Paediatric Severe Community-Acquired Pneumonia in India

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ABSTRACT

Aim: To evaluate the prescribing patterns of antibiotics and antipyretics and their dosage for severe community-acquired pneumonia (SCAP) in a paediatric population before and after an educational intervention in a rural Indian hospital.

Method: Physician prescribing patterns for SCAP were collected prospectively in a cohort of paediatric patients (pre-intervention group). An educational intervention strategy was developed and implemented using data from baseline prescribing patterns and the *Therapeutic Guidelines: Antibiotic* recommendations for treatment of SCAP. An analysis to evaluate the impact of drug selection and dosing following the intervention was conducted in a second patient cohort (post-intervention group).

Results: There were 146 patients in the pre-intervention group and 155 in the post-intervention group. Antibiotic choices were within the guidelines in both groups. All of the patients in the pre-intervention group received dexamethasone with every dose of antibiotic. Post-intervention, the use of dexamethasone was eliminated. For the pre-intervention group, 97% of the antibiotic doses and 55% of the antipyretic doses were classified as inappropriate. Inappropriate prescribing of antibiotic and antipyretic doses was significantly reduced to 89% ($p = 0.002$) and 10% ($p < 0.001$) respectively, following the intervention.

Conclusion: There was some improvement in prescribing appropriate doses of antibiotics and antipyretics for SCAP following the educational intervention.

J Pharm Pract Res 2005; 35: 183-6.

INTRODUCTION

Lower respiratory tract infections are a common cause of mortality in developing countries and are a major cause of morbidity in children worldwide.[1] The incidence of pneumonia in these countries is up to ten times higher than in developed countries. Pneumonia can place an enormous economic and public health burden on the healthcare system of a developing country.[2,3]

Each year approximately two million children under the age of five years die of pneumonia, accounting for one-fifth of childhood deaths worldwide.[4] Children in developing countries have a high incidence of bacterial pneumonia, risk factors that predispose them to severe infections, and limited access to effective medical care. The risk factors include large family size, overcrowding, being the youngest in the family, low birth weight, lack of breastfeeding, malnutrition, vitamin A deficiency and exposure to smoke from cooking on open stoves with biomass fuels.[5,6]

In India health insurance is uncommon especially in rural areas. Most patients pay physician fees and hospital and drug costs from the family income. The ability to pay has obvious implications for the prescribing of drugs and subsequent treatment of infections in this patient group. Almost all of the current knowledge of prescribing trends has been derived from studies conducted in developed countries. This data may not be relevant for developing countries in view of differing health and financial problems, and priorities. The lack of data prompted this study in a rural paediatric hospital in India. Local physician prescribing patterns for the treatment of severe community-acquired pneumonia (SCAP) was reviewed.

The aim of the study was to evaluate the prescribing patterns of antibiotics and antipyretics and their dosage for SCAP in a paediatric population before and after an educational intervention.

METHOD

A prospective cohort study was conducted at Srujan Hospital for Sick Children, a 60-bed rural paediatric hospital in Andhra Pradesh, India. The study population was divided into two groups: a pre-intervention group (studied in July 2002 for three weeks) and a post-intervention group (studied in September 2002 for three weeks). The educational intervention was introduced on 5 August 2002.

All outpatients under 18 years of age and diagnosed with SCAP were included. Inpatients were excluded from the study. Pre-intervention patients were excluded from the study in the post-intervention phase. The diagnosis of SCAP was made by the paediatrician and indicated on the prescription. Although hospitalisation is common with SCAP, it is not affordable for many in rural India. It is therefore common for this population to receive treatment as an outpatient.

The intervention strategy involved a verbal presentation of the pre-intervention study results to the paediatricians and the recommended drugs and dosages for SCAP according to the *Therapeutic Guidelines: Antibiotic* (TG:A)—Appendix 1.[7] A dosing chart was provided to the prescribers with dosing schedules according to patient weight. The dosing charts were also placed in physicians' consulting rooms and wards.

According to the study criteria, an inappropriate choice of drugs were those in variance with the TG:A.[7] An appropriate dosage was one prescribed within ± 25% of the recommended dose. The designated dosage error of ± 25% was based on the common variability allowed in dosage forms and bioequivalence studies.

An investigator collected data from the prescription while the patients were paying their fees after visiting the paediatrician. The patients had no insurance or fee-for-service coverage. The data was collected during hospital visiting hours during a three-week period before and after the intervention.

Data collected were patient demographics (age, weight, sex); drug name, dosage, frequency, route and number of doses prescribed. The weight of most patients was not available on the prescription. The investigator weighed each patient in his office in the pre-intervention group. In the post-intervention group, patients were weighed and results were written on the empty prescription forms by nursing assistants before patients visited the paediatrician. The nursing assistants notified

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the investigator whenever the diagnosis of SCAP was recorded. The study did not collect data on how the paediatrician made a diagnosis of SCAP. The hospital does not have a pharmacist or nursing staff. All prescribing was by paediatricians.

The prescribing data were compared for appropriateness with TG:A[7] and *Therapeutic Guidelines: Analgesic*.[8] Populations were compared for demographics and the influence of the intervention by chi-square analysis. Differences in parametric data were tested using Student's t-test. Based on a = 0.05 and b = 0.2 and a 20% change in drug prescribing and dose prescribing required, a minimum sample of 80 patients in each group was needed to achieve statistical significance.

As this study involved an analysis of patients' prescription data, ethical issues related to confidentiality and release of data. A unique non-patient identifiable code was allocated to each prescription to enable re-identification (if necessary) from the hospital's duplicate copy of the prescription. Any coded data to leave the hospital was kept secure in accordance with the National Health and Medical Research Council guidelines, with only group data released from the research.[9] Informed consent was not required, since the study was classified as a quality control audit and the treatment was within standard of care for SCAP and prescribed independently of the study. The Curtin University of Technology Ethics Committee approved this study.

RESULTS

There were 301 patients of which 146 were in the pre-intervention group and 155 in the post-intervention group. There were 61 (42%) females and 85 (58%) males in the pre-intervention group and 63 (41%) females and 92 (59%) males in the post-intervention group (p = 0.8). The mean age of patients in the pre-intervention group was 2.4 years and in the post-intervention group was 3.6 years with a statistically significant difference between the two groups (p < 0.001).

Pre-Intervention Group

In the pre-intervention group, 99% of patients received antibiotics that met TG:A recommendations for SCAP (144 with ceftriaxone and two with cefotaxime). In addition to antibiotic therapy all patients received dexamethasone (200–500 mg/kg/per day) with every dose of antibiotic (to prevent an anaphylactic reaction).

Of the 144 patients on ceftriaxone in the pre-intervention group, the appropriate dose was prescribed in 3 (2%) and 141 (98%) received doses less than recommended (Table 1). The only other antibiotic prescribed in pre-intervention group patients was cefotaxime. Of the two patients treated with cefotaxime, one received three doses and was on an appropriate dosage. The other patient received 10 doses that were 26 to 50% below the recommended dosage.

Antipyretics, specifically paracetamol, are commonly prescribed in children with SCAP. There were 137 (94%) patients in the pre-intervention group receiving paracetamol and the other 9 (6%) did not receive an antipyretic. Of the patients who received paracetamol, 61 (45%) were on an appropriate dosage and 76 (56%) were on doses below or above the recommended dosages (Table 2).

Post-Intervention Group

There were 155 patients in the post-intervention group with all patients receiving ceftriaxone for SCAP, in line with the TG:A recommendations. Post-intervention, none of the patients received dexamethasone with the antibiotic (p < 0.001). Antibiotic dosing improved significantly from the pre-intervention group to the post-intervention group (p = 0.002). In the post-intervention group, 17 (11%) patients were on an appropriate dosage and 138 (89%) were on doses below the recommended level. There were 152 (98%) patients in the post-intervention group who received paracetamol. Dosing of paracetamol also improved significantly (p < 0.001) with 137 (90.1%) patients in the post-intervention group receiving the correct dose (Table 2).

Table 1. Ceftriaxone dosage in pre-intervention and post-intervention groups

	Pre-intervention		Post-intervention	
Category	**No. patients (n = 144)**	**No. doses (n = 1021)**	**No. patients (n = 155)**	**No. doses (n = 1354)**
Appropriate dose	3 (2%)	16 (1.6%)	17 (11%)	146 (11%)
26-50% below recommended dose	136 (95%)	971 (95%)	14 (9%)	124 (9.1%)
51-75% below recommended dose	5 (3.5%)	34 (3.3%)	121 (78%)	1060 (78%)
76-100% below recommended dose	-	-	3 (1.9%)	24 (1.8%)

Table 2. Paracetamol dosage in pre-intervention and post-intervention groups

	Pre-intervention		Post-intervention	
Category	**No. patients (n = 137)**	**No. doses (n = 1501)**	**No. patients (n = 152)**	**No. doses (n = 1992)**
Appropriate dose	61 (45%)	687 (46%)	137 (90%)	1806 (91%)
26-50% below recommended dosage	9 (6.6%)	108 (7.2%)	14 (9.2%)	171 (8.6%)
51-75% below recommended dosage	1 (0.7%)	9 (0.6%)	-	-
26-50% above recommended dosage	24 (18%)	241 (16%)	-	-
51-75% above recommended dosage	27 (20%)	300 (20%)	1 (0.7%)	15 (0.7%)
76-100% above recommended dosage	7 (5.2%)	72 (4.8%)	-	-
> 100% above recommended dosage	8 (5.8%)	84 (5.6%)	-	-

DISCUSSION

Results of this study showed that there was an improvement in the choice and dosage of antibiotics and antipyretics prescribed for patients with SCAP following an educational intervention. Although our study demonstrated some improvement in the appropriate ceftriaxone dosage, there were still a number of patients on inappropriate antibiotic dosages. Suboptimal dosing of antibiotics has two potential consequences: therapy failure and emergence of bacterial resistance. In developing countries the widespread misuse of antibiotics, in combination with the spread of antibiotic resistance, has rendered several conventional antibiotics virtually useless.[10]

In the pre-intervention group, 98% of patients were prescribed antibiotic dosages below the recommended dose, compared to 89% in the post-intervention group. The prescriber has the responsibility to ensure the delivery of an appropriate antimicrobial to the site of an infection in concentrations that exceed those needed to inhibit the growth of the pathogen involved. This was not occurring enough in the patient group studied.

There was a significant difference in the mean age of patients in the two groups and, while the difference was small, it may have had an impact on the prescribing patterns and data analysis. The paediatricians tended to prescribe ceftriaxone dosages according to the strengths available (125 mg, 250 mg, 500 mg, 1 g) rather than calculate the dose based on the patient's weight. Therefore, patients were either receiving low doses or high doses and sometimes by chance receiving the correct doses. The slight improvement in the prescribing of ceftriaxone dosage in the post-intervention group (11% vs 2%) may be due to chance rather than the impact of the intervention and is most likely clinically insignificant. As only 11% of patients received the correct antibiotic dosage, it is apparent that the impact of the intervention was very low.

A possible reason for the large number of post-intervention group patients receiving 51 to 75% below the recommended dosage (78% vs 3.5%), is the older population in the pre-intervention group. Since the paediatricians were prescribing fixed strengths of ceftriaxone, the slightly older post-intervention group were probably heavier in weight, leading to the lower amount (as mg/kg) of ceftriaxone prescribed.

Most paediatric patients with SCAP in rural India are treated as outpatients. Most families cannot afford inpatient treatment due to high hospital costs. The majority of families have both parents working so there would also be a loss of income if one or both of the parents stayed with their child for inpatient treatment. Most families are from small villages surrounding the hospital and tend to visit for a consultation and medicines only. The hospital cannot accommodate every sick child due to a limited number of beds available.

Possible reasons for inappropriate prescribing included: high antibiotic costs, low monthly incomes, poverty, no medical insurance, and lack of government subsidised medicines. For example, the cost of ceftriaxone treatment for a patient with SCAP weighing 25 kg and below 10 years of age, would be Rs 165 (US$3.75).[11] The mean duration of treatment for SCAP is 7 to 10 days. It therefore costs between Rs 1155 (US$26.25) and Rs 1650 (US$37.5) per course for antibiotic treatment. In comparison to the antibiotic costs, the consultation fees, cost of paracetamol and other indirect costs are very low.

In India, monthly per capita consumer expenditure was Rs 531 (US$12) for rural areas in July to December 2002.[12] Most patients cannot afford the total treatment costs; they buy medications for a reduced number of days than the prescribed number. In an attempt to enhance patient compliance over the total duration of the course, paediatricians tended to prescribe low antibiotic dosages as evidenced in the prescribing of dosages of ceftriaxone following the intervention. This was not the case with paracetamol since it is affordable. Prior to our intervention, prescribers were not routinely aware of the weight of the patient. Once the dosing chart and weights of the patients were provided, there was a significant improvement in the doses of paracetamol prescribed. Although the intervention was relatively small and short, it demonstrated that pharmacists can have a positive impact on drug prescribing.

Ceftriaxone, a broad spectrum third-generation cephalosporin with a long half-life, and excellent bioavailability when administered intramuscularly, allows once-daily treatment for pneumonia and other severe community-acquired infections. It is also effective against many bacterial infections.[13-15]

In a study by Dagan et al, infants and children with community-acquired serious infections were safely and effectively treated as outpatients using a regimen of once-daily intramuscular ceftriaxone.[15] A retrospective study, showed that ceftriaxone was efficacious for the completion of therapy on an outpatient basis after the drug had been initiated during hospitalisation for infants and children with serious infections.[16]

Dagan et al. have also shown that there was a saving of 376 days of hospitalisation for the 72 successfully treated patients.[15] The only cost during their treatment was for ceftriaxone and the daily clinic visits. This represents a considerable financial saving compared with the cost of inpatient management for those conditions. Furthermore all successfully treated patients and their parents resumed normal activity within three days of initiation of treatment.

At Srujan Hospital, dexamethasone was prescribed with every dose of parenteral antibiotic to prevent an anaphylactic reaction. TG:A does not recommend steroid administration with parenteral antibiotics. Steroids in pharmacological doses depress cell-mediated immunity more than humoral immunity, leading to an impairment of monocyte/macrophage killing, antigen processing, and cytokine release. They may potentiate infection with intracellular pathogens due to suppression of release of γ-interferon, interleukin-1, and interleukin-2 from T-lymphocytes.[17] Stuck et al. have reported that the overall rate of infection in patients receiving systemic corticosteroids was 13%.[18] Dexamethasone was prescribed for all patients in the pre-intervention group and none in the post-intervention group. No patients were readmitted to the hospital due to an anaphylactic reaction during the study period.

Paracetamol, an antipyretic, is widely used in children. It has a good safety profile within the recommended dosage range. The antipyretic effect of paracetamol is directly related to its plasma concentration.[19] However, toxicity has been rarely reported with therapeutic doses when administered over several days in children who have concurrent illnesses such as fever, vomiting, or diarrhoea.[8]

In this study, 45% of children in the pre-intervention group received antipyretic doses above those recommended. Of particular concern were the eight children who were prescribed more than 100% of the recommended dose. In addition to the immediate concern, medically prescribed dosages of medicines that are easily available over-the-counter, such as paracetamol may lead to these dosages being continued.

In India, the government subsidises health care with free medical care and medicines, available in public hospitals. According to the 1998-1999 annual report from the Government of India, there were 14 000 hospitals, 810 538 hospital beds, 22 243 primary healthcare centres and 131 471 subprimary health centres of which all are government owned. In all, 503 900 doctors were providing services to patients.[20] Considering the size of the population, the number of facilities available is low and below the World Health Organization recommendations. Many patients, therefore, visit private hospitals or clinics run by physicians to ensure access to medical care.

The World Health Organization recommends intramuscular ampicillin/penicillin for children under five years of age diagnosed with severe pneumonia. The physicians at Srujan Hospital for Sick Children argue that the patients who regularly visit the hospital have developed resistance to these drugs. No published data in India or elsewhere is available to support this argument. We believe the prescription of third-generation cephalosporins for SCAP for this patient group is more due to social and cultural factors than a lack of prescribing knowledge.

Following the intervention, there was little impact on the level of appropriate prescribing of ceftriaxone dosage and paediatricians have continued prescribing low doses of antibiotics to enhance patient compliance. Significant improvement was achieved in the level of appropriate prescribing of paracetamol dosage and following the intervention none of the patients were prescribed dexamethasone. Social and economic factors may influence the prescribing of expensive drugs in rural India. Review of prescribing practices may optimise the use of drugs in this region and assist in rationalising therapy to give the best patient outcome for the money spent.

Acknowledgements
We are grateful to Dr KP Rao, paediatrician, Srujan Hospital for Sick Children, for his invaluable support during the data collection and KC Coley, Associate Professor, School of Pharmacy, University of Pittsburgh in the preparation of the manuscript. We also thank J Ramesh, M Venkatesh, G Suresh, T Tirupathi and all the staff at the hospital for their assistance during the study.

Competing interests: None declared.

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Submitted: October 2004
Accepted after external peer review: June 2005

Appendix 1. Recommendations for severe community-acquired pneumonia[7]

Patient category	Antibiotics recommended
Children > 10 years	erythromycin 10 mg/kg up to 0.5-1 g IV, 6-hourly PLUS benzylpenicillin 30-60 mg/kg up to 1.2 g IV, 4 to 6-hourly PLUS gentamicin 6 mg/kg IV, daily
Children > 10 years (hypersensitive to penicillin)	ceftriaxone 50 mg/kg up to 1 g IV, daily OR cefotaxime 50 mg/kg up to 1 g IV, 8-hourly
Children < 10 years	cefotaxime 50 mg/kg up to 1 g IV, 8-hourly OR ceftriaxone 50 mg/kg up to 1 g IV, daily PLUS di(flu)cloxacillin 50 mg/kg up to 2 g IV, 4-hourly
All children	If required, oral paracetamol 20 mg/kg 6-hourly or 15 mg/kg 4-hourly