicrobial drugs with the broadest possible spectrum (8). This system of care promotes inappropriate antimicrobial drug selection and duration of treatment, a practice that is known to promote emergence of resistant strains (9).

The World Health Organisation recommends (10) the use of ampicillin and gentamicin as the first-line empirical treatment in suspected neonatal sepsis in developing countries. Most organisms isolated in our study showed lower susceptibility to ampicillin and gentamicin (<40% in 1991/92 and <10% in 2001/02 for gram negative isolates) than that of other developing countries. In 1995 hospital workers in Nigeria (11) reported 85.7% susceptibility to gentamicin; while in Pakistan (12) 56.8% were susceptible in 2001. Our findings highlight the importance of monitoring the pattern of antimicrobial resistance in local settings as general recommendations may not be applicable to local conditions.

The increase of *coagulase negative Staphylococcus* and reduced prevalence of other gram positive bacteria confirms the finding by other researchers that bacterial pathogens in neonatal infections vary geographically and change over time (13,14). The emergence of CONS as the predominant cause of all bacteraemia ten years later was unexpected because our unit did not provide invasive neonatal intensive care services that are usually associated with CONS infections. However, it may be a reflection of poor infection control practices and spread of multi-drug resistant strains in the unit because an environmental microbiological surveillance of the unit in 2002 showed that CONS was the most common organism isolated (15).

Infections caused by multi-drug resistant bacteria are very costly in both human and financial terms. Newer high potency antimicrobial agents are beyond the reach of many parents in developing countries. Adherence to infection control procedures in neonatal units significantly reduces the spread of multi-drug resistant bacteria (16). However, the lack of understanding about these procedures and the poor attitude to infection control practices hinder the benefits in many neonatal units. Poor resource hospitals with overcrowded neonatal units like ours should urgently review infection control practices and institute systems to monitor antimicrobial use and resistance as a measure to reduce neonatal morbidity and mortality.

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