Study on Antimicrobial Susceptibility of Bacteria Causing Neonatal Infections: A 12 Year Study (1987 - 1998)

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ABSTRACT

Objective: The method of Manual of Clinical Microbiology was used to identify bacteria. We investigated the epidemiological characteristics of bacterial agents and their antimicrobial susceptibility as empirical treatment for neonatal infections. Disk diffusion tests were also done for antimicrobial susceptibility.

Results: From January 1987 to December 1998, 2244 bacterial strains were isolated in our neonatal ward. The first three predominant species were *Staphylococcus epidermidis* (23.9%), *Staphylococcus saprophyticus* (19.9%) and *Escherichia coli* (12.6%) in group I (infections acquired outside of hospital). *Escherichia coli*, *Klebsiella* and *Pseudomonas aeruginosa* accounted for 18%, 15.2% and 12.6% respectively in group II (nosocomial infections). The sensitivity rates of those antimicrobials that are seldom used for newborns were found to be higher, while the resistant rates of the commonly used antimicrobial drugs have increased significantly. The resistant rates of bacterial isolate from group II to antimicrobial agents including penicillin and ampicillin were significantly higher than those isolated from group I ($p<0.05$) The sensitivity rate was 82.2% (717/833) by using amikacin only, when combined with penicillin, rose to 89%(741/833).

Conclusions: Gram-negative bacteria were mainly responsible for nosocomial infections of neonates in our hospital. Infections acquired outside the hospital were mainly caused by Gram-positive bacteria. Nosocomial pathogens produced drug resistance easily. Combination of amikacin and penicillin can be recommended as the initial antibiotics for treatment of neonatal infections.

Keywords: infections, nosocomial, antimicrobial susceptibility tests, antimicrobial drugs, China, hospital

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INTRODUCTION

There have been very high incidence of infections in hospitalised neonatal infants[1]. Recently, the spectrum and resistance of the pathogenic bacteria have constantly changed year after year because of wide applications of antimicrobial drugs. It may be necessary to treat neonatal infections by empirical use of antimicrobial drugs as soon as possible so as to reduce the mortality of newborn by knowing the epidemiology of bacteria, antimicrobial susceptibility, etc.

MATERIAL AND METHOD

Culture and identification of pathogenic bacteria

The clinical specimen was isolated on culture medium containing blood and incubated, the single colony was selected for identification by using the method of Manual of Clinical Microbiology[2].

Source of specimens

From January 1987 to December 1998, 2244 bacterial strains were isolated in the neonatal ward of the Children's Hospital of the Chongqing University of Medical Sciences, Sichuan, China. There were 897 strains (40%) taken from sputum of infants with pneumonia; 815 strains (36.3%) from the blood of infants with sepsis; 317 strains (14.1%) from umbilical discharges; 165 strains (7.4%) from eye discharges due to conjunctivitis, 32 strains (1.4%) from impetigo; and 18 strains from others.

Antimicrobial susceptibility tests

We used disk diffusion tests to perform antimicrobial susceptibility tests. The disk and M-H agar were purchased at Institution of Test attached to the Epidemic Prevention Station, Zhejiang Military Area. The quality control strains were as follows: ATCC 25923 (*Staphylococcus aureus*), ATCC 25922(*Escherichia coli*) and ATCC 27853 (*Pseudomonasa aeruginosa*).

STATISTICS

The functions including filtration and sum under Microsoft FoxPro were applied. SAS program was used for comparing rates of two swatches and x^2 – square analysis.

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Table I. The composing ratio (%) of pathogens causing several common diseases in neonatal infants.

		Gram-negative bacteria					Gram-positive bacteria					
Diseases	n	E.coli	Klebsielleae	P.aeruginosa	Other	Total	S.aureus	S.epidermidis	S.saprophyticus	Streptococcus	Other	Total
Pneumonia	897	20.6	14.5	5.8	15.7	56.6	6.0	12.5	13.7	2.9	2.3	43.4
Omphalitis	317	18.0	7.3	2.5	26.4	54.2	9.8	12.3	19.6	3.2	0.9	45.8
Sepsis	815	5.8	3.1	2.0	27.9 *	38.8	4.0	27.6	20.9	1.2	7.1	61.1
Impetigo neonatorum	32	3.1	6.3	6.3	3.1	18.8	46.9	15.6	18.6	0.0	0.0	81.1
Conjunctivitis	165	7.9	7.3	8.8	18.0	42.0	9.1	24.0	18.9	3.0	3.0	58.0

* among them Acinetobacter accounts for 9.9%.

Table II. The pathogens isolated from between infections acquired outside of hospital and nosocomial infections.

	Outside of hospital		Nosocomial			
Bacteria	No.	%	No.	%	Total	%
S.epidermidis	436	23.9	41	9.7	477	21.3
S.saprophyticus	361	19.9	36	8.6	397	17.8
S. aurcus	136	7.5	15	3 6	151	6.7
E.coli	230	12.6	76	18.0	306	13.6
Klebsielleae	130	7.1	64	15.2	194	8.6
P.aeruginosa	42	2.3	53	12.6	95	4.2
Streptococcus	40	2.2	11	2.6	51	2.3
Micriococcus	58	3.2	10	2.4	68	3
Acinetobacter	92	5	22	5.2	114	5.1
Serratia	39	2.1	8	1.9	47	2.1
E.cloacac	43	2.4	24	5.7	67	3
Othcr Pscudomonas	88	4.8	29	6.9	117	5.2
Other Gram-negative bacteria	18	1	3	0.7	21	0.9
Other Gram-positive bacteria	110	6	29	6.9	139	6.2
Total	1823	100	421	100	2244	100

RESULTS

Pathogenic Bacteria

Pathogenic bacteria causing infections of newborns in our hospital were as follows:

1. Gram-negative bacteria most commonly caused neonatal pneumonia accounted for 56.6%, of which 20.6% were *Escherichia coli*. Omphalitis was most caused by *Staphlococcus saprophyticus*, accounting for l9.6%. 48.5% of neonatal sepsis were caused by *Staphylococcus epidermidis* and *Staphylococcus saprophyticus*. 46.9% of impetigo neonatorum were caused by *Staphylococcus aureus* and 42.9% of conjunctivitis by *Staphylococcus epidermidis* and *Staphylococcus saprophyticus* (Table I).
2. Comparing the results of bacterial culture from samples taken from infections acquired outside of hospital (<48 hours after hospital admission) and nosocomial infections (≥48 hours after admission) of neonates in our hospital as shown in Table II: The most predominant species were *Staphylococcus epidermidis* and *Staphylococcus saprophyticus* in the group of infections acquired outside of hospital, while *Escherichia coli, Klebsiella* and *Pseudomonas aeruginosa* accounted for most in the group of nosocomial infections.

Antimicrobial susceptibilty and resistance

1. The situation of total antimicrobial susceptibility in the isolates from our neonatal ward is shown in Table III.

2. Table IV shows that the bacterial resistant rate to 15 kinds of antibiotics in nosocomial infections is significantly higher than infections acquired outside of hospital.
3. Total antimicrobial susceptible rate and resistant rate to antibiotics are in; Table III and Table IV, respectively.
4. The antimicrobial susceptible rate by combining two antibiotics is showed in Table V .

DISCUSSIONS

Bacterial infection is prevalent in newborn infants, especially the premature and very low birth weights (VLBW) infants. It is the important cause of neonatal death. With poor immunological functions, neonates may frequently be infected by the opportunistic or saprophytic bacteria which usually do not cause infections in older infants and adults, so there are various and complex pathogens in newborns. *Staphylococcus epidermidis* and *Staphylococcus saprophyticus* were prominent pathogens causing various neonatal diseases. These accounted for sepsis and conjunctivitis respectively, and caused pneumonia, im.petigo and omphalitis. To a certain extent, it reflects the epidemiological characteristic. of pathogens in neonates in our district in Chongqing.

In a hospital in Germany, 64% of nosocomial infections of preterm infants hospitalised in neonatal intensive care unit (NICU) were due to *Staphylococcus epidermidis*[3]. It is obvious that *Staphylococcus epidermidis* is an important pathogen of the newborns. From the distribution of bacteria between group I (infections acquired outside of hospital) and group II (nosocomial infections), *Staphylococcus epidermidis*, *Staphylococcus saprophyticus* and *Escherichia coli* were the three predominant species in Group I, while *Escherichia coli*, *Klebsiella* and *Pseudomonas* aeruginosa

Table III. The fatal susceptibility to bacteria1 iso1ates in neonatal infants.

Antimicrobial drugs	No.	Sensitive No.	Sensitive rate(%)
Ciprofloxacin	21	20	95.2
Tienam	73	64	87.7
Vancomycin	214	175	81.8
Norfloxacin	613	483	78.8
Amikacin	1747	1366	78.2
Cefoxitine	64	50	78.1
Polymyxin B	76	58	76.3
Ceftazidine	188	134	71.3
Cefotaxime	299	189	63.2
Cefoperazone	160	101	63.1
Cefuroxine	440	268	60.9
Cefazolin	1336	811	60.7
Tobramycin	77	43	55.8
Gentamycin	1631	878	53.8

Table IV. Comparing of the resistant rates belween infections acquired outside of hospital and nosocomial infections.

Antimicrobial drugs	Outside of hospital			Nosocomial			χ^2	p
	n	Resistant No.	Resistant rate (%)	n	Resistant No.	Resistant rate (%)		
Penicillin	948	774	81.6	175	161	92.0	10.6	0.0011
Ampicillin	940	777	82.7	250	240	96.0	27.2	0.0001
Oxacillin	364	200	54.9	43	32	74.4	5.2	0.0228
Erythromycin	991	704	71	184	155	84.2	13.1	0.0003
Cefazoline	1084	371	34.2	252	154	61.1	60.8	0.0001
Cefaperazole	118	36	30.5	42	23	54.8	6.8	0.009
Cefuroxime	378	132	34.9	62	40	64.5	18.4	0.0001
Cefradine	85	38	44.7	17	14	82.4	F *	<0.007
Cefotaxime	248	79	31.9	51	31	60.8	14.0	0.0002
Gentamycin	1327	555	41.8	304	198	65.1	53.1	0.0001
Amikacin	1419	280	19.7	328	101	30.8	18.5	0.0001
Karamycin	706	393	55.7	216	160	74.1	22.6	0.0001
Tobramycin	67	26	38.8	10	8	80.0	F *	<0.02
Chloromycetin	644	335	52	189	130	68.8	16.0	0.0001
Vancomycin	185	25	13.5	29	14	48.3	18.1	0.0001

* Fisher's exact test

Table V. Comparing of bacterial sensitive rates between single and combining two antimicrobial drugs.

Antimicrobial drugs and codes			Sensitive rates (%)		
a	b	n	a	b	a/b
Penicillin	Amikacin	833	17.8	86.2	89.0
Penicillin	Gentamycin	801	16.7	56.9	59.7
Penicillin	Karamycin	477	14.7	43.0	47.6
Penicillin	Chloromycetin	347	14.4	42.4	47.3
Penicillin	SMZ Co	243	17.7	23.5	35.4
Penicillin	Ampicillin	578	16.3	18.9	21.6
Cefazoline	Amikacin	1132	57.3	75.8	79.6
Cefazoline	Karamycin	445	44.5	38.2	58.4
Cefazoline	Ampicillin	806	55.1	13.8	56.1

were the three predominant species in Group II. Selection of antimicrobial drugs should be done by differentiating the above two types of infections. Table IV shows that the bacterial resistant rate to penicillins, cephalosporin, aminoglycosides, erythromycin, chloramphenicol and vancomycin in nosocomial infections group is significantly higher than that in the group of infections acquired outside of hospital. Preventing nosocomial infections could effectively control transmission of bacterial resistance.

Table III shows there are 14 kinds of antibacterials whose total bacterial sensitive rate was more than 50%, and heading the list was ciprofloxacin, a rate of 95.2%. The sensitive rate of norfloxacin to those bacteria was 78.8%. The above two drugs belong to the quinolones that are appropriate for treatment of infective diseases in neonates. But their adverse effcet on developing cartilage in the newborns is a deterrent factor and their use in pediatrics is restricted. Nevertheless, many reports on the outcome of the long-term use of quinolones in neonates and children have shown no definite skeletal, joint and cartilaginous toxicity[4,5].

The sensitive rate of amikacin to bacteria isolated in our hospital was up to 78.2%. Gotoff also recommended the use of amikacin in NICU if the infant had been prescribed other antimicrobial drugs recentIy or been infected by resistant strains[1], and are comparatively nontoxic. Susceptivity rates of tiernam and vancomycin were 87.7% and 81.8% respectively; they had better be used as second or third selection in our country because they are costly. For cephalosporin, especially the third - generations, the sensitivity rate ranged between 60.7% and 78.1%. Odio had reported that third-generation cephalosporins cover more of the pathogens implicated in neonatal sepsis and meningitis[6], hence are better choice as well.

It must be attended that 82.7% of strains isolated from infections acquired outside of hospital and 96% of strains isolated from nosocomial infections were resistant to ampicillin in our hospital, but only 6.7% of bacterial isolates in a medical unit of Norway is resistant to ampicillin[7]. Eighty-nine per cent of the methicllin-resistant coagulase-negative staphylococci were susceptible to netimicin as opposed to 17% to gentamycin[7], because presently netimicin is seldom used compared to gentamycin, whereas ampicillin was too widely used in our country causing a large number of ampicillin resistant strains to emerge. This is consistent with Gotoff's viewpoints that the frequently used antibiotics would speedily produce resistant bacterial strains[1].

CONCLUSIONS

Our experience showed that Gram-negative bacteria were mainly responsible for nosocomial infections of neonates in our hospital. Mainly, Gram-positive bacteria cause infections acquired outside of hospital. Nosocomial pathogens produced drug resistance readily. Combination of amikacin and penicillin can be recommended as empirical antibiotics for treatment of neonatal infections before the results of bacterial cultures and antimicrobial susceptibility tests are known. Antimicrobials must be administered according to the results of susceptibility tests. There exist different predominant pathogens and different antimicrobial sensitive patterns in different regions during this period.

REFERENCES

1. Gotoff SP. Infection of the neonatal infant. In: Behrman RE, Kliegmen RM, Jenson HB, eds. Nelson textbook of pediatrics. 16th ed. Philadelphia: Saunders, 2000; 546-9.
2. Murray PR, Baron EJ, Pfaller MA, et al. Manual of Clinical Microbiology, 6th ed, Washington DC: Amer Soc Microbiol, 1995.
3. Naumeister B, Kastner S, Conrad S, et al. Characterisation of coagulase-negative staphylococci causing, nosocomial infections in preterm infants. Eur J Clin Microbial Infect Dis 1995; 14:856-63.
4. Schaad UB. Use of fluorquinolones in pediatrics consensus report of an international society of causing nosocomial infections in preterm infants. Eur J Cin Microbial Infect Dis 1995; 14:856-63.
5. Schaad UB, Sander E, Wedgwood J, et al. Morphologic studies for skeletal toxicity after prolonged ciprofloxacin therapy in two juvenile cystic fibrosis patients. Pediatr Infect Dis J, 1999; 37:47-8.
6. Odio CM. Cefotaxime for treatment of neonatal sepsis and meningitis. Diagn Microbio Infect Dis 1995; 22(12):111-7.
7. Ronnostad A, Abrahamson TG, Gaustad P, et al. Antibiotic susceptibility of blood culture isolates after nearly two decades with netilmicin and ampicillin in neonatal septicacmia. APMIS 1999; 107:257-62.