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Research Article

Comparison of efficacy of amoxicillin-clavulanate and levofloxacin in the 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 Levofloxicin 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 Levofloxicin Group) received Oral Levofloxicin250 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. Even though most patients with acute rhinosinusitis recover promptly without antibiotic therapy, it should be considered in patients with prolonged or more severe symptoms. Due to its evolution, rhinosinusitis is considered to be acute (viral or non-viral origin) if it lasts less than 12 weeks, chronic when it exceeds this time period and recurrent acute when three or more acute episodes are suffered in one year. Rhinosinusitis symptoms resolve spontaneously in 40% of the patients without any treatment. However, medical treatment is indicated to provide symptomatic relief, accelerate the resolution of the clinical picture, prevent possible complications and avoid evolution to chronicity.[2]

The primary goals of management of acute sinusitis are to eradicate the infection, decrease the severity and duration of symptoms, and prevent complications. Most patients with acute sinusitis

are treated in the primary care setting. 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.

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.

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.[5-7] In mild acute rhinosinusitis without previous antibiotic therapy, the treatment of choice is amoxicillin-clavulanate or cefadraxil, 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 (cacosmia) 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, β-lactam antibiotic used to treat bacterialinfections 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

STUDY DESIGN: Randomized Controlled trial.

SETTING: Department of Otorhinolaryngology, Head & Neck Surgery, Allied Hospital Faisal Abad.

DURATION OF STUDY: January 2017 to June 2017

Inclusion Criteria: All patients fulfilling the case definition of acute bacterial sinusitis after clinical examination done by an ENT specialist.

- Age 15 to 55 years, either gender.

Exclusion Criteria:

- 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 Levofloxicin
- Patient with previous sinus/conventional nasal surgery
- Patients with history of diabetes mellitus
- History of Pregnancy and actively lactating mothers.

DATA COLLECTION PROCEDURE:

Patients were collected from outdoor department of Otorhinolaryngology, Head & Neck Surgery, Allied Hospital Faisal Abad. Patient's demographic data along with registration number was entered on Proforma. After the informed consent, patients were randomly assigned into two groups based on Lottery method in Group A and Group B. Patients of 15 to 55 years of age were included based on the presence of any four or more symptoms and two or more signs described in inclusion criteria. Patients were excluded by history if they were already on any antibiotics, if non-compliant, if have any drug allergy or if any previous nasal surgery. Blood sugar was checked in suspected diabetic patients, if required. Pregnant women were excluded by history and urine pregnancy test, if required. 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 Levofloxicin Group) received Oral Levofloxicin250 mg every 12 hours for 10 days. All the patients were kept under strict survellience 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. (Annexure I)

DATA ANALYSIS PROCEDURE:

All data would be entered and analyzed using SPSS version 10. Mean and standard deviation was calculated for age and duration of sign and symptoms. Frequency and % age was calculated for gender and efficacy. Chi-Square test was used to determine the difference in efficacy in two groups. Potential effect modifiers like sex, age and duration of rhinosinusitis at presentation were controlled through stratification and post-stratification chi square was applied to see their effect on efficacy. P- value ≤ 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. Majority of the patients 129 (35.83%) were between 31 to 45 years of age as shown in Table I. Out of these 360 patients, 143 (39.72%) were male and 217 (60.28%) were females with ratio of 1:1.5 (Figure I).

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. Majority of the patients 215 (59.72%) were ≤ 4 weeks of duration of disease as shown in Table II.

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 as shown in Figure II.

Stratification of efficacy in both groups with respect to age groups has shown in Table III. Table IV & Table V have shown stratification of efficacy according to gender and duration of disease in both groups respectively.

Table-I: Age distribution for both groups (n=360).

Age (years)	Group A (n=180)		Group B (n=180)		Total (n=360)	
	No. of patients	%age	No. of patients	%age	No. of patients	%age
15-30	51	28.33	53	29.44	104	28.89
31-45	66	36.67	63	35.0	129	35.83
46-55	63	35.0	64	35.56	127	35.28
Mean ± SD	**35.73 ± 7.31**		**35.91 ± 8.24**		**35.79 ± 7.86**	

Figure I: %age of patients according to Gender (n=360)

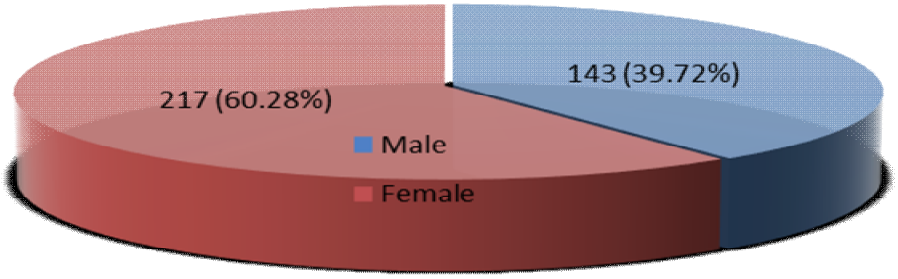
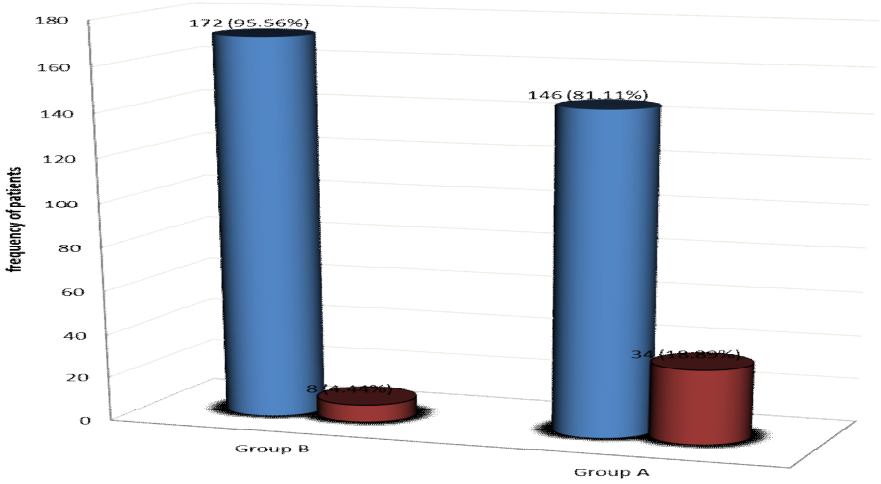


Table II: %age of patients according to duration of disease.

Duration of disease	Group A (n=180)		Group B (n=180)		Total (n=360)	
	Frequency	%age	Frequency	%age	Frequency	%age
≤4 weeks	109	60.56	106	58.89	215	59.72
>4 weeks	71	39.44	74	41.11	145	40.28
Mean ± SD	**4.33 ± 2.72**		**4.28 ± 2.60**		**4.19 ± 2.36**	

Figure II: Percentage of patients according to Efficacy in both groups (n=360).



P-value = 0.000 which is statistically significant.

Table III: 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 IV: 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 V: 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

Acute bacterial rhinosinusitis (ABRS) is a bacterial infection involving the paranasal sinuses and is usually preceded by a viral upper respiratory tract infection (URTI; i.e., the "common cold") or an acute exacerbation of an allergic disorder.[13] In 1996, the American Academy of Otolaryngology–Head and Neck Surgery Foundation developed working definitions of sinusitis in an attempt to standardize communication among health-care providers and researchers.[14] Because sinusitis is generally preceded by rhinitis and rarely occurs without concurrent rhinitis, the more appropriate term for this condition is "rhinosinusitis." Bacterial superinfection may occur at any time point after viral infection but is generally assumed to have occurred if symptoms have persisted for >10 days or have worsened after 5–7 days.[14]

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.[15] 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.

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[16] 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.

The German sinus treatment guidelines recommend amoxicillin as empirical first-line therapy.[17] Many alternatives are listed in those guidelines, including β-lactam/β-lactamase inhibitor combinations, second-generation oral cepahlosporins, macrolides, ketolides, TMP-SMZ, doxcycline, and clindamycin. For patients with more-severe disease (risk factors) or for whom first-line therapy failed, amoxicillin-clavulanate, second-generation cephalosporins, or, alternatively, respiratory fluoroquinolones or third-generation cephalosporins are the recommended therapies. Treatment guidelines for ABRS have also been published by the Spanish Society of Chemotherapy and the Spanish Society of Otorhinolaryngology and Cervico-Facial Pathology.[18] These recommendations were based on the following susceptibility data for the geographic region: *S. pneumoniae* was highly susceptible to moxifloxacin (99.6%), levofloxacin (99.6%), telithromycin (98.92%), and high-dose amoxicillin (94.9%).

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 clavulanatet.i.d.) for 10–14 days.[19] 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 Adelglasset al[20] 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.

In another trial, Jareoncharsriet al[21] compared the clinical efficacy and bacteriological response of levofloxacin and amoxicillin/clavulanic acid (co-amoxiclav) in sixty patients having purulent maxillary sinusitis for 14 days. This study demonstrated that levofloxacin 300 mg orally once daily was as effective and safe as amoxicillin/clavulanic acid 625 mg three times a day in the treatment of maxillary sinusitis, either acute or acute exacerbation. Both drugs showed bacteriological efficacy that was not significantly different. On the whole, it is concluded that levofloxacin has better efficacy than amoxicillin-clavulanate in the treatment of acute bacterial rhinosinusitis in terms of signs and symptoms relief.

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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