Utilisation of Antimicrobials in Hospitalised Paediatric Patients

Medha A Joshi, MD*
Sathyendra Kasyap JV, MD**

ABSTRACT

To study the pattern of utilisation of antimicrobials, a one year prospective survey in a paediatric unit, including neonataology, was undertaken at MS Ramaiah Medical Teaching Hospital, Bangalore, India. The parameters studied to assess the appropriateness of the use were the choice of drug, dosage, duration, route of administration and whether the prescribing was therapeutic or prophylactic. Of the 200 cases analysed, 85% received antimicrobial agents (AMAs); 49% of these were found to be appropriate. The choice was inappropriate in 20%, the duration was too long in 28% and dosage was wrong in 3%. The most common route of administration was parenteral. In the paediatric ward prescription was largely therapeutic, whereas in neonataology it was prophylactic in 59% of the patients. Amikacin and cefotaxime were the two most commonly prescribed AMAs in neonatology. The clinical relevance of the prescription is discussed.

A study of the utilisation of antimicrobial agents (AMAs) is necessary for a positive approach to many problems arising from antimicrobials, their high cost and sequlae of use. Several studies of antimicrobial usage in hospitals from different parts of the world have reported 25-56% use of AMAs in hospitalised patients[1-3]. However, there are few reports on the paediatric services[4,5], which deal with somewhat different problems from those of the general population and may require a different approach in antimicrobial usage[6,7].

Children are more prone to viral infections which do not require AMA therapy and are also vulnerable to serious bacterial infections which require vigorous and prompt treatment.

Forceful promotion by medical representatives from various pharmaceutical industries, along with the ready availability of newer AMAs has brought a change in the approach of doctors towards their patients. Various problems of resistance, long term adverse reactions, high cost and irrational therapy need careful consideration[3,8,9]. One approach which would help to solve these problems would be to study the utilisation of antimicrobial agents in various disciplines. This study was undertaken in order to define the prescribing patterns in paediatric wards (including neonatology) at MSR Medical College, Bangalore, India.

METHODS

A prospective study of 200 randomly selected cases, out of 490 hospitalised paediatric patients, was conducted for a period of one year (January 1992 to December 1992). The proforma included information regarding age, sex, diagnosis, the number of AMAs prescribed, frequency of administration, dosage, route and duration of therapy, whether culture and sensitivity (C/S) tests were done and whether the AMAs were used prophylactically or therapeutically. An attempt was made to calculate whether the diagnosis of particular AMAs was justified and if the selection of AMAs was influenced by C/S tests.

*Professor & Head
**Assistant Professor

Department of Pharmacology
MS Ramaiah Medical College
Bangalore, India

Table 1
Number of AMAs, Prescription, Percentage of Patients Exposed

*No. of AMAs**	*Patients*	*Percentage*
Single AMA	58	29%
Two AMAs	110	55%
Three AMAs	19	9.5%
Four AMAs	10	5%
Five and above	3	1.5%

*AMA – antimicrobial agents

Table 2
Culture and Sensitivity Tests

*C/S Tests Done	22.5%
Appropriate AMAs** according to C/S report	22.2%
Treatment not according to C/S report	26.69%
No growth	51.11%

*C/S – Culture and Sensitivity
**AMAs – antimicrobial agents

RESULTS

Of the 200 cases selected for the study, 79 were from neonataology and 121 from paediatric unit. During the study period, 85% of these patients received antimicrobial agents. A total of 28 different AMAs were prescribed. The average number of AMAs given per patient per day was 2.5. Table 1 shows the percentage of patients receiving AMAs. The C/S test results are summarised in Table 2.

In the paediatric ward the use of AMAs was therapeutic, whereas in neonataology it was prophylactic, with 59% of the patients showing no signs of sepsis. The common route of administration was parenteral (intravenous / intramuscular), whilst the oral route was advised at the time of discharge. The duration of the stay ranged from 2 to 45 days (average 19.8 days) and in most of the cases, the patient received antimicrobials throughout the hospital stay.

Table 3
Commonly prescribed AMAs and their indications

Indications	*Commonly Prescribed AMA Combinations and AMAs#*						
	Cefotaxime + Amikacin	*Cefotaxime + Gentamicin*	*Ampicillin + Gentamicin*	*Crystalline Pencillin + Chloram-Phenicol*	*Ampicillin*	*Gentamicin*	*Cipro-floxacin*
Preterm *SFD/RDS/HMD	50	17	3	—	—	1	1
Respiratory Infections	6	1	14	1	25	2	—
Encephalitis	1	—	—	—	2	1	—
Congenital Anomalies	3	1	—	—	—	—	—
Pyogenic Meningitis	—	—	3	8	—	1	—
Gastroenteritis	—	—	3	—	2	11	—
Pericarditis	—	—	—	1	2	1	—
Enteric Fever	—	—	—	—	1	1	12
Liver Diseases	—	—	—	—	1	—	—
Renal Diseases	—	—	—	—	1	—	—
Post-Invasive Procedure	—	—	—	—	2	—	—
Staph. Pyemia	—	—	—	—	—	1	—
Miscellaneous	2	—	1	—	2	2	—
Total	62	19	24	10	38	21	13

AMAs – antimicrobial agents *SFD - Small For Date
* RDS – Respiratory Distress Syndrome
* HMD – Hyaline Membrane Disease

Table 3 shows the most common AMAs prescribed, along with their indications. The neonatal indications of antimicrobial use are summarised in Table 4.

Table 4
Indications for the use of *AMAs in Neonatal Ward

	Indications	*Number Affected*
1	Pre-term *SFD+*HMD+*RDS+Hypothermia Muconium aspiration + Pneumonia Birth asphyxia, Pneumothorax	51
2	Pre-term SFD + Hyperbilirubinaemia	7
3	Septicaemia Pre-term SFD + Sepsis Term SFD + Sepsis	12
4	Congenital Anomalies Tracheo-esophageal fistula with cleft palate Pre-term obstruction uropathy with valve with Hydronephrosis	3
5	Miscellaneous Term SFD with Hypoxic ischemia Encephalopathy with intracranial haemorrhage Meningitis, Ventriculitis	6
	Total	79

*AMAs – antimicrobial agents
*SFD – Small For Date
*HMD – Hyaline Membrane Disease
*RDS – Respiratory Distress Syndrome

Respiratory tract infections (87 patients) and gastroenteritis (21 patients) were the most frequent conditions seen in the paediatric ward. Ampicillin (27.55%) or gentamicin and ampicillin combination (14%) were frequently used in respiratory tract infections whereas gentamicin was used in 52.4% of patients with gastroenteritis. Of the enteric fever cases, 12 (66.6%) were treated with ciprofloxacin and none were given chloramphenicol.

In neonatology, for Small For Date (SFD) babies with Hyaline Membrane Disease (HMD) with or without clinical sepsis, cefotaxime and gentamicin or cefotaxime and amikacin were most frequently prescribed. The duration of therapy varied from 7 to 15 days.

DISCUSSION

The incidence of antimicrobial use reported from hospitalised patients in developing countries has been 57% in Bangladesh[10] and 56.1% in India[11], but only 26.5% to 32% in South African University Hospital[2]. Various studies have shown a steady increase in antimicrobial use over the last decade[11,12]. In our study, the 85% usage may be due to the fact that our centre is a tertiary referral hospital which receives serious cases only, also because of better diagnostic facilities and increased availability of AMAs.

It was observed that during the period of study gentamicin was the common aminoglycoside prescribed for neonates for the first three months of study, after which amikacin was substituted without substantial bacteriological support. Amikacin has the unique advantage of being resistant to aminoglycoside inactivating enzymes and should be kept as a reserve drug for nosocomial gram negative infections resistant to gentamicin. Routine use of this drug with the resultant development of resistance will leave us without a reserve drug for life threatening infections[14]. Though organisms were sensitive to AMAs such as furazolidine, cephalexin and neomycin, gentamicin was the most common AMA prescribed for gastroenteritis. International recommendations put ampicillin, cefazolin, furazolidine and nalidixic acid before gentamicin as the first line of treatment.

Ciprofloxacin was used routinely for the treatment of enteric fever. Though some reports[15,16] have shown the four newer quinolines to be safer in the paediatric age group, the long term side effects like development of arthropathy and haematuria[17,18] make their use undesirable. So, if salmonella typhi is resistant to the older established drugs, third generation cephalosporins like ceftriaxone and cefaperazone could be used instead of ciprofloxacin[19,20].

The duration of therapy, mainly prolonged therapy, was also found to be inappropriate. Unnecessarily prolonged therapy leads to adverse reactions and promotes emergence of resistant strains and superinfections. In one case of pyogenic meningitis, crystalline penicillin and chloramphenicol were given for 25 days. The recommended duration in the paediatric age group is a minimum of ten days, or five days after the patient has become afebrile. In the same case the dose of penicillin administered (6 million units/day) was also much higher than the recommended dose of 400,000 units/kg/day (2 million units in this patient). Although penicillin is

usually a very safe drug, during meningial infections the CSF concentration reached is higher and can result in convulsions.

There was also another patient with tracheobronchitis who was treated with cephalexin for 15 days, cephazolin for 9 days and gentamicin for 18 days. Such unscientific use of antimicrobial combinations should be discouraged. The dosage and dose interval were appropriate in almost all patients.

With the exception of one case in which thrombocytopenia was recorded after the use of cefotaxime, no adverse reactions were noted. Lack of data on adverse effects does not necessarily indicate the absence of such events. It is necessary to be vigilant, and recording relevant observations is especially important when newer drugs are being used.

In the neonatal ward, all infants (n=79) admitted were put on AMAs. In 47 patients (59%), their use was prophylactic. In 25 patients (32%), the infants were clinically septic and in seven of those there was bacteriologically proven sepsis. The other indication for prophylactic use of AMAs was positive testing for CRP, which was done in 27 cases and found to be positive in 23 of these. There were 27 patients with no strong clinical evidence of sepsis and one negative investigation for sepsis; this patient received antibiotics which were continued for more than 48 hours.

The possible reasons for the absence of sepsis in these patients were (i) the non-specific nature of signs of sepsis in neonates (ii) physicians' reluctance to stop AMAs once started and (iii) the logistic difficulty of obtaining routine culture results at weekends. In these cases a combination of cefotaxime and gentamicin or amikacin was used prophylactically as well as therapeutically. Sensitivity of gram negative organisms to a single AMA like gentamicin (74%) or cefotaxime (79%) was much less, compared to the combination of cefotaxime and gentamicin (94%) or cefotaxime and amikacin (96%). Hence the use of AMA combination is bacteriologically justifiable although change of aminoglycoside is not.

Appropriate use of AMAs was seen in only 49% of patients. The choice was inappropriate in 20% of patients. Inappropriate use was seen in the continued use of a particular AMA even after the C/S reports showed resistance. This was seen in 27% of the samples sent for C/S tests. This could be due to good clinical response in spite of the in-vitro resistance. The total number of samples sent for the C/S test was also very low (22.5%). A similar trend is seen in other countries too[13]. The reasons why use of AMAs was deemed inappropriate were (i) the unnecessary change of one AMA to another, (ii) the continued use of a drug against organisms resistant to its effect, and (iii) use of AMAs which are contraindicated in the paediatric age group. The duration of therapy was too long in 28% of patients whereas the dosage was too high in 3% of patients.

CONCLUSION

In the study period of one year, 85% of the patients received antimicrobials. The prescription was appropriate in 49% of patients. AMA combinations were prescribed in 51%. The use of ciprofloxacin should be avoided in the paediatric age group. In neonatology the prophylactic use was for too long a period. This high prevalence of exposure to potentially toxic AMAs needs to be restricted to a minimum. Periodic drug utilisation surveys such as this will help to monitor the shortcomings in pharmacotherapy and avoid repetition in the future.

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