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A RANDOMISED CONTROLLED TRIAL TO FIND OUT THE BETTER TREATMENT CHOICE OF ACUTE BACTERIAL RHINOSINUSITIS

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Abstract:

Objective: *The research objective is the comparison of the effectiveness of Levofloxacin and Amoxicillin-Clavulanate in the dealing of acute bacterial rhinosinusitis.*

Materials & Methods: *A sample size of 360 acute bacterial sinusitis patients of both genders, ageing from fifteen to fifty-five was selected. Those patients were excluded who had pneumonia, diabetes mellitus, and allergy to levofloxacin. Two random groups were made; Group A were given 01 gram, 02 times a day, of Amoxicillin-clavulanate for ten days and Group B were given 250 grams, 02 times a day, of Levofloxacin for ten days. Before the start of antibiotic and after the treatment on 11th day, symptoms were recorded of all patients.*

Results: *Group A patients have (35.73 ± 7.31) years as mean age and group B have (35.91 ± 8.24) years. Male patients were 39.72% (143) and females were 60.28% (217) with having (1:1.5) ratio. In Levofloxacin (group B) patients, efficacy was found 95.5% (172) and in Amoxicillin-clavulanate (group A) patients, 81.11% (146) having p-value (p=0.000).*

Conclusion: *The study concludes that to treat acute bacterial rhinosinusitis, levofloxacin provides better efficacy with the low cast than amoxicillin-clavulanate regarding symptoms and signs of relief.*

Keywords: *Amoxicillin-Clavulanate (AC), Levofloxacin, Acute Rhinosinusitis (ARS), Acute Sinusitis (AS), Acute Bacterial Rhinosinusitis (ABRS), Stratification of Efficacy (SOE), Randomized Controlled Trials (RCTs), Levofloxacin (LEV), Co-Amoxiclav (COA).*

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INTRODUCTION:

ARS is a bacterial/acute viral infection, which causes paranasal sinuses and inflammation of nose mucosa [1]. However, acute viral rhinosinusitis occurs most commonly. It is better considered a symptom of severity and prolonged ARS if it is recovered early without the use of antibiotic therapy. If rhinosinusitis is cured before twelve weeks, it is considered acute, if it exceeds twelve weeks, chronic, and if it occurs for three episodes in a year, it is considered recurrent acute. Although 40% of the symptoms of rhinosinusitis are resolved promptly without treatment, even then medical treatment is started promptly to increase the speed of symptomatic resolution, avoid possible complications and evolution to chronicity [2]. The essential objective in dealing with AS is the eradication of infection, and decrease of severity. If the deterioration and symptoms exist even though antibiotic is continued, nosocomial infection or complication persists, or sinusitis episodes are present, then otolaryngologist's evaluation is recommended. It is the main goal of the treatment of AS to treat the bacterial pathogens systematically and provide adequate drainage to it. It is suggested by Joint Task Force on Practice Parameters for Allergy and Immunology to continue assessment of symptoms after three to seven days of therapy continue treatment for seven days more if improvement is noticed. Symptoms are reduced effectively with the combination of intra-nasal corticosteroid and antibiotic [3]. To avoid septic complications, patients with AS should be treated with intensive care. Drainage can be carried out either medically or surgically, considering the removal of nasogastric and nasotracheal tubes. Pynnonen et al. retrospective cohort study suggested that depending on the provider, (whether a medical trainee or emergency medicine providers) patients (66%) are given with the overuse of antibiotics for a mild AS [4]. Whether a controlled or rigorous clinical trial, the use of topical nasal corticosteroids (with or without the combination of anti-microbial agents) for treatments has showed therapeutic utility [5 – 7]. The treatment of choice for mild, moderate, and severe ARS is amoxicillin-clavulanate/cefadroxil, levofloxacin or moxifloxacin, and cefotaxime/cefixime/ceftriaxone respectively [8 – 10]. The collected data of Europeans suggests the efficacy of using amoxicillin-clavulanate over levofloxacin is higher [11 – 12]. No Pakistani data at this regard is available. The purpose of the study was to compare the efficacy of using two mostly used medicines in the treatment of ARS among Pakistanis (sample population). The use of Levofloxacin is more cost-effective than amoxicillin-clavulanate in treating ARS among our sample size. Clinical parameters included; the complaints of patients like blockage of nose, headache, feeling bad smell or unable to smell; discharge from nasal cavity, the frequency of episodes per hour and per day. The assessment of physical symptoms by an ENT specialist like post-nasal drip, mucopurulent nasal discharge in meatus, swollen and nasal turbinate. The inclusion of at least four symptoms and two signs occurred for more than ten days or seven days with severity of symptoms is the requirement for the diagnosis of ABRS. Amoxicillin-Clavulanate treats the bacterial infections due to microorganisms using a moderate spectrum, β-lactam antibiotic, and bacteriolytic. Dose of 01gm/12 hour for ten days is used on Group (A). Levofloxacin treats the severe bacterial infections or any of those bacterial infections, which remain uncured by any other antibiotics. It is a synthetic-chemotherapeutic-antibiotic from the class of fluoroquinolone drug. Dose of 250mg/12 hours for ten days on Group (B).

MATERIAL AND METHODS:

Our RCT (Randomized Controlled Trial) research was carried out from March 2016 to August 2017 at Mayo Hospital, Lahore in the Otorhinolaryngology department. All the patients who are declared with acute bacterial sinusitis, fulfilling case definition, by an ENT specialist were included in the research within the age group of fifteen to fifty-five years wither male or female. We did not include all the cases such as antibiotic consumer, incomplete dosage of treatment, existence of complication (Pneumonia etc.), history of allergies to AC/Levofloxacin, patients who had sinus previously, having history of diabetes mellitus and females who were actively lactating and pregnant.

A Performa of patient's registration number and demographic record was filled, with informed consent. Lottery-based division of patients (15 – 55 years age group) into Group A & B was carried out. Patients with at least 04 symptoms and 02 signs of inclusion criteria were included. Patients with drug allergies, previous sinus, history of antibiotics, and pregnant women were excluded. Blood of suspected diabetic patients was checked for sugar level. Same dose of nasal decongestant with nasal spray of xylometazoline and steam inhalation was given to all patients for equal duration. Group A of AC dose received one-gram oral AC every twelve hours for ten days. Levofloxacin group (Group B) received 250 mg of oral levofloxacin every twelve hours for ten days. All patients were observed for side effects and followed up through telephone contact. Signs and symptoms of patients were recorded before the start and after the completion of treatment. Performa was

used for data collection.

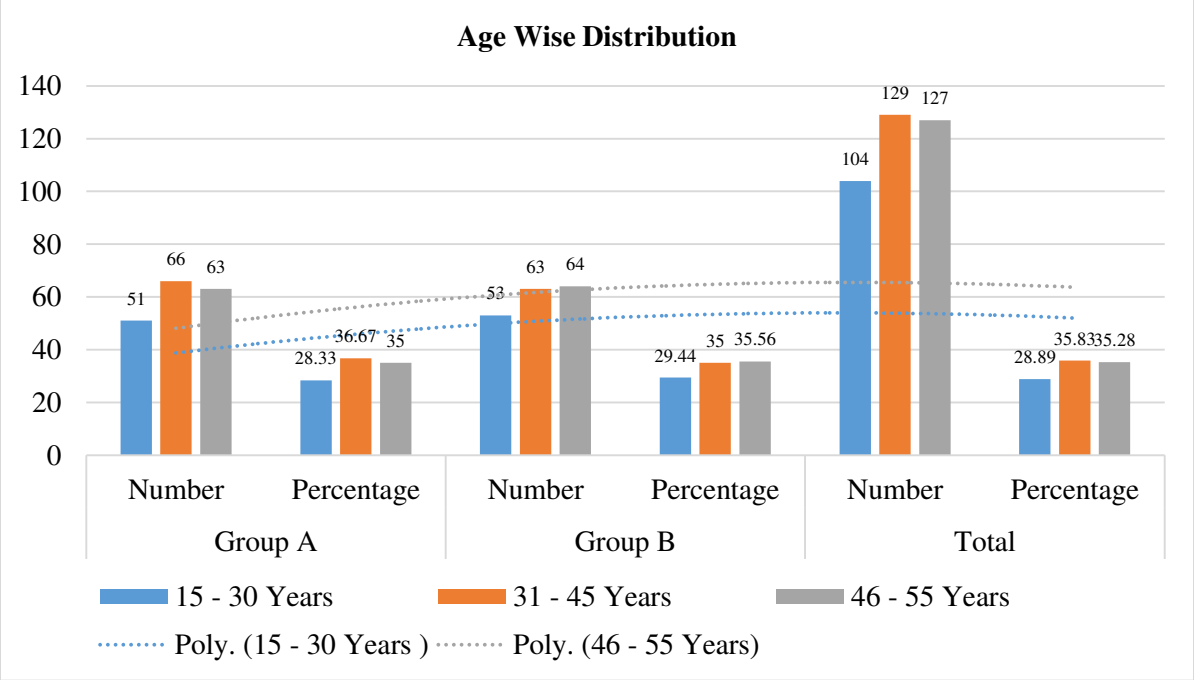
Data analysis would be carried out using SPSS calculating standard and mean deviation for the duration of symptoms and sign. Efficacy and gender's percentage and frequency was calculated with efficacy difference between both groups determined through Chi-Square test. Effecting variables like age, sex and ARS duration were controlled pre and post-stratification, suing Chi-Square to observe effects on efficacy. Significant p-value was taken ≤ 0.05.

RESULTS:

The study included patients of 15 – 55 years age having (35.7 ± 7.8) years as mean age. Group A patients have (35.73 ± 7.31) years as mean age and group B have (35.91 ± 8.24) years. Age group of 31 – 45 years were in majority 35.83% (129) (Table – I).

Table – I: Age Wise Distribution

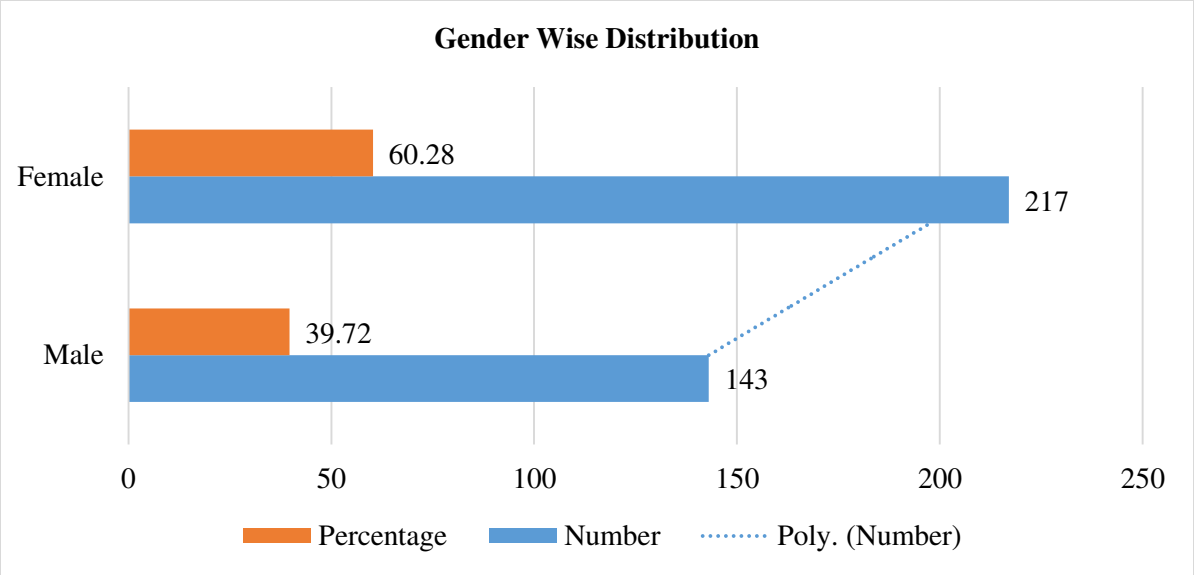
Age	Group A		Group B		Total	
	Number	Percentage	Number	Percentage	Number	Percentage
15 - 30 Years	51	28.33	53	29.44	104	28.89
31 - 45 Years	66	36.67	63	35	129	35.83
46 - 55 Years	63	35	64	35.56	127	35.28
Mean ± SD	**35.73**	**7.31**	**35.91**	**8.24**	**35.79**	**7.86**



Male patients were 39.72% (143) and females were 60.28% (217) with having 1:1.5 ratio (Table – II).

Table – II: Gender Wise Distribution

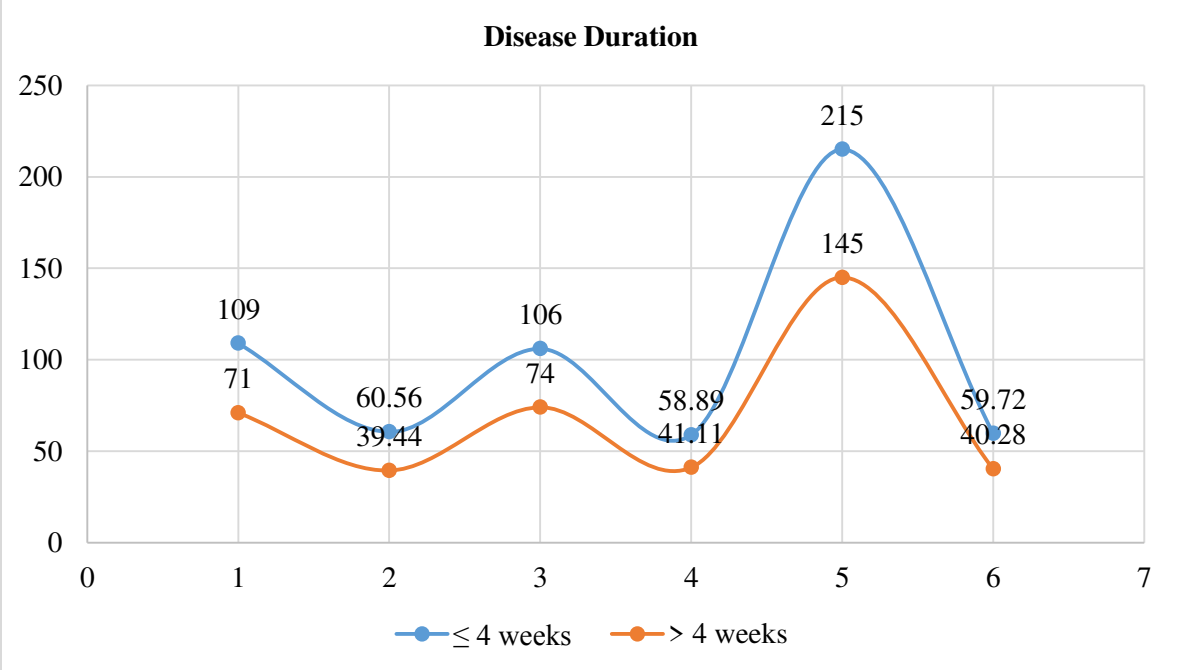
Gender	Number	Percentage
Male	143	39.72
Female	217	60.28



For 4.19±2.36 weeks of mean duration, symptoms existed on the other hand, for disease, mean duration for group A & B is 4.33±2.72 and 4.28±2.6 weeks respectively. Total 59.72% (215) patients had a duration of disease as ≤ 4 weeks (Table – III).

Table – III: Patients' (360) percentage with respect to the duration of disease.

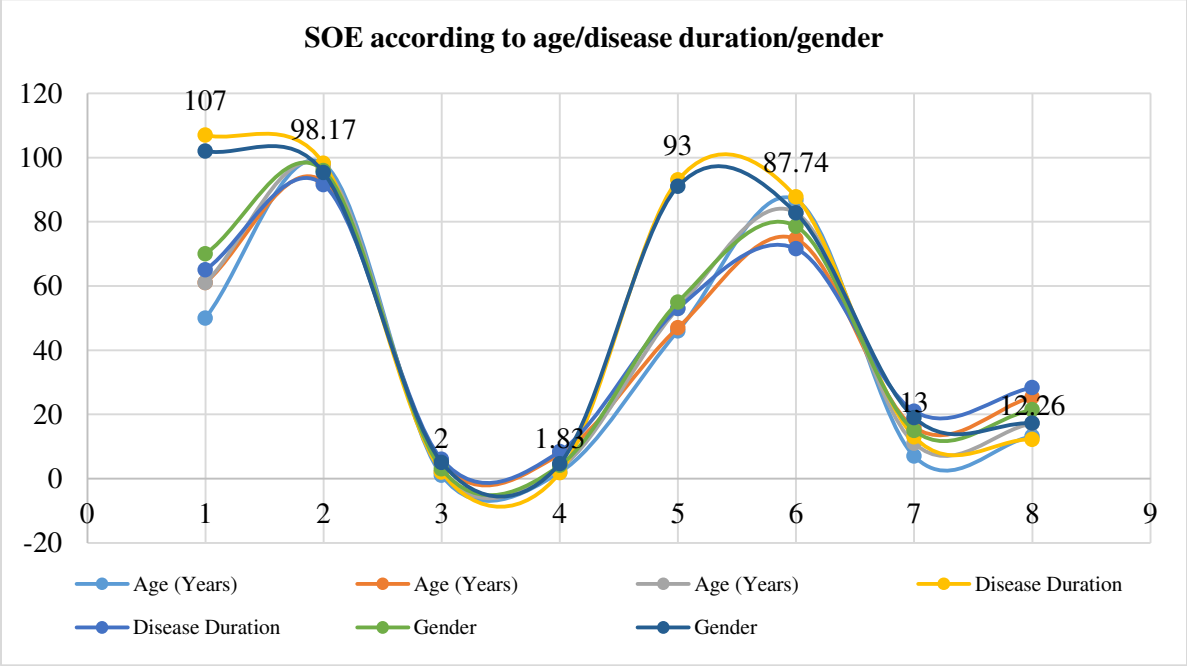
Disease Duration	Group A		Group B		Total	
	Number	Percentage	Number	Percentage	Number	Percentage
≤ 4 weeks	109	60.56	106	58.89	215	59.72
> 4 weeks	71	39.44	74	41.11	145	40.28
Mean ± SD	4.33	2.72	4.28	2.6	4.19	2.36



Efficacy rate was 95.5% (172) and 81.1% (146) patients in Group B and A respectively. SOE with respect to the duration of disease and gender in both groups is as below.

Table – IV: SOE according to age/disease duration/gender

Age/Duration/Gender		Group B (180)				Group A (180)				P-value
		Yes		No		Yes		No		
		No	%	No	%	No	%	No	%	
Age (Years)	15-30	50	98.04	1	1.96	46	86.79	7	13.21	0.031
	31-45	61	92.42	5	7.58	47	74.60	16	25.40	0.006
	46-55	61	96.83	2	3.17	53	82.81	11	17.19	0.009
Disease Duration	≤ 4 Weeks	107	98.17	2	1.83	93	87.74	13	12.26	0.003
	> 4 Weeks	65	91.55	6	8.45	53	71.62	21	28.39	0.002
Gender	Male	70	95.89	3	4.11	55	78.57	15	21.43	0.002
	Female	102	95.33	5	4.67	91	82.73	19	17.27	0.003



DISCUSSION:

ABRS is an infection of paranasal sinuses that occurs after an acute exacerbation of an allergic disorder or a common cold (upper respiratory tract infection) [13]. To communicate in a standard way with health care researchers, Head and Neck Surgery Foundation of American Academy of Otolaryngology created sinusitis definition in 1996 [14]. The term "rhinosinusitis" is made because sinusitis is most of the times preceded by rhinitis [14]. Sinus aspirate has not been used for the treatment of ABRS before in RCTs, other than in non-standardized trials, which has shown some bacterial cure. Antibiotics like Amoxicillin and TMP-SMX (trimethoprim-sulfamethoxazole) with placebo have compared with 05 RCTs and 02 Meta-analysis, where the former showed a more improved clinical outcome [15]. During ten to fourteen days, 47% patients with antibiotics and 32% patients of the control group were cured. Patients cured/improved with antibiotic were 81% and 66% were cured/improved with the control group. Efficacy was observed as 'yes' (p-value=0.000) among 95.5% (172) and 81.1% (146) patients in Group B (Levofloxacin) and A (AC) respectively in this study. The efficacy in treating purulent maxillary sinusitis was compared between the use of levofloxacin and co-amoxiclav in this study [16]. For fourteen days, 60 patients received either 625mg co-amoxiclav 3-times a day or 300mg levofloxacin once a day. Radiological improvement of 61.80% and 60.50% found with a resolution of 41.20% and 26.90% and improvement of 20.60% and 34.60% for levofloxacin and co-amoxiclav respectively. The percentage of pre-treatment of maxillary antral aspiration found positive in 82.40% (28) and 76.90% (20) for levofloxacin group and

COA group respectively. LEV group achieved 78.50% bacteriological eradication and COA group achieved 70%. The rate of eradication for major pathogens of AS was 66.70% and 0% for P. aeruginosa, 100% and 75.0% for H. Influenza, 100% and 50% for Neisseria species, 100% and 100% for S. aureus, and 100% and 100% for S. pneumonia, in group LEV and COA respectively. Amoxicillin is recommended by German for sinus treatment as 1st-line therapy [17]. Patients who were not cured with first-line therapy or severe risk factor, AC, 2nd or 3rd generation cephalosporins are suggested recommendations. Spanish Society of Chemotherapy/Otorhinolaryngology and Cervico-Facial Pathology has published ABRS treatment guidelines [18]. In a trial, 535 clinically evaluated patients could receive 500mg/day LEV or AC for ten to fourteen days [19]. The results (cured/improved) with LEV and AC group were 88.40% and 87.30% after two to five days of therapy. Adelglass et al. study show 88.40% success (cured and improved) for 267 patients and 87.30% success with 268 patients using LEV and AC respectively [20]. The outcome suggests using single LEV a day than using 3 AC/day for the treatment of AS. Another study Jareoncharsi et al. also suggests that LEV 300mg/day orally is as effective as AC or COA 625mg 3 times/day for fourteen days [21]. Both drugs are significantly effective but LEV has relatively better efficacy than AC as a whole in the cure of ABRS considering signs and relief of symptoms.

CONCLUSION:

The study concludes that while treating ABRS, LEV shows better and cost-effective outcomes than AC in terms of relief of symptoms and signs. Therefore, LEV is our recommendation for the symptoms relief and signs of ABRS.

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