Original Research Article

Usage of antibiotics and monitoring of drug interactions in pediatrics at a tertiary care teaching hospital

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ABSTRACT

Background: Respiratory tract infections (RTI) are more common in pediatrics. Especially in developing countries like India, RTI causes more death in children. Antibiotics are used to treat RTI even in case of viral infections. Hence rational use of antibiotics is very much needed to avoid antibiotic resistance. In this study we have analysed the prescribing pattern of antibiotics and their drug interactions involved in the management of respiratory tract infections in a tertiary care teaching hospital.

Methods: A prospective observational study was conducted in the department of pediatrics at a tertiary care teaching hospital for a period of 6 months (November 2019-April 2020). A total of 144 patients were included in the study and their prescription was analysed for their antibiotic prescribing pattern and interactions.

Results: Infants were more prone to RTI infections. Among RTI, lower RTI were more common in children. We have analysed prescribing pattern of antibiotics in which, mono antibiotic therapy were more commonly used. Ampicillin was the frequently prescribed antibiotic. Azithromycin had the most possible interactions among the antibiotics prescribed.

Conclusions: More than 336 antibiotics were used for all types of RTI, even in the case of viral infections. So rational use of antibiotics is needed. Among 144 children who were enrolled in the study, none of them were subjected to culture sensitivity test. As of which, all of them were treated empirically. Penicillin and cephalosporin are the mostly prescribed antibiotics in RTI. Cephalosporin prescribed children had less hospital stay and hardly interactions were found.

Keywords: Antibiotics, Children, Respiratory tract infection, Cephalosporin

INTRODUCTION

Respiratory tract infection (RTI) is defined as any type of infection that occurs in the upper and lower respiratory tract. Children and infants are more sensitive to this type of infection. RTI results in 1.9 million death per year in developing countries, of these 20% are from India. In developing countries, children younger than 5 years are more susceptible to acute RTI and carry high mortality rate especially in children less than age of 24 months.1 Most of the respiratory tract infections are due to viruses and only few are due to bacteria. The most common bacteria that causes infection include Streptococcus pneumonia, Haemophilus influenza, and Moraxella catarrhalis. Viruses which are responsible for infection in children and infants includes rhinovirus, para influenza virus, adenovirus, measles virus and corona virus disease (COVID) (one of the recently identified disease which is affecting many countries globally).2
Upper RTI and lower RTI are the two types of RTI. Although most of the RTIs are caused due to viruses, antibiotics were prescribed as primary treatment. Most of the children had received antibiotics once they were diagnosed as RTI patient. In some cases inappropriate use of antibiotics results in antibiotic resistance, morbidity and mortality. Rational use of antibiotics will reduce the problems associated with antibiotic usage such as antibiotic resistance, morbidity and mortality. Drug interactions occurs usually when the prescribed drug reacts with one another or with foods and other beverages consumed by the patients. Sometimes this type of reaction produces harmful effects. Harmful interactions is one of the important causes of 10-20% of the adverse reactions. These conditions require hospitalisation and some of them are life threatening.

Objective of the study is to analyse the antibiotic usage in the management of RTI on paediatric patients. And monitoring drug interactions of antibiotics in the management of RTI on paediatric patients.

METHODS

It was a prospective observational study. The study was conducted in the department of paediatrics at Rajah Muthiah Medical College and Hospital, Annamalai University, Chidambaram, Tamilnadu, a 1400 bed multi-specialty tertiary care teaching hospital located in south India. The duration of the study was 6 months (November 2019 to April 2020).

Statistical tool

Microsoft excel 2013 was used as the statistical tool.

Ethical approval

The study was approved by institutional human ethics committee (approval letter no. IHEC573/2019)

Sample size

Rao soft sample size calculator was used. Sample size was 144. For 95% confidence level, confidence interval was 8%.

Inclusion criteria

Patient of both gender who were less than 12 years of age with RTIs and patients who were admitted in the department of paediatrics were included in the study.

Exclusion criteria

Patient who had other infections other than RTI and patients who were unwilling to participate in the study were excluded.

In this study the patient’s data and their prescription data was collected. From the above collected data, the antibiotics and their prescribing pattern were analysed. Their drugs chart was analysed to find the possible drug interactions and it was recorded.

RESULTS

A total of 144 RTI patients data were collected among which N=76 (52.7%) were infants (28 days – 2 years) (Table 1).

Table 1: Age wise classification of RTIs.

| Age classes          | No. of RTI | Percentage |
|----------------------|------------|------------|
| Neonates (0-28 days) | 6          | 4.16       |
| Infants (28 days-2 years) | 76      | 52.7       |
| Young child (2 years-6 years) | 36      | 25         |
| Child (6 years-12 years) | 26       | 18.05      |
| Total               | 144        | 100        |

Lower RTIs are more common in children. In the 144 RTI patients N=88 (61%) were males (Table 2).

Table 2: Disease wise classification of RTIs.

| Disease                | No. of male affected | No. of female affected | Total |
|------------------------|----------------------|------------------------|-------|
| URTI (unspecified)     | 6                    | 2                      | 8     |
| Common cold            | 2                    | 0                      | 2     |
| Pharyngitis            | 10                   | 6                      | 16    |
| Tonsillitis            | 14                   | 0                      | 14    |
| Laryngitis             | 0                    | 0                      | 0     |
| Sinusitis              | 0                    | 0                      | 0     |
| LRTI (unspecified)     | 22                   | 14                     | 36    |
| Bronchopneumonia       | 12                   | 18                     | 30    |
| Bronchitis             | 14                   | 10                     | 24    |
| Both                   | 8                    | 6                      | 14    |
| Total                  | 88                   | 56                     | 144   |

Ampicillin was the most frequently used antibiotics in the treatment of RTI. Mono antibiotic therapy N=68 (47%) was more commonly used prescribing pattern of RTIs. In mono antibiotic therapy, cephalosporin prescribed patients had the least hospital stay (N=24) 3.7 days (Table 3 and 4).

Table 3: Patterns used in RTI.

| Pattern                  | Number of used | Percentage |
|--------------------------|----------------|------------|
| Mono antibiotic therapy  | 68             | 47         |
| Dual antibiotic therapy  | 58             | 40         |
| Triple antibiotic therapy| 18             | 13         |
Among all the three therapies, mono therapy cephalosporin class drugs had the least hospital stay to prove some efficacy. In cephalosporin third generation drugs such as cefotaxime and ceftriaxone were the mostly used drugs (Table 5).

**Table 4: Mono antibiotic therapy.**

| Antibiotics classes | No. of times used | Average hospital stay (days) |
|---------------------|-------------------|-----------------------------|
| Cephalosporin       | 24                | 3.7                         |
| Macrolide           | 4                 | 4                           |
| Penicillin          | 40                | 4.1                         |

Dual antibiotic therapy was mostly used after mono therapy. In this penicillin and aminoglycosides had less hospital stay of (N=10) 4.4 days. In penicillin class piperacillin, amoxicillin and ampicillin are mostly used in aminoglycosides, amikacin and gentamicin are mostly used (Table 6).

Trio antibiotic therapy was used for severe RTI patients only. It has long hospital stay than other therapy and used in least amount of patients (Table 7).

Totally 85 possible drug interactions were founded. Azithromycin had 32% of drug interactions. Most of the interactions were moderate drug interactions. Cephalosporin had no drug-drug interactions. These are possible drug Interaction which analyzed from their prescription. Azithromycin mostly interact with ampicillin, amoxicillin, piperacillin (Figure 1 and 2).

**Table 5: Usage of antibiotics in RTI.**

| Antibiotics used for RTI | No. of times used | Percentage |
|--------------------------|-------------------|------------|
| Amikacin                 | 12                | 10.61      |
| Ceftriaxone              | 13                | 11.50      |
| Gentamicin               | 11                | 9.73       |
| Ampicillin               | 26                | 23         |
| Azithromycin             | 14                | 12.38      |
| Amoxicillin              | 14                | 12.38      |
| Cefotaxime               | 16                | 14.15      |
| Cefpodoxime              | 5                 | 4.42       |
| Doxycycline              | 1                 | 0.88       |
| Norfloxacin              | 1                 | 0.88       |

**Figure 1: Percentage of drug interactions in antibiotics.**

| Class 1     | Class 2     | No. of times used | Average hospital stay (days) |
|-------------|-------------|-------------------|-----------------------------|
| Macrolides  | Cephalosporin | 8                 | 6                           |
| Penicillin  | Macrolides  | 16                | 5.1                         |
| Aminoglycosides | Cephalosporin | 14               | 4.5                         |
| Penicillin  | Cephalosporin | 4                 | 4.5                         |
| Penicillin  | Aminoglycosides | 10              | 4.4                         |
| Penicillin  | Fluroquinolones | 6              | 7                           |

**Table 6: Dual antibiotic therapy.**

| Class 1         | Class 2     | Class 3     | No. of times used | Average hospital stay (days) |
|-----------------|-------------|-------------|-------------------|-----------------------------|
| Penicillin      | Macrolides  | Aminoglycosides | 6                 | 4.3                         |
| Aminoglycosides | Macrolides  | Cephalosporin | 8                 | 8                           |
| Cephalosporin   | Penicillin  | Macrolides  | 2                 | 12                          |
| Aminoglycosides | Penicillin  | Fluroquinolones | 2              | 5                           |

**Table 7: Triple antibiotic therapy.**
In this study a total of 144 respiratory tract infected patients were included based on the inclusion and exclusion criteria. Among them demographic results shows that infants (28 days to 2 years) were more sensible (53%) to the RTIs. Prescribing pattern of antibiotics were classified into mono antibiotic therapy, dual antibiotic therapy, triple antibiotic therapy. The effectiveness of antibiotics were studied by average hospital stay of patients prescribed with different classes of antibiotics because in 144 patients, none were advised to or had undergone culture sensitivity test. The issues related to antibiotic resistance can be solved by making the practitioners aware of the treatment for RTI. There are many studies related to antibiotic use in hospitals. The information regarding antibiotics use provides a constructive approach in solving problems arising from multiple antibiotic use.\textsuperscript{5}

Prescribing indicators has been developed by World Health Organization (WHO) in a collaborative work with international network for rational use of drugs. Prescribing indicators is defined as the indicators used to measure the performance of health care providers in several key dimensions related to appropriate use of drugs. It is being used to detect various problems in prescribing practices such as polypharmacy, inclination for branded products, overuse of antibiotics or injections and prescribing out of formulary or essential drug list.\textsuperscript{5,6}

Males are more likely to get RTI which to be found similar in (58.57%) in Choudhry et al this study conducted in India at Gauhati hospital.\textsuperscript{7}

Average hospital stay for RTI is more than 5 days which to be found similar in Akbari et al study which was 6 days.

Macrolides had more drug interactions than other antibiotics (32%), which similar in the other study by Akbari et al conducted in Sagar hospital, Bengaluru, India.\textsuperscript{8}

But triple antibiotic therapy was used for severe RTI patients so ultimately they had much longer hospital stay than others the same reflected in this study. Triple antibiotic therapy patients had more average hospital stay. Average hospital stay in triple antibiotic therapy was 7 days.\textsuperscript{9,10}

In the current study all the study patients diagnosed with LRTI were prescribed with antibiotics. However, in a study conducted by Malladi et al, the antibiotic prescribing for LRTI was found to be 57%.\textsuperscript{11} The percentage of antibiotics prescribed for LRTI in a study conducted by Naik et al was found to be 46.87%.\textsuperscript{12} In the present study the most commonly prescribed antibiotics is penicillin (35.59%), macrolides (23.38%), cephalosporin (30.08%) and aminoglycosides (20.35%). The study conducted by Tobia et al found the following antibiotic class being commonly prescribed, macrolides (27%), penicillin (22%), quinolones (12%) and cephalosporin (1%). The study conducted by Malladi et al found that cephalexin’s were the most commonly prescribed antibiotics. The study conducted by (Naik et al., 2013) found the antibiotic use for RTI as follows: cephalexin’s (55.55%), macrolides (37.77%), penicillin (11.11%), and quinolones (8.88%).\textsuperscript{13,14}

In this study cephalexin antibiotics were not involved in any kind of drug interactions. In those 85 interaction which found to be similar with Akbari et al conducted in Sagar hospital, Bengaluru, India.\textsuperscript{15}

Limitation of this study is in all 144 efficacy of antibiotics only studied from prescription analysis only. None of them are monitored from patients so all are possible drug interactions only.

**CONCLUSION**

The most commonly affected pediatric population were infants. Male children were more likely to get RTI. Mono antibiotic therapy was mostly used in this study than dual and triple antibiotic therapy.

Macrolides have more drug interactions. Cephalexin has less hospital stay and has no drug interactions. From this study it can be concluded that the rational and cautious use of antibiotics will reduce the event of multi-drug resistance.

The medication error and drug interactions are moderate in RTI although clinical pharmacist will be needed in health care setting for early detection and monitoring of rational use of drug and also monitoring drug interactions. This will be helpful for further improvement in the reduction of incidence in antibiotic resistance and drug incidence.
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