A RANDOMISED CONTROL STUDY TO COMPARE THE EFFICACY OF CEFUROXIME, CLARITHROMYCIN, AND LEVOFLOXACIN IN THE MANAGEMENT OF PAEDIATRIC UPPER RESPIRATORY TRACT INFECTION

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Received: 30 July 2021, Revised and Accepted: 10 September 2021

ABSTRACT

Objective: The upper respiratory infections cause considerable morbidity mainly in children due to the fact that they mainly affect children. Accordingly, a study was conducted on antibiotics to compare the effectiveness of clarithromycin, cefuroxime, and levofloxacin for treating upper respiratory tract infections (URTI) in children.

Methods: A prospective observational study for a period of 6 months was conducted in the pediatrics department of RVM hospital. Outpatients under the age of 14 years given antibiotics for the treatment of URTI were included in the study. A total of 99 study subjects were included in the study, divided into three groups each containing 33 sample sizes (clarithromycin, cefuroxime, and levofloxacin). Patient data was collected using a form and verbal consent was obtained from patients/patient representatives, and drugs were given using the lottery method. Follow-up was done and noted for the 3rd, 5th, 7th day through telephonic calls, and the collected data were evaluated using statistical analysis.

Results: Pool data from 99 patients shows that many patients belong to 0–5 years age groups (age distribution), and males were more than female (gender distribution). Clarithromycin (cure rate 3 days) and cefuroxime (cure rate 5 days) showed an equal rate of cure percentage (94%), while levofloxacin for 3–5 days with a 3% failure rate. A significant difference of p<0.05 (p=0.000) was observed and no adverse events were noted.

Conclusion: The study findings showed, out of 3 drugs, clarithromycin and cefuroxime showed an equal efficacy rate of 94%, but clarithromycin showed shorter duration of outcome, i.e., 3 days. Hence, clarithromycin is effective than the other two drugs in the treatment of URTI.

Keywords: Upper respiratory tract infections, Clarithromycin, Cefuroxime, Levofloxacin, Pediatrics.
Study design
A prospective, interventional, randomized double-blind, observational study was conducted among subjects with URTI attending the outpatient pediatric department of RVM hospital. The three antibiotics (cefuroxime, clarithromycin, and levofloxacin) commonly prescribed for URTI were assessed and compared for their therapeutic efficacy. The strength doses (15 mg/kg/7 days) and duration of treatment of the three antibiotics were given as per the WHO model formulary for children and Model List of Essential Medicines 2019 to ensure that given drug in prescribed dose is safe in children [9,10].

A. Clarithromycin syrup – CLARINOVA – 125 mg/5 ml
B. Cefuroxime syrup – CEFAKIND – 125 mg/5 ml
C. Levofloxacin syrup – L-CIN – 125 mg/5 ml

The physician was kept unaware of the codes given to each antibiotic to ensure blinding. When a subject meets inclusion criteria approaches the outpatient department, the prescriber selected a chit written with the code A, B, or C by lottery method. The pharmacist was requested to dispense antibiotics as mentioned above upon receiving the study prescriptions. The study was initially approved by the institutional ethical committee (code: GCPR/I/EC/JUNE2019-20/B04) and consent was obtained from the study subjects [parents/guardians] before the study. They were explained about the telephonic follow-up before the study (Fig. 1).

Inclusion and exclusion criteria
Outpatients ≥14 years with diagnosed with URTI in the pediatric department of RVM hospital were included in the study. Patients other than URTI >14 years and inpatients of pediatric department of RVM hospital were excluded from the study.

Sample size and data collection
A total of 99 sample size was collected having 33 samples in each category of antibiotics. Before including in the study, a written informed was taken from study subjects. During the 6 months of study, relevant information was collected from the patient representative, by asking questionnaires including chief complaints, past/present medication history, etc., and entered into pre-designed data collection forms. Follow-up regarding alleviation of symptoms, ADR, if any, and adherence was done through telephonic interview starting at 3rd day followed by 5th and 7th day based on necessity and till symptoms subsided.

Classification of outcomes
The outcomes of the study subjects were classified as:

Cured
If, patient is completely relieved from symptoms by the treatment.

Improved
If, the patient’s condition is better than before by the treatment.

Failed
If, the patient’s situation is deteriorated or no betterment is observed by the treatment.

Statistical analysis
Descriptive statistics and graphical presentation of data analysis were shown as frequency, percentage, mean, and SD. Comparisons of categorical data between groups were done using Pearson χ² analysis, Kruskal Wallis Test, and 1-way analysis of variance (ANOVA). Statistical analysis, using SPSS statistical software, version 22, was performed.

RESULTS
Out of 99 patients, the patient’s near age was noticed to be 4.92±3.65 years with average weight of 13.9±12.0 kg. Most patients fall under the peer group of 0–5 years (68%). Out of 99 patients, 52 are male and 47 are female (Table 1).

On the telephonic interview, the treatment outcomes were observed and the effects of three drugs were compared. A χ²-test was applied to check the homogeneity of the attributes in respect of a particular characteristic. The results showed that clarithromycin and cefuroxime appeared effective than levofloxacin. Among 33 subjects received levofloxacin, 52% of subjects reported complete cure, 45% improved their clinical symptoms, while 3% reported no improvement upon antibiotic treatment (Table 2 and Fig. 2).

The findings of duration of treatment outcomes showed that majority of subjects receiving clarithromycin (73%) showed improvement in their symptoms within three days while it was 5 days for cefuroxime (73%) and 7 days for levofloxacin (58%). One way ANOVA is performed to correlate the effects of the drugs by the period of outcome, i.e., 3 days/5 days/7 days (parametric) and was found that clarithromycin has shown more efficacy within less duration i.e., 3 days (Table 3 and Fig. 3).

DISCUSSION
Among 99 pediatric study subjects, the prevalence of URTI is high in 0–5 years’ age group may be due to low immunity. On the telephonic follow-up of patients, we checked on the compliance of subjects and established that patients in all drug groups were adherent to every medication prescribed to them. So failure to receive medication was not a factor for the efficacy shown by the test drugs. No ADR was reported

Table 1: Age, gender, and body weight-wise distribution of the study population

| Parameter          | Frequency (n=99) | Total (%) |
|--------------------|-----------------|-----------|
| Age                |                 |           |
| 0–5 years          | 27 (27)         | 67 (68)  |
| 6–10 years         | 3 (3)           | 12 (22)  |
| 11–14 years        | 3 (3)           | 10 (10)  |
| Total              | 33 (33)         | 99 (100) |
| Mean±SD            | 3.7±3.5         | 4.9±3.65 |
| IQR                | 0.2–13          | 0.6–13   |
| Gender             |                 |           |
| Male               | 19 (19)         | 52 (53)  |
| Female             | 14 (14)         | 47 (47)  |
| Average weight     | 10.9±10.1       | 13.9±12.0|

Table 2: Comparison of treatment outcomes of three antibiotics given for URTI in paediatrics

| Drugs    | Outcome | χ², p<0.05 |
|----------|---------|------------|
| Drug A   | 31 (94) | 0 (6) 0 (0.0000)* |
| Drug B   | 31 (94) | 0 (6) 0 (0.0000)* |
| Drug C   | 17 (52) | 1 (3) 1 (0.1000)  |
| Total    | 79      | 19 1  |

Table 3: Comparison of duration of treatment outcomes of three antibiotics given for URTI in paediatrics

| Drugs    | Duration of outcome in days n (%) | F, p<0.05 |
|----------|----------------------------------|-----------|
| Drug A   | 24 (73) 6 (18) 3 (9) 3.7±1.31     | 24.87, 0.0000 |
| Drug B   | 7 (21) 24 (73) 2 (6) 4.7±1.02     | 1.02, 0.3000 |
| Drug C   | 4 (12) 10 (30) 19 (58) 5.9±1.42   | 5.91, 0.0000 |
| Total    | 35 40 24 |

*p<0.05; Duration of Outcome mean values are statistically noticeable between drugs by using one-way ANOVA, URTI: Upper respiratory tract infections
by the patient’s caregivers upon telephonic inquiry. However, it does not mean that there won’t be any ADR with the test drugs.

Among the clarithromycin, cefuroxime and levofloxacin groups, clarithromycin and cefuroxime have shown a 94% cure rate whereas levofloxacin showed 52% cure rate. Collating with the study conducted by Siepman in the year, 1998, it was found that these 2 drugs were equally efficacious [11]. A study by Guay et al, expressed that clarithromycin has high effects than cefuroxime. Another study by Henry concluded that cefuroxime (250 mg, twice daily) is as potent as amoxicillin (500 mg, TID) that provide baseline data for the utility of these selected antibiotics in URTI [11,12]. A study by AdelGlass et al, in contrast to the above results, concluded that levofloxacin and clarithromycin showed equal efficacy but the standards of life for levofloxacin are higher [13]. In a randomized comparative study of levofloxacin versus amoxicillin/clavulanate for treatment of pediatric patients with bronchitis and various factors that could not be studied here. Clarithromycin has shown cure before completing three days in 73% of individuals whereas cefuroxime has shown 73% within 5 days. Moreover, 50% of them were healed between 3 and 5 days of treatment. The time of treatment is longer in the levofloxacin group, most patients took more than 5 days for improvement in symptoms.

Antibiotic resistance has made infections more difficult to treat today, leading to life-threatening situations. Despite this, there are numerous encouraging research opportunities in antibiotic use, particularly in children. In the global context, antibiotic usage, awareness, knowledge, and practice need to be understood. As reported by the WHO, India is among the countries with a high rate of drug resistance coupled with the irrational use of antimicrobial agents. Despite developing research on antimicrobial stewardship, the country is primarily interested in drug discovery and development [16,17].

**CONCLUSION**

By considering our study conducted on 99 patients, we conclude that all three drugs are not equally efficacious in treating URTI in pediatric patients. Amidst three antibiotics, clarithromycin is more preferable. The study can be repeated in a larger sample size to increase reliability. As our study is conducted with limited resources, the study can be strengthened by culture sensitivity data and patient compliance was 100% and no side effects were observed. However, it cannot be extrapolated to the bigger sample or population. So advance research in some more populations can be held to know safety with these antibiotics in pediatric population.

**ACKNOWLEDGMENTS**

The investigators extend gratitude to RVM institutes of medical sciences and research center, for permitting to conduct the present study.

**CONFLICTS OF INTEREST**

The authors confirm that this article content has no conflicts of interest.

**FUNDING**

Not applicable.

**AUTHORS CONTRIBUTION**

The authors have made considerable contributions to the work reported in the manuscript.

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