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KEY WORDS:

A COMPARATIVE STUDY OF AMOXICILLIN, ERYTHROMYCIN, CEFADROXIL, AND GATIFLOXACIN IN TREATMENT OF ACUTE LOWER RESPIRATORY TRACT INFECTIONS

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ABSTRACT

Introduction: Community-acquired acute lower respiratory tract infection (LRTI) incorporates a spectrum of diseases from acute bronchitis, acute exacerbation of chronic obstructive pulmonary disease (COPD) and pneumonia. It is the most common cause for consulting general practice and OPD. This study was undertaken to compare older and newer antimicrobials in terms of clinical efficacy, tolerability and cost for the initial treatment for OPD management of LRTI in a government medical college setup. **Material And Methods:** This randomized, prospective study was conducted in the Medicine OPD of a government medical college, over a period of one year.Patients of either sex, aged between 16-60 yrs satisfying following definitions of acute bronchitis (with secondary bacterial infection), acute exacerbation of COPD and community acquired pneumonia were selected for the study.

Patients were randomly assigned to one of the following treatment groups:

- Group I- Amoxicillin 500 mg three times a day for 7 days.
- Group II - Erythromycin 500mg four times a day for 7 days
- Group III - Cefadroxil 500mg two times a day for 7 days
- Group IV-Gatifloxacin 400mg once a day for 7 day

Efficacy and safety of all antimicrobials were assessed and compared

Results: Satisfactory clinical outcome as cure and improvement was obtained in 48 % and 36% in amoxicillin, 52% and 33% in erythromycin 49% and 38% in cefadroxil, 64% and 27% in gatifloxacin group respectively. Unsatisfactory clinical outcome as failure was recorded in 16%, 15%, 13% and 9% of amoxicillin, erythromycin, cefadroxil and gatifloxacin groups respectively. **Conclusions:** All the four drugs were equally effective with more than 80% efficacy in treatment of LRTI. The treatment groups did not differ in incidence of adverse events. All the adverse effects were mild and did not require cessation of therapy.

INTRODUCTION

Community-acquired acute lower respiratory tract infection (LRTI) incorporates a spectrum of diseases from acute bronchitis, acute exacerbation of chronic obstructive pulmonary disease (COPD) and pneumonia. It is the most common cause for consulting general practice and OPD. LRTIs lead to morbidity in terms of more days of bed disability, restricted activity and absence from work than any other category of acute illness.

LRTIs are the leading reason for prescription of antimicrobials. There are an increasing number and variety of antimicrobials being produced which often have no clear-cut advantage over those available. Moreover, they are promoted irrationally. In such circumstances the value of antimicrobials must be assessed against competitors by price as well as its clinical efficacy.

This study was undertaken to compare older and newer antimicrobials in terms of clinical efficacy, tolerability and cost for the initial treatment for OPD management of LRTI in a government medical college setup.

AIMS AND OBJECTIVE

To study Amoxicillin, Erythromycin, cefadroxil and Gatifloxacin in acute lower respiratory tract infections in outdoor patients in the following aspects.

1) Clinical efficacy
2) Tolerability / safety
3) Cost of an antimicrobial agent per patient

MATERIAL AND METHODS

Study design: This randomized, prospective study was conducted in the Medicine OPD of a government medical college, over a period of one year

Inclusion criteria:

Patients of either sex, aged between 16-60 yrs satisfying following definitions of acute bronchitis (with secondary bacterial infection), acute exacerbation of COPD and community acquired pneumonia were selected for the study.

Acute bronchitis (with secondary bacterial infection) was defined as, presence of at least 2 of the following signs/ symptoms: recent onset (within 7 days of enrolment) of productive cough, increased in daily volume of sputum and purulent change in sputum in the absence of COPD, pneumonia or sinusitis.

Acute exacerbation of COPD was defined as known. case of COPD presenting with recent onset of following clinical features: increase breathlessness, increase in sputum volume and increase in sputum purulence.

Community acquired pneumonia was defined as recent onset of rales and egophony (focal chest signs) on pulmonary auscultation and at least two of the following signs and symptoms: fever, chest pain, cough, purulent sputum, chills, malaise or radiological findings consistent with pneumonia.

Exclusion Criteria

1. Patients with known or suspected hypersensitivity reaction to any of the study drugs

2. Patients already taking antimicrobials or who had received antimicrobials within 72 hours prior to enrolment

3. Patients with symptoms of LRTI but diagnosed as pulmonary tuberculosis, HIV, asthma, malignancy

4. Patients who were pregnant or lactating or were of childbearing potential and not using acceptable methods of contraception

5. Patients suffering form renal or hepatic impairment or GIT disease, which might hamper the absorption of drug

6. Patients of LRTI satisfying the inclusion and exclusion criteria but presenting with serious kind of ailment which required hospitalization or parenteral therapy Institutional ethics committee approved the study protocol and all patients provided written informed consent.

Patients were randomly assigned to one of the following treatment groups:

- Group I- Amoxicillin 500 mg three times a day for 7 days.
- Group II - Erythromycin 500mg four times a day for 7 days
- Group III - Cefadroxil 500mg two times a day for 7 days
- Group IV-Gatifloxacin 400mg once a day for 7 day

Patients were instructed to come for follow up on Day 3. Day 7 and Day 10.

Assessment of Clinical efficacy:

Clinical efficacy of study drugs was assessed semiquantitatively by change in severity of three cardinal symptoms of LRTI namely productive cough, sputum volume, or sputum purulence.

Each symptom was assessed semiquantitatively as Absent that is no symptoms, Mild that is symptom is present but not affecting work, Moderate that is symptom is present during day but not affecting sleep, and Severe that is symptom is there throughout day and night. Assessment of each symptom was done at each follow up visit by taking detailed history. Other symptoms like fever, breathlessness. chest pain, rales and rhonchi were also assessed.

Clinical response in a given patient was defined as

- cure:absent symptoms 1 to 3 days post treatment
- improvement:substantial reduction but not complete resolution of symptoms 1-3 days post treatment
- Failure: no apparent response to treatment 1-3

Safety evaluation:

At each follow up visit, drug related adverse events were assessed for severity, duration and relationship to the treatment.

Cost of antimicrobial per patient:

Cost of Antimicrobials treatment per patient for 7 days of therapy with study drugs was calculated in the end. Cost was taken according to the DMER rate contract list. Also, the market cost of antimicrobials was studied.

Statistical Methods.

Demographic data were assessed by paired t-test. Pretreatment symptom similarity and adverse events among the groups were analysed by chi-square test. Clinical efficacy within the group and among the groups was also assessed by chi square test. significant.

OBSERVATIONS AND RESULTS

Two hundred patients with LRTI were enrolled in this prospective randomized study and were allocated randomly to four treatment groups.

Out of 200 patients of LRTIS, 117 patients were diagnosed to be suffering from acute bronchitis (with secondary bacterial infection), 43 as mild-moderate community acquired pneumonia and 40 patients as acute exacerbation of COPD.

Overall dropout rate was 38% (76 out of 200 patients, that is 19 patients in amoxicillin, 17 in erythromycin, 20 each in cefadroxil and gatifloxacin group). **(table1)**

There was no significant difference in the treatment groups with respect to gender. **(table 2)**

Satisfactory clinical outcome as cure and improvement was obtained in 48 % and 36% in amoxicillin, 52% and 33% in erythromycin 49% and 38% in cefadroxil, 64% and 27% in gatifloxacin group respectively. Unsatisfactory clinical outcome as failure was recorded in 16%, 15%, 13% and 9% of amoxicillin, erythromycin, cefadroxil and gatifloxacin groups respectively. Therefore, clinical response rate was 84% in amoxicillin, 85%, in erythromycin, 87% in cefadroxil and 91% in gatifloxacin groups respectively. **(table 3)**

Tolerability Evaluations:

Patients with one or more adverse events were reported in 40% of amoxicillin treated patients, 30% of erythromycin, 30% of cefadroxil and 20% of gatifloxacin group There was no significant difference in overall incidence of adverse events among all groups ($p>0.05$). All adverse events reported were non-serious. Most common drug-related adverse events in case of amoxicillin were of gastrointestinal system mainly diarrhoea while in case of erythromycin it was abdominal pain. For cefadroxil, the most common adverse event was In postural hypotension. (table 4)

When the cost of antimicrobials per patient for 7 days of therapy was studied. Amoxicillin required RS.110/-, erythromycin RS. 104/-, cefadroxil RS.22/-and gatifloxacin required RS.11/-, according to DMER rate contract list When market cost of antimicrobial was studied for amoxicillin lowest cost was 247.8 and highest cost RS. 306.11- For erythromycin, cost range was RS. 126.3/- to 417.6/-, for cefadroxil RS. 50.66/- to 184.56/- and gatifloxacin RS. 43.79/- to 45.54/-.

According DMER rate contract list, amoxicillin (500mg - three time a day), erythromycin (500mg - 4 times a day) and cefadroxil (500mg -twice a day) were costly compared with gatifloxacin (400mg once a day). Cost was counted on the basis of dosage, frequency and duration of antimicrobial therapy.

DISCUSSION

In this study satisfactory clinical outcome (clinical cure + improvement) was seen in 84% in amoxicillin, 85% in erythromycin, 87% in cefadroxil and 91% in gatifloxacin group. Henry et al have reported satisfactory clinical outcome in 86% of patients treated with amoxicillin + clavulanic acid in their study[1]. Erythromycin has produced a satisfactory outcome in 85% of patients which is in agreement with other studies on this topic[2]. Cefadroxil has shown satisfactory clinical outcome in 87% patients of LRTIs in this study. In previous studies, cefadroxil has been used successfully in therapy of bacterial infections of the lower respiratory tract[3]. For the Gatifloxacin group, a satisfactory clinical outcome was seen in 91% of patients of LRTIs in this study. Similar results have been reported in a prospective, multicentre, noncomparative trial of Gatifloxacin in LRTIs[4].

In our study, patients were more compliant with gatifloxacin (94% patients took 92% of tablets) followed by cefadroxil 86% of the patients took 85% of the tablets. The compliance was less with amoxicillin and erythromycin (80% of the patients took 77% of the tablets and 73% of the patients 71% of the tablets respectively.

Patients with one or more adverse events were 12, 9, 13, 8 in amoxicillin, cefadroxil, erythromycin and gatifloxacin groups respectively. Most common adverse effect with amoxicillin was diarrhoea which is consistent with adverse events reported in literature. In one study, overall incidence of adverse effects with cefadroxil was 6.3% and most frequent among them have been GI disturbances such as nausea and vomiting and less frequently diarrhoea. In the erythromycin group, GI related adverse events were most common and

most predominant was abdominal pain which is consistent with ADR reported in literature.

When two drugs do not differ significantly in clinical efficacy and tolerability profile, the cost of therapy determines the choice of drug in given condition. The cost of 7 days of antimicrobial treatment with amoxicillin, erythromycin, cefadroxil and gatifloxacin was calculated according to government rates. Cost of therapy with amoxicillin and erythromycin was found to be more than cefadroxil and gatifloxacin.

This is the first time when amoxicillin, erythromycin-well established antimicrobials in acute LRTIs, cefadroxil-very commonly prescribed by general practitioners in our are and gatifloxacin - a promising new fluoroquinolone were studied together in the treatment of LRTIs. Another strong point of this study was the use of cardinal symptoms for calculation of cure, failure,or improvement of the disease. This study included almost all patients of LRTIs treated by general practitioners with antibiotics.

Further studies with larger sample size are required on this subject to validate the findings of this study.

Conclusions

This study compared the safety, efficacy and cost of Amoxicillin, Erythromycin, cefadroxil and Gatifloxacin in acute lower respiratory tract infections in outdoor patients in a government medical college.

- All the four drugs were equally effective with more than 80% efficacy in treatment of LRTI.
- The treatment groups did not differ in incidence of adverse events. All the adverse effects were mild and did not require cessation of therapy.
- Cost of therapy with amoxicillin and erythromycin was found to be more than cefadroxil and gatifloxacin in this study.

Table 1 Patient selection

Groups	Number of patients enrolled	Number of patients followed up
Amoxicillin	50	30
Erythromycin	50	32
Gatifloxacin	50	31
Cefadroxil	50	30

p>0.05

Table 2 Demographic data

	Amoxicillin	Erythromycin	Gatifloxacin	Cefadroxil
Mean age	39 ± 14	35 ± 12	37 ± 12	37 ± 12
Percentage of male patients	66%	51%	66%	56%
Percentage of female patients	34%	39%	34%	34%

p>0.05

Table 3: Clinical efficacy in percentage

Clinical outcome	Amoxicillin	Erythromycin	Gatifloxacin	Cefadroxil
Satisfactory cure	48	52	64	49
Improvement	36	33	27	38
Failure	16	15	9	13
Clinical response rate	84	85	91	87

Table 4:Safety

	Amoxicillin	Erythromycin	Gatifloxacin	Cefadroxil
Patients with one of more ADE	12	12	8	9
Diarrhea	6	3	1	5
Nausea or vomiting or abdominal pain	3	7	3	2
Other adverse reactions	4	5	1	3

p>0.05

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