Research Article

Study on safety and efficacy of Cephalosporins with macrolides in the treatment of lower respiratory tract infection in a tertiary care teaching hospital

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Abstract

Background: The objective of present study was to find out the different combinations of azithromycin and cephalosporins generally prescribed, compare their efficacy and safety (adverse drug reactions). **Materials and methods:** A prospective observational study was conducted in the pulmonary and general medicine ward at Navodaya Medical College Hospital & Research Centre, Raichur, Karnataka. The data was analyzed to interpret different parameters of the study. Efficacy was determined based upon the clinical response (reduction in symptoms) and length of hospital stay. Safety was determined by assessing the occurrence of ADR and their severity. In the study period, 85 patients were included based on the inclusion criteria. **Results:** Results revealed that male patients were more 45 (52.94%).More numbers of patients are at the age group of 60-69 years (31.76%) followed by 50- 59 years (28.24%) with a Mean± SD of age 54.95 ± 14.545. **Conclusion:** Different combinations prescribed were azithromycin + ceftriaxone, azithromycin + cefixime, and azithromycin + cefpodoxime. The most commonly prescribed combination was found to be ceftriaxone with azithromycin. The ceftriaxone group showed statistically significant difference in the reduction of clinical symptoms thereby indicating greater efficacy. The patients experienced ADRs which were mild in nature with none severe indicating that all the combinations were safe**.**

Keywords: Azithromycin, Ceftriaxone, efficacy, lower respiratory tract infections, safety

Introduction

World Health Organization (WHO) global burden of disease study estimated that lower respiratory infections (LRTIs) where 429.2 million episodes of illness worldwide and accounts for 94.5million disability adjusted life years (DALYs).In adults aged over 59 years, it causes 1.6million deaths annually **(**WHO, 2012**)**. Lower respiratory tract infection (LRTI) is a broad terminology which includes acute bronchitis, pneumonia, acute exacerbations of chronic obstructive pulmonary disease/chronic bronchitis (AECB), and acute exacerbation of bronchiectasis. Acute LRTIs (ALRTIs) are one of the common clinical problems in community and hospital settings. Beta-lactam antibiotics, macrolides, and fluoroquinolones are routinely prescribed medicines for the management of ALRTIs. Macrolides are time-tested and effective agents for the treatment of LRTIs. The role of antibiotics in the management of broader population of patients with LRTI is less clear (Smucny et al., 2004). The standard antibacterial treatments for lower respiratory tract infections in the past have been macrolides, in particular macrolides, the penicillins, or cephalosporins **(**Kryfti et al., 2013**)**. Adverse drug reactions (ADRs) lead to a number of medical and economic consequences, e.g. they extend hospital stay, increase the cost of treatment and exposure to possible harm and death almost two-fold. Thus, there is an impelling need to create awareness among physicians and patients towards the need for ADR monitoring (ASHP guideline, 1995). There are virtually few literatures and no efficacy and safety studies from North Karnataka, India. The objective of present study was:

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1) To find out the different combinations of azithromycin and cephalosporins generally prescribed for LRTI in general medicine and pulmonology department.

2) To compare efficacy of azithromycin with various cephalosporins in the treatment of LRTI based upon the clinical response i.e, reduction in the symptoms.

3) To examine the duration of symptoms after therapy initiation.

4) To record any adverse effects after therapy initiation

Materials and methods

A prospective observational study was carried out for a period of 6 months from September 2017 to February 2018 after the approval from Institutional Ethics Committee of Navodaya Medical College Hospital & Research Centre, Raichur. A total of 85 patients were included in this study. All adult and geriatric hospitalized patients of general medicine and pulmonology department who were diagnosed with LRTI with prescription containing combination of azithromycin with cephalosporins and patients who give oral consent to participate in this study were included and patients who are not willing to or unable to give oral consent to participate in the study, pregnant/lactating women and pediatric patients, patients visiting OPD, patients admitting in ICU and casuality were excluded from the study.

The data collection form was developed by consulting physicians and staff of Pharmacy Practice Department. The following information like patient demographic details(name, age, reason for hospitalization, duration of suffering, smoking history, etc), laboratory investigations, co-morbidities, drug combination of azithromycin with cephalosporins, length of hospital stay were collected. Patient follow up was carried out until discharge. Efficacy was determined based upon the clinical response i.e. reduction in the symptoms such as sputum production, cough, wheezing, dyspnoea, fever, discolored sputum and length of hospital stay. The patients were monitored throughout till discharge. The patients were also monitored for any adverse drug reactions during the treatment. A descriptive statistical analysis has been carried out in the present study. The difference in the reduction of symptoms in different treatment groups were statistically analyzed by Chi-square test.

Results

Among the 85 patients, 45(52.94%) were male and 40(47.06%) were female. More number of patients were in the age group of 60-69years (Figure 1 & 2). More number of patients were diagnosed with AECOPD (48.24%) making it highest among others (Table 1). Majority of the patients (88.23%) complained of cough followed by breathlessness (69.41%). The other symptoms observed were fever (57.64%), sputum production (47.05%), dyspnea (7.06%), loss of appetite (7.05%), chest pain (2.36%), vomiting (2.35%), headache and back pain (1.18%) (Table 2).

Maximum patients (75.29%) were prescribed with the combination of azithromycin + ceftriaxone followed by azithromycin + cefixime (12.94%) and azithromycin +cefpodoxime (11.76%) (Table 3).

The length of the hospital stay ranged from 1 to 12 days. Maximum patients (79.99%) got discharged between 5-8 days followed by 1-4 days (14.12%) and 9-12 days (5.89%). (Table 4)

Among the study population, change in sputum production was greater in case of combination of azithromycin + ceftriaxone compared to cefixime and cefpodoxime group of patients (Table 5).

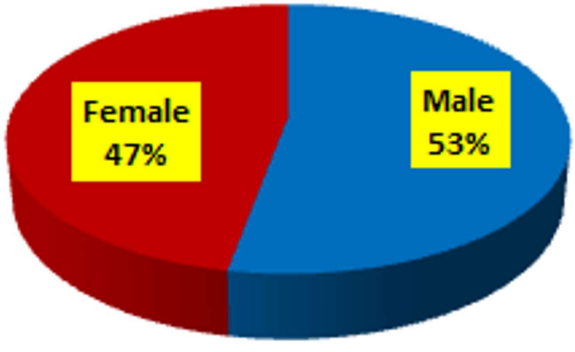

Figure 1. Distribution according to gender (N=85)

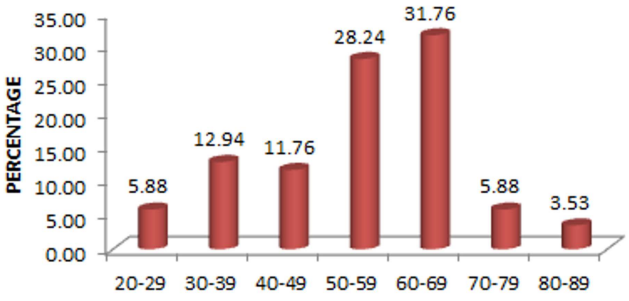

Figure 2. Distribution according to age group (N=85)

Table 1. Different diagnosis (N=85)

Diagnosis	No. of cases	Percentage
Pneumonia	19	22.35
AECOPD	41	48.24
AEBA	4	4.71
Bronchitis	5	5.88
LRTI	16	18.82
Total	85	100

Table 2. Details of complaints presented by patients with LRTI (N=85)

Clinical symptoms	Azithromycin+ Ceftriaxone		Azithromycin+ Cefixime		Azithromycin+ Cefpodoxime		Total	
	N	%	N	%	N	%	N	%
Sputum production	32	50	5	45.4	3	30	40	47.05
Cough	59	92.1	8	72.7	8	80	75	88.23
Dyspnea	3	4.6	1	9	2	20	6	7.06
Fever	35	54.6	8	72.7	6	60	49	57.64
Breathlessness	46	71.8	7	8.2	6	60	59	69.41
Vomiting	2	3.1	0	0	0	0	2	2.35
Chest pain	1	1.5	0	0	1	10	2	2.36
Headache	1	1.5	0	0	0	0	1	1.18
Loss of appetite	5	7.8	1	9	0	0	6	7.05
Back pain	1	1.5	0	0	0	0	1	1.18

Table 3. Details of combinations of azithromycin and cephalosporin therapy prescribed to the patients with LRTI (N=85)

Combinations	No. of cases	Percentage
Azithromycin+Ceftriaxone	64	75.29
Azithromycin+Cefixime	11	12.94
Azithromycin+Cefpodoxime	10	11.76
Total	85	100

Table 4. Distribution according to the length of hospital stay (N=85)

No. of days	Length of hospital stay Azithromycin+ Ceftriaxone		Azithromycin+ Cefixime		Azithromycin+ Cefpodoxime		Total	
	N	%	N	%	N	%	N	%
1 to 4	12	14.12	0	0	0	0	12	14.12
5 to 8	48	56.47	10	11.76	10	11.76	68	79.99
9 to 12	4	4.71	1	1.18	0	0	5	5.89
Total	64	75.3	11	12.94	10	11.76	85	100

Further evaluation of symptoms was done individually to assess their severity. The results are depicted in the following table 6, 7, 8, & 9.

In case of patients given the combination of azithromycin with ceftriaxone, there were complaints of headache (3), dizziness (1), constipation (1) and abdominal pain (1).In case of azithromycin with cefixime there were complaints of headache (1), dizziness (1) and in case of azithromycin with cefpodoxime there were complaints of headache (1), constipation (1). None of the ADRs were severe and life threatening.

Discussion

During the study period, out of 85 patients 45 (52.94%) were male and 40 (47.06%) were female. It was similar as study done by (Khan et al., 2009). The age of patients ranged from 20 to 89 years. Maximum number of patients 27(31.76%) were in the age group of 60-69 years whereas 3(3.53%) belong to the age group of 80-89 years as in the similar study (Tamm et al., 2007). The reason for higher incidence in this group is due to severe disease condition by increase in age. In our study it was found that 53% were

Table 5. Change in sputum production (N=40)

Change in sputum	Day 0						Day of discharge					
Treatment	Severe		Moderate/ Mild		Absent		Severe		Moderate/Mild		Absent	
	N	%	N	%	N	%	N	%	N	%	N	%
Azithromycin+ Ceftriaxone	24	61.5	9	23	0	0	2	5.1	25	64.1	6	15.3
Azithromycin+ Cefixime	4	10.2	0	0	0	0	0	0	2	5.1	2	5.1
Azithromycin+ Cefpodoxime	2	5.1	1	2.5	0	0	1	2.5	2	5.1	0	0
							x^2=18.730					
							P=0.001<0.05significant					

Table 6. Change in cough (N=75)

Change in cough	Day 0						Day of discharge					
Treatment	Severe		Moderate/ Mild		Absent		Severe		Moderate/Mild		Absent	
	N	%	N	%	N	%	N	%	N	%	N	%
Azithromycin+ Ceftriaxone	34	45.3	25	33.3	0	0	1	1.3	44	58.6	14	18.6
Azithromycin+ Cefixime	8	10.6	0	0	0	0	7	9.3	0	0	1	1.3
Azithromycin+ Cefpodoxime	4	4.7	4	4.7	0	0	0	0	7	9.3	1	1.3
x^2=5.818 P=0.055>0.05 notsignificant							x^2=56.587					
							P=0.000<0.05 significant					

Table 7. Change in breathlessness (N=59)

Change in breathlessness	Day 0						Day of discharge					
Treatment	Severe		Moderate/Mild		Absent		Severe		Moderate/Mild		Absent	
	N	%	N	%	N	%	N	%	N	%	N	%
Azithromycin+ Ceftriaxone	25	42.3	21	35.5	0	0	0	0	40	67.7	6	10
Azithromycin+ Cefixime	3	5	4	6.7	0	0	2	3.3	5	8.4	0	0
Azithromycin+ Cefpodoxime	4	6.7	2	3.3	0	0	1	1.6	3	5	2	3.3
x^2=0.739 P=0.691>0.05 notsignificant							x^2=11.395					
							P=0.022<0.05 significant					

smokers, 23% were alcoholic, 12% were tobacco chewing and 12% were with no social habits. It was similar as study done by (Tamm et al., 2007). Majority of the patients 41(48.24%) were diagnosed with AECOPD followed by 19 patients with pneumonia (22.35%), 16 patients with LRTI (18.82%), 5 patients with bronchitis (5.88%) and 4 patients with AEBA (4.71%). In our study, it was found that out of 88 patients, 40% were diagnosed with pneumonia followed by acute exacerbation of COPD (23%), bronchitis (23%) and AEBA (14%) which was similar to studies conducted by Khan et al., 2009. It was observed that maximum patients (75.29%) were prescribed with the combination of azithromycin + ceftriaxone followed by azithromycin + cefixime (12.94%) and azithromycin + cefpodoxime (11.76%).A study by Geetha S et al.,2009 observed that maximum patients were prescribed with the combination of azithromycin with cefotaxime group. Azithromycin was prescribed along with the cephalosporins to the enrolled patients at a dose of 500mg O.D. In case of ceftriaxone, the dose prescribed to the patients was 1gm B.D. In case of cefixime, the dose prescribed to the patients was 200mg B.D and cefpodoxime was prescribed at a dose of 325mg B.D.

The efficacy of medications was evaluated mainly by observing the reduction of symptoms from the time of admission up to the day of discharge. According to the table 5,6,7,8,&9, it was found that reduction in symptoms was

Table 8. Change in dyspnea (N=6)

Change in dyspnea	Day 0						Day of discharge					
Treatment	Severe		Moderate/Mild		Absent		Severe		Moderate/Mild		Absent	
	N	%	N	%	N	%	N	%	N	%	N	%
Azithromycin+ Ceftriaxone	2	33.3	1	16.6	0	0	0	0	3	50	0	0
Azithromycin+ Cefixime	1	16.6	0	0	0	0	0	0	1	16.6	0	0
Azithromycin+ Cefpodoxime	1	16.6	1	16.6	0	0	0	0	2	33.3	0	0
x^2=.750 P=0.687>0.05 notsignificant												

Table 9. Change in fever (N=49)

Change in fever	Day 0				Day of discharge			
Treatment	Yes		No		Yes		No	
	N	%	N	%	N	%	N	%
Azithromycin+Ceftriaxone	35	71.4	0	0	2	4	33	67.3
Azithromycin+Cefixime	8	16.3	0	0	3	6.1	5	10.2
Azithromycin+Cefpodoxime	6	12.2	0	0	2	4	4	8.1
					x^2=7.399 P=0.025<0.05 Significant			

greater in case of the combination of azithromycin with ceftriaxone group compared to the other two groups. As the percentage of reduction in severe symptoms was greater in combination of azithromycin with ceftriaxone compared to cefixime and cefpodoxime group of patients, ceftriaxone combination seems more effective in reducing the symptoms. Statistically there was a significant difference found in the reduction of sputum production, cough, fever and breathlessness between the treatment groups. However, there was no statistically significant difference in the dyspnea with different combinations. Safety of the treatment was evaluated by monitoring the adverse drug reactions of the treatment groups throughout the study period. In case of patients given the combination of azithromycin with ceftriaxone, there were complaints of headache, dizziness, constipation and abdominal pain. In case of azithromycin with cefixime there were complaints of headache, dizziness and in case of azithromycin with cefpodoxime there were complaints of headache, constipation. None of the ADRs were severe and life threatening.

Conclusion

Azithromycin along with various cephalosporins used for the treatment of LRTI were ceftriaxone,cefixime and cefpodoxime.The combinations prescribed were appropriate with respect to the diagnosis.All the three combinations showed a decrease in the clinical symptoms of the patients, but ceftriaxone group of patients showed a faster decreased compared to other two groups.Combination of azithromycin with ceftriaxone was more efficatious than azithromycin with cefixime and cefpodoxime. All the three combinations showed adverse drug reactions which were mild in nature and none of them were serious and life threatening.Thus, it can be concluded that combination of azithromycin with ceftriaxone was the best among the three combinations in treating the LRTI.

Conflict of interest

No conflict of interest.

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