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ORIGINAL ARTICLE

Comparison of Ciprofloxacin and Amoxicillin/Clavulanic Acid in the Treatment of Chronic Rhinosinusitis

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ABSTRACT

Objective: To compare ciprofloxacin with amoxicillin/ clavulanic acid in the treatment of chronic rhinosinusitis (CRS) in terms of frequency of improvement in symptom score.

Patients and Methods: This randomized control trial was conducted at Department of Otorhinolaryngology, Capital Hospital Islamabad, from March 2015 to March 2016. Study population included 190 cases of Chronic Rhino Sinusitis (CRS) of either gender, aged 18 to 50 years and excluding confounders, divided in two groups. Group A received Ciprofloxacin 500 mg BD and Group B received Amoxicillin/ clavulanic acid 625 mg TDS for 10 days. Symptom score was recorded at start of treatment and finally at 16th week. Data analysis was done by SPSS 17.0. Chi Square was used to compare improvement of two groups. P-value ≤ 0.05 was considered significant.

Results: The sample population comprised of 190 cases of CRS aged 18 to 50 years with mean and standard deviation of 31.85 ± 10.07 years. Improvement in symptom score was in the range of 1 - 28, with mean and standard deviation of 10.52 ± 3.94. Male population was 54.7% (104/190) while females 45.3% (86/190). A significant association of treatment group on symptom score having p-value = 0.001 was found. Ciprofloxacin group showed higher improvement (90.53%) compared to Amoxicillin/ clavulanic acid group (71.58%).

Conclusion: Ciprofloxacin showed significantly better results than Amoxicillin/ clavulanic acid in the treatment of CRS in terms of frequency of improvement in symptom score.

Key words: Amoxicillin/ clavulanic acid, Chronic Rhinosinusitis, Ciprofloxacin, Symptoms Score

Author`s Contribution
[1] Conception, synthesis, planning of research and manuscript writing Interpretation and discussion
[2-3] Data analysis, interpretation and manuscript writing, Active participation in data collection.

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Article info.
Received: January 22, 2017
Accepted: July 10, 2018

Cite this article. *Shahan Z, Saqulain G, Ahmed J. Comparison of Ciprofloxacin and Amoxicillin/Clavulanic Acid in the treatment of Chronic Rhinosinusitis. JIMDC.2018; 7(4):*

Funding Source: *Nil*
Conflict of Interest: *Nil*

Introduction

Multidisciplinary expert panels have defined Chronic rhinosinusitis (CRS), as inflammatory disease of sinonasal mucosa lasting 12 weeks or longer including objective evidence of mucosal inflammation, despite attempts at medical management.[1,2] The signs/ symptoms of CRS are taken as diagnostic criteria, which include two or more symptoms, of which one should be either blockage of nose/ obstruction, congestion or discharge (anterior/ posterior), ± facial pain or pressure and ± loss/ reduction of smell.[3] This should also include either endoscopic signs including mucopurulent discharge and/or nasal polyps, and/or oedema in middle meatus. In leu of endoscopic signs mucosal changes within the ostiomeatal complex and/or sinuses on CT Scanning is also acceptable.[3] Prevalence of CRS varies significantly, 2% to 16% in the United states [4,5] and 7% to 27% in

European, south Africa and Caribbean Region.[6-8] CRS is typically diagnosed among young or middle-aged [9] with mean age of 39 years with women disproportionately affected [4,8] and it also results in loss of work days.[10]

Aim of treatment is to maintain nasal patency, reduce inflammation and eliminate pathogens. The pathogenesis is uncertain, however polymicrobial biofilms can contribute.[11-13] Therefore, antibiotics are indicated.[13] In a local study cephalosporin (cefuroxime) was found to be more frequently prescribed than amoxicillin in treatment of CRS.[14] However, treatment also includes antihistamines, analgesics, decongestants, corticosteroids and mucolytic with antihistamines being commonly prescribed.[14] Nasal septal deviations are commonly seen in CRS [15] so are nasal polyps[16], therefore surgery is reserved for such cases and when abscess is revealed on CT and if it shows clinical deterioration.[13] CT may also be helpful in the diagnosis of fungal infection involving paranasal sinuses.[17]

Antibiotics are used against common isolates including staphylococcus aureus and anaerobes, including beta lactam producing organisms, pseudomonas aeruginosa and facultative Gram-negative rods. Therefore, the spectrum of antibiotic should include these organisms.[18] A number of antibiotics are used in CRS especially in acute exacerbations including amoxicillin and clavulanic acid combinations and fluoroquinolones. In a local study efficacy for resolution of signs and symptoms of CRS with both Amoxicillin-Clavulanate and Levofloxacin was found similar [19], however, no local study is available comparing the efficacy of Amoxicillin-Clavulanate and quinolones for CRS.

The objective of this study was to compare Ciprofloxacin with Amoxicillin/ clavulanic acid in the treatment of chronic rhinosinusitis (CRS) in terms of frequency of improvement in symptom score.

Patients and Methods

This randomized control trial was conducted at the ENT department, Capital Hospital Islamabad, from March 2015 to March 2016, after approval from the institutional ethical committee. Other ethical issues were taken into account. Presence of female attendant in cases of females being examined was made mandatory. The sample size was 190 cases calculated with 5% level of significance, 80% power of test, and anticipated population proportion of 83.3% in Group A and 67.6% in Group B with minimum sample size of 95 in each group. Non-probability consecutive sampling technique was used. All the diagnosed cases of CRS who consented for the study were included in the study. These included cases of both genders aged 18 to 50 years. Cases which could act as confounders, were excluded from the study. These included cases with previous sinus surgery/FESS, or nasal lavage within a week of presentation; cases with allergic rhinitis, allergy to test drugs, fungal sinusitis, nasal deformities and nasal polyposis. Moreover, cases who used antibiotics within the last one week before presentation, those with chronic use of steroids or immunosuppressive cases with co morbidities, and pregnant females were also excluded from the study.

Patients with CRS fulfilling the selection criteria were selected from ENT outpatient's department of Capital Hospital. Informed consent was taken and patients were randomly divided into two groups (Group A and Group B), by balloting. Patients were diagnosed as CRS clinically by the research supervisor. This included nasoendoscopy and where required CT scanning was performed. Performa was filled by the patient and symptom score calculated by the researcher. All 13 symptoms (Major Symptoms: nasal obstruction, post nasal discharge, nasal discharge, facial pain or pressure, hyposmia / anosmia, nasal congestion, headache; Minor Symptoms: halitosis, fever, fatigue, dental pain, cough, ear pain or fullness) were scored. Each symptom was scored on the following scale:

None = No Symptom = 0

Mild = Symptom occurs in/ or continues for less than 6 hours. = 1

Moderate = Symptom recurs in/ or continues for 6 to 12 hours. = 2

Severe = Symptom recurs in/ or continues for more than 12 hours = 3

As, all 13 symptoms were scored the maximum score was 39 (13 x 3).

Group A patients were given Ciprofloxacin 500 mg twice daily and Group B cases were given Amoxicillin/ clavulanic acid 625 mg thrice daily. Treatment was instituted for 10 days. Patients in both groups were also instituted Xylometazoline nasal spray, Tab. Loratadine

Table.1: Stratification of gender and age					
Stratification	Treatment Group	Improvement		Total	P-value
		Yes	No		
Male (n=104)	Group A: Ciprofloxacin	49 (90.74%)	5 (9.26%)	54	0.002
	Group B: Amoxicillin/Clavulanic Acid	33 (66%)	17 (34%)	50	
	Total	82	22	104	
Female (n=86)	Group A: Ciprofloxacin	37 (90.24%)	4 (9.76%)	41	0.118
	Group B: Amoxicillin/Clavulanic Acid	35 (77.78%)	10 (22.22%)	45	
	Total	72	14	86	
< 35 Years (n= 118)	Group A: Ciprofloxacin	55 (91.67%)	5 (8.33%)	60	0.003
	Group B: Amoxicillin/Clavulanic Acid	41 (70.69%)	17 (29.31%)	58	
	Total	96	22	118	
≥35 Years (n = 72)	Group A: Ciprofloxacin	31 (88.57%)	4 (11.43%)	35	0.095
	Group B: Amoxicillin/Clavulanic Acid	27 (72.97%)	10 (27.03%)	37	
	Total	58	14	72	

10mg once daily and saline nasal douches thrice daily. Symptom score was recorded at first visit and final outcome was measured at 16th week. Follow up was ensured by taking contact number and address. Data collected included Medical Record number, age, sex and contact detail and sinus score at first visit and at 16th week.

The Data collected was recorded, organized and analyzed on SPSS 17.0. Qualitative variables like gender were measured in terms of frequency and percentage. Quantitative variables like age and symptom score were measured in terms of mean and standard deviation. Chi Square was used to compare improvement of two groups. P ≤ 0.05 was significant. Effect modifier like age and gender were controlled by stratification. Post stratification Chi Square was applied.

Results

Among the 190 patients included in the study, 104 (54.7%) were males while 86 (45.3%) were females with a male to female ratio of 1.2:1. The patient age range was from 18 to 50 years with mean and standard deviation of the age as 31.85 ± 10.07. The range of improvement in symptom score following treatment ranged from 1-28, with mean and standard deviation of 10.52 ± 3.94. Among males, a significant association was found between treatment group and improvement in symptom score, with p-value of 0.002 while no significant association between treatment group and improvement in symptom score was found in females with p-value of 0.118. In < 35 years of age group, significant association was found between treatment group and improvement in symptom score with p-value 0.003 while no significant association was found in patients > 35 years of age group, between treatment group and improvement in symptom score with p-value 0.095 (table 1).

Overall, the treatment group has shown significant association on symptom score having p-value = 0.001. It was noted that after instituting 10 days' treatment and recording the symptom score on 16th week, Ciprofloxacin group showed more improvement [n = 86 (90.53%)] compared to Amoxicillin/ clavulanic acid group [n=68 (71.58%)] as shown in (Table 2).

Table.2: Comparison of improvement in both Groups (n = 190)				
Treatment Group	Improvement		Total	P-value
	Yes	No		
Ciprofloxacin treatment	86 (90.53%)	9 (9.47%)	95	0.001
Amoxicillin treatment	68 (71.58%)	27 (28.42%)	95	
Total	154	36	190	

Discussion

Since CRS is an inflammatory disease of sinonasal mucosa lasting 12 weeks or longer [1,2], the aim of treatment in CRS include steps to eliminate infection, reduce sinonasal inflammation, and maintain patency of sinonasal passage to facilitate drainage. Management of precipitating risk factors is also recommended [20], in addition to antibiotics for the short-term treatment of CRS with exacerbations.[3] A number of antibiotics are in use. Amoxicllin/ clavulanic acid combinations have increased effectiveness against B-Lactamase producing bacteria.[21] Also, fluoroquinolones including ciprofloxacin have good activity against most of Gram -ve and Gram +ve organisms.[22] A number of studies comparing different drugs for the treatment of CRS have been documented.[23-25] Namyslowski et al,[24] compared Cefuroxime axetil with amoxicillin/ clavulanic acid with no significant difference in clinical response and bacterial eradication. Zaman et al., in a local study found that in context with resolution of signs and symptoms of CRS efficacy of both Amoxicillin-Clavulanate and Levofloxacin was similar.[19] Legent F et al., compared the Ciprofloxacin with Amoxicllin/ clavulanic acid in terms of cure rate with assessment done on 40th day [23]. In slight contrast, the objective of our research was to compare Ciprofloxacin with Amoxicillin/ clavulanic acid in the treatment of chronic rhinosinusitis (CRS) in terms of frequency of improvement in symptom score at 16th week. For this we conducted a randomized control trial in which one hundred and ninety patients of CRS were included which fulfilled the selection criteria by using, non-probability consecutive sampling. These included patients aged 18 years to 50 years, with mean and standard deviation of the age as 31.85 ± 10.07 years. In our study males were 104/190 (54.7%) while females were 86/190 (45.3%). The minimum symptom score was 1 and maximum score was 28 with mean and standard deviation as 10.52 ± 3.94.

Several organisms (both aerobes and anaerobes) associated with chronic rhinosinusitis have been isolated, [26,27] which strengthens the role of antibiotics. Role of amoxicillin/ clavulanic acid [2,24], ofloxacin, and erythromycin [25] is there. Piromchai P et al., concluded in a small study to support the use of systemic antibiotics for the curative treatment of chronic rhinosinusitis in adults and there is limited evidence in support of use of antibiotics and that further good quality trials, with large sample sizes, are needed to evaluate the use of antibiotics in chronic rhinosinusitis.[28] However, due to emerging resistance ciprofloxacin is proving to have a pivotal role in treatment,[23] but not many studies have been conducted to prove its role.

Legent F.et al.[23] reported in their study that after 9 days' treatment, nasal discharge disappeared in 71/118 (60.2%) patients of the ciprofloxacin group and in 69/123 (56.1%) of those in the amoxycillin/clavulanic acid group. The clinical cure and bacteriological eradication rates were 58.6% versus 51.2% and 88.9% versus 90.5% for ciprofloxacin and amoxycillin/clavulanic acid, respectively. These differences were not significant, however, amongst patients who had a positive initial culture and who were evaluated 40 days after treatment. Ciprofloxacin recipients had a significantly higher cure rate than those treated with amoxycillin/clavulanic acid (83.3% vs. 67.6%, p = 0.043). Our treatment groups have shown significant association of symptom score with p-value of 0.006. After instituting 10 days' treatment and recording symptom score at 16th week, Ciprofloxacin group revealed a higher improvement (90.53%) in symptom score compared to Amoxicillin/ clavulanic acid group (71.58%). Thus Ciprofloxacin has shown to be a better antibiotic, in terms of improvement, in symptom score. However, more studies need to be conducted to further strengthen its role in CRS.

Conclusion

Ciprofloxacin shows significantly better results than Amoxicillin/ clavulanic acid in the treatment of Chronic Rhinosinusitis, in terms of improvement in symptom score. Also treatment group was significantly associated with improvement in symptom score in males and in less than 35 years of age group.

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