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EFFICACY OF AMOXICILLIN-CLAVULANATE AND LEVOFLOXACIN TREATMENT OF ACUTE BACTERIAL RHINOSINUSITIS

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ABSTRACT

Objective: To compare the efficacy of Amoxicillin-Clavulanate and Levofloxacin in the treatment of acute bacterial rhinosinusitis**. Materials & Methods:** A total of 360 patients with acute bacterial sinusitis of age ranges from 15-55 years of both gender were included. Patients with pneumonia, h/o allergy to allergy to Amoxicillin-Clavulanate or Levofloxacin and diabetes mellitus were excluded. Patients were randomly assigned into two groups based on Lottery method in Group A and Group B. Group A (The Amoxicillin-Clavulanate Group) received oral Amoxicillin-Clavulanate 1 g every 12 hours for 10 days. Group B (The Levofloxacin Group) received Oral Levofloxacin 250 mg every 12 hours for 10 days. Symptoms and signs were recorded at visit one before the start of antibiotics and at day 11 after completion of treatment. **Results:** The mean age of patients in group A was 35.73 ± 7.31 years and in group B was 35.91 ± 8.24 years. Out of these 360 patients, 143 (39.72%) were male and 217 (60.28%) were females with ratio of 1:1.5. Efficacy was seen as yes in 172 (95.56%) patients in group B (Levofloxacin group) group A (Amoxicillin-Clavulanate group) and 146 (81.11%) patients in with p-value of 0.000. **Conclusion:** This study concluded that levofloxacin has better efficacy and cost-effective than Amoxicillin-Clavulanate in the treatment of acute bacterial rhinosinusitis in terms of signs and symptoms relief.

KEYWORDS: Bacterial, rhinosinusitis, levofloxacin, amoxicillin.

INTRODUCTION

Acute rhinosinusitis (ARS) is defined as an acute viral or bacterial infection characterized by inflammation of the mucosa of the nose and paranasal sinuses.[1] Although most cases of acute rhinosinusitis are viral in origin, acute bacterial rhinosinusitis is also a fairly common occurrence. In most of the cases patients with acute rhinosinusitis get recovered without antibiotic course. Antibiotic therapy should be considered in patients with chronic prolonged or more severe symptoms. Rhinosinusitis is considered an acute illness (viral or non-viral origin) if it lasts less than 12 weeks, after exceeding this time period it become chronic. Rhinosinusitis symptoms resolve spontaneously in 40% of the patients without any treatment. However, the purpose of medical treatment is to provide symptomatic relief, speed up the resolution of the clinical sign and symptoms, prevent possible complications and avoid evolution to chronicity.[2] Most patients with acute sinusitis are treated in the primary care hospital or clinics. Further evaluation by an otolaryngologist is recommended when (1) continued deterioration occurs with appropriate antibiotic therapy, (2) episodes of sinusitis recur, (3) symptoms persist after 2 courses of antibiotic therapy, or (4) comorbid immunodeficiency, nosocomial infection, or complications of sinusitis are present. The goals of management of acute sinusitis are the provision of adequate drainage and appropriate systemic treatment of the likely bacterial pathogens.[3] The Joint Task Force on Practice Parameters for Allergy and Immunology suggests assessing response to symptoms after 3-5 days of therapy and continuing for an additional 7 days if there is improvement. Combining an intranasal corticosteroid with an antibiotic reduces symptoms more effectively than antibiotics alone.[3] Drainage of the involved sinus can be achieved both medically and surgically.

Aggressively treat patients in intensive care who develop acute sinusitis in order to avoid septic complications. Consider removal of nasotracheal and nasogastric tubes and promote drainage either medically or surgically.[4] A retrospective cohort study by Pynnonen et al, conducted at a single academic institution, suggested that antibiotics are being overused in the treatment of patients with mild acute sinusitis of short duration. The investigators found that 66% of such patients were being given antibiotics, with antibiotic use varying according to the individual provider, the provider's specialty (with emergency medicine providers tending to use more antibiotics), and whether a medical trainee was present.[4] Antimicrobial agents and topical nasal corticosteroids (used alone or in

combination with antimicrobial agents) are the treatments that have demonstrated therapeutic utility in rigorous and controlled clinical trials.[57] In mild acute rhinosinusitis without previous antibiotic therapy, the treatment of choice is amoxicillin-Clavulanate or cefadroxil, while when it is moderate or mild in patients previously treated with antibiotics, levofloxacin or moxifloxacin are preferable and are good alternatives, while in the severe forms, third generation cephalosporins, such as cefotaxime or ceftriaxone or cefixime are indicated.[8-10] In Europeans, available clinical data suggests higher efficacy of amoxicillin/Clavulanate over levofloxacin.[11-12] However, no such data is available for Pakistani population. The rationale of this study was to compare clinical efficacy of two commonly used medications for treatment of acute rhinosinusitis in a sample of Pakistani population. Levofloxacin has the potential to be a cost effective alternative for amoxicillin/Clavulanate in the treatment of acute bacterial rhinosinusitis in our patients.

Operational Definitions

1. Acute Bacterial rhinosinusitis: The following clinical parameters were considered for diagnosis:

a. Patient's complaints including feeling of stuffiness or blockage in nose, discharge from nasal cavity, headache, inability to smell or feeling of bad smell was recorded. The duration in hours per day and frequency of episodes per day of these complaints was recorded.

b. Physical findings include red and swollen nasal turbinates, mucopurulent nasal discharge in meatus and post nasal drip was assessed by clinical examination by an ENT specialist.

2 A diagnosis of acute bacterial rhinosinusitis requires presence of any four or more symptoms and two or more signs, persistence of symptoms for longer than 10 days or a worsening of symptoms after 7 days.

3 Efficacy: Efficacy was assessed by using the following parameter on day 11 in the term of: a. Complete Resolution of clinical signs and symptoms.

4 Amoxicillin-Clavulanate: It is a moderate spectrum, bacteriolytic, βlactam antibiotic used to treat bacterial infections caused by susceptible microorganisms. We used it in a dose of 1gm every 12 hours for 10 days in our study (Group A).

Levofloxacin: It is a synthetic chemotherapeutic antibiotic of the fluoroquinolone drug class and is used to treat severe bacterial infections or bacterial infections that have failed to respond to other antibiotic classes. We used it in a dose of 250 mg every 12 hours for 10 days in our study (Group B).

MATERIAL AND METHODS

This randomized controlled trial was conducted at Department of Otorhinolaryngology, Victoria Hospital Bahawalpur, from January 2018 to June 2018. Total 360 patients with patients fulfilling the case definition of acute bacterial sinusitis after clinical examination, age 15 to 55 years, either gender were selected for this study. Patients already on some other antibiotics, patients who fail to complete the duration and prescribed dosage of the treatment, with complications like Pneumonia, any history of allergy to Amoxicillin-Clavulanate or Levofloxacin, patient with previous sinus/conventional nasal surgery, patients with history of diabetes mellitus, history of Pregnancy and actively lactating mothers. Selected patients were divided into two equal groups (A and B) randomly. All patients were given xylometazolin nasal spray along with nasal decongestant and steam inhalation in the same dosage and duration. Group A (The Amoxicillin-Clavulanate Group) received oral Amoxicillin-Clavulanate 1 g every 12 hours for 10 days. Group B (The Levofloxacin Group) received Oral Levofloxacin250 mg every 12 hours for 10 days. All the patients were kept under strict surveillance and side effects if any, were noted. Follow up was ensured by taking telephone contacts. All the patients were assessed for signs and symptoms resolution. Symptoms and signs were recorded at visit one before the start of antibiotics and at day 11 after completion of treatment. Data was collected using proforma. Collected data was entered in SPSS version 16 and analyzed. Numerical data was presented as mean and SD categorical data was presented as frequencies and percentages.

Efficacy of treatment was compared between the both treatment groups by applying chi-square test. P value less than 0.05 was taken as significant.

RESULTS

Age range in this study was from 15 to 55 years with mean age of 35.79 ± 7.86 years. The mean age of patients in group A was 35.73 ± 7.31 years and in group B was 35.91 ± 8.24 years. Mean duration of symptoms were 4.19 ± 2.36 weeks. The mean duration of disease in group A was 4.33 ± 2.72 weeks and in group B was 4.28 ± 2.60 weeks. Comparison of efficacy between the both groups was done. Treatment was found effective in 146 (81.11%) patients of group A and 172 (95.56%) patients of group B. Statistically significant difference of efficacy between the both groups was observed with p value 0.000. (Table 1)Patients were divided into three age groups i.e. age group 15-30 years, age group 3145 years and age group 46-55 years. Treatment was found effective in 50 (98.04%) patients of group B and in 46 (86.79%) patients of group A. The difference of efficacy between the both groups was statistically significant with p value 0.031. In age group 31-45 years, efficacy of treatment was noted in 61 (92.42%) patients of group B while in 47 (74.60%) patients of group A and the difference of efficacy between the both groups was

statistically significant with p value 0.006. In age group 46-55 years, treatment was found effective in 61 (96.83%) patients of group B while in 53 (82.81%) patients of group A and the difference was significant with p value 0.009. (Table 2)In ≤4 weeks duration of disease, efficacy of treatment was noted in 107 (98.17%) patients of group B while in 93 (87.74%) patients of group A. Difference of efficacy between the both groups was statistically significant with p value 0.003. In >4 weeks duration of disease group, treatment was found effective in 65 (91.55%) patients of group B and in 53 (71.62%) patients of group A and the difference was significant with p value 0.002. (Table 3) In 70 (95.89%) male patients of group B and 55 (78.57%) male patients of group A treatment was found effective and the difference was significant with p value 0.002. In 102 (95.33%) female patients of group B and 91 (82.73%) female patients of group A, treatment was effective and the difference was statistically significant with p value 0.003. (Table 4).

Table 1: Comparison of efficacy between both groups.

Group	Efficacy		Total	P value
	Yes	No		
A	146 (81.11%)	34 (18.89%)	180	0.000
B	172 (95.56%)	8 (4.44%)	180	

Table 2: Stratification of efficacy in both groups with respect to age of patients.

Age of patients	Group B (n=180)		Group A (n=180)		p-value
	Efficacy		Efficacy		
	Yes	No	Yes	No	
15-30 years	50 (98.04%)	01 (1.96%)	46 (86.79%)	07 (13.21%)	0.031
31-45 years	61 (92.42%)	05 (7.58%)	47 (74.60%)	16 (25.40%)	0.006
46-55 years	61 (96.83%)	02 (3.17%)	53 (82.81%)	11 (17.19%)	0.009

Table 3: Stratification of efficacy in both groups with respect to duration of disease.

Duration of disease (weeks)	Group B (n=180)		Group A (n=180)		p-value
	Efficacy		Efficacy		
	Yes	No	Yes	No	
≤4 weeks	107 (98.17%)	02 (1.83%)	93 (87.74%)	13 (12.26%)	0.003
>4 weeks	65 (91.55%)	06 (8.45%)	53 (71.62%)	21 (28.39%)	0.002

Table 4: Stratification of Efficacy in both groups with respect to Gender.

Gender	Group B (n=180)		Group A (n=180)		p-value
	Efficacy		Efficacy		
	Yes	No	Yes	No	
Male	70 (95.89%)	03 (4.11%)	55 (78.57%)	15 (21.43%)	0.002
Female	102 (95.33%)	05 (4.67%)	91 (82.73%)	19 (17.27%)	0.003

DISCUSSION

There have been no randomized controlled trials (RCTs) of antibiotic treatment for ABRS using sinus aspirate cultures before and after treatment, although nonrandomized trials have demonstrated bacteriologic cures. Five RCTs and two meta-analyses have compared antibiotics, usually amoxicillin and trimethoprim-sulfamethoxazole (TMP-SMX; Bactrim, Septra), with placebo, with clinical improvement as the outcome, which is the more clinically relevant patient-oriented outcome.[13] About 47 percent of patients treated with antibiotics and 32 percent of the control group were cured at 10 to 14 days. Eighty-one percent of patients treated with antibiotics and 66 percent of the control group were cured or improved, meaning one patient benefited for every seven treated with antibiotics. The treatment effect in these trials may have been underestimated because the lack of specificity of diagnosis diluted the effect of treatment.[13]

Amoxicillin-Clavulanate potassium (Augmentin), cephalosporins (cefuroxime [Cetin] and cefixime [Suprax]), and macrolides (azithromycin and clarithromycin), have been studied extensively.[14] All have demonstrated similar clinical success rates—generally above 85 percent. The use of fluoroquinolone for ABRS is relatively new. Ciprofloxacin (Cipro) and cefuroxime had 90 percent resolution rates when administered to patients in a primary care setting.[15] In an open label RCT, levofloxacin (Levaquin) and clarithromycin had 96 and 93 percent clinical success rates, respectively.[16]

In our study, efficacy was seen as yes in 172 (95.56%) patients in group B (Levofloxacin group) group A

(Amoxicillin-Clavulanate group) and 146 (81.11%) patients in with p-value of 0.000. The study.[17] compared the clinical efficacy and bacteriological response of levofloxacin and co-amoxiclav in the treatment of purulent maxillary sinusitis. Sixty patients randomly received either levofloxacin 300 mg orally once daily or co-amoxiclav 625 mg three times a day for 14 days. Radiological improvement was 61.8% with levofloxacin (41.2% resolution, 20.6% improvement) and 61.5% with co-amoxiclav (26.9% resolution, 34.6% improvement). Pretreatment maxillary antral aspiration cultures were positive in 28 patients (82.4%) in the levofloxacin group and 20 patients (76.9%) in the co-amoxiclav group. Bacteriological eradication was 78.5% in the LEV group and 70.0% in the COA group, which was not significantly different. In the LEV group, the eradication rate for major pathogens of acute sinusitis was 100% for H. influenzae, 100% for S. pneumoniaeand S. aureus, 100% for Neisseria species, and 66.7% for P. aeruginosa. The eradication rate in the COA group was 75% for H. influenzae, 100% for S. pnumoniae and S. aureus, 50% for Neisseria species, and 0% for P. aeruginosa. In one trial, a total of 535 patients who could be clinically evaluated randomly received levofloxacin (500 mg/day) or amoxicillin-Clavulanate (500 mg of amoxicillin t.i.d. and 125 mg of Clavulanate t.i.d.) for 10–14 days.[18] Clinical cure/improvement rates, 2–5 days after therapy, were 88.4% for levofloxacin-treated patients, compared with 87.3% for amoxicillin-Clavulanate treated patients. In another such study by Adelglass et al.[19] compared amoxicillin- Clavulanate and levofloxacin in ABRS. The success rates (cured and improved) 2 to 5 days after the end of treatment were 88.4% for the 267 clinically evaluable patients who received levofloxacin and 87.3% for the 268 clinically evaluable patients who received amoxicillin-Clavulanate. The results of this study show that once-daily administration of levofloxacin is as effective and better tolerated than amoxicillin-Clavulanate administered 3 times daily in treating acute sinusitis in adult patients.

CONCLUSION

This study concluded that levofloxacin has better efficacy and cost-effective than Amoxicillin-Clavulanate in the treatment of acute bacterial rhinosinusitis in terms of signs and symptoms relief. So, we recommend that levofloxacin should be used routinely in general practice for treatment of acute bacterial rhinosinusitis in terms of signs and symptoms relief.

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