Original Article

Role of Amoxicillin, Azithromycin and Moxifloxacin in the empirical treatment of community acquired bacterial sinusitis – An open label randomized study

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Abstract

Background: The study was conducted to compare the safety and efficacy of Amoxicillin, Azithromycin and Moxifloxacin in the empirical treatment of acute bacterial sinusitis. **Materials**: Inthis open label randomized study, Sixty patients of both sexes in the age group of 18 to 65 years showing clinical and radiological evidence of acute bacterial sinusitis were randomly allocated to three groups namely Group 1 receivedamoxicillin 500 mg three times a day for 7 days, group 2 received azithromycin 500 mg OD for 3 days while the third group received moxifloxacin 400 mg OD for 7 days. The patients were followed to look for signs of clinical improvement, to repeat the investigations and for any drug induced adverse reactions. **Results**: Data of 50 patients who completed the study including 16 patients in Group 1 and 2, 18 patients in group 3 was analyzed. Overall symptomatic improvement was almost similar, 81.25% with amoxicillin, 82.50% with azithromycin and 88.46% with moxifloxacin. The clinical cure rate with azithromycin was 75% compared to 77.7 % with moxifloxacin and 68.75% with amoxicillin. Physical signs of acute sinusitis evidenced by rhinoscopy improved better with azithromycin (66.66%) than amoxicillin (50%) and moxifloxacin (55.55%). Significant reduction in Neutrophil count was seen with all the three drugs. The improvement in radiological appearance was slightly lower with amoxicillin. Adverse effects reported were mild and subsided after treatment. **Conclusion:** The clinical cure of acute sinusitis is high with moxifloxacin but compliance would be much better with azithromycin because of its three day course.

Keywords: Amoxicillin, Azithromycin, Moxifloxacin, Community acquired sinusitis, Bacterial sinusitis.

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INTRODUCTION

Sinusitis is one of the commonest varieties of community acquired upper respiratory tract infections leading to large number of outpatient visits to health providers and utilize a large portion of health care resources. It is characterized by inflammation of paranasal sinuses secondary to bacterial invasion after viral rhinitis.[1] In community acquired acute bacterial sinusitis, the organisms most frequently isolated are Streptococcus pneumoniae and Hemophilus influenza in 50-70% cases. Moraxella catarrhalis causes the disease in 20% of children but to a lesser extent in adults. Other Streptococcoal species and Staphylococcusaureus contribute to a small percentage of cases. Methicillin Resistant Staphylococcus aureus is an emerging cause of the disease. The treatment of acute sinusitis is primarily medical, based on empirical goals to avoid complications. In routine practice, the antibiotic of choice to treat acute sinusitis isamoxicillin with or without clavulanic acid. Other alternative agents used are trimethoprim-sulfamethoxazole, cephalosporins, macrolidesand fluoroquinolones.[2] Most of the causative bacteria are becoming resistant to amoxicillin due to their long term and sometimes, indiscriminate use. Patient compliance apparently diminishes with increased duration of therapy, especially for oral antibiotics. Drugs with

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once daily dosing face less resistance and have few adverse effects when compared with old conventional drugs. There are a number of studies comparing the efficacy of co-amoxiclav with either azithromycin or moxifloxacin. Number of studies using amoxicillin is limited. Keeping this in view, the present study was planned to compare the safety and efficacy of three drugs in the treatment of acute bacterial sinusitis namely capsule Amoxicillin 500 mg thrice daily for 7 days, tablet Azithromycin500 mg OD for 3 days and tablet Moxifloxacin 400 mg OD for 7 days.

MATERIALS AND METHODS

A total of 60 patients, both males and females in the age group of 18 to 65 years, were taken for this open label randomized study with the aim of comparing the efficacy and tolerability of three drugs namely amoxicillin, azithromycin and moxifloxacin. The Institutional Ethical Committee approved all the procedures used in the study. Written informed consent was obtained from all the patients. Patients with history of chronic sinusitis, peptic ulcer or any other condition affecting drug absorption, treatment with any other antibiotics within the previous 72 hours, evidence of major systemic disease, pregnant/lactating women, patients who underwent sinus surgery in the past were all excluded from the study. Patients showing the typical features of acute sinusitis such as headache, facial pain, nasal discharge, nasal blocking, fever, sinus tenderness lasting for less than 12 weeks duration were selected. Thorough Medical history was taken and patients were subjected to general physical examination, ENT examination and baseline investigations like complete blood picture and X ray Paranasal sinuses. They were then randomly distributed in equal number to three treatment groups

Group I: Received Amoxicillin 500 mg three times a day for 7 days

Group II: Received Tab Azithromycin 500 mg OD for 3 days

Group III: Received Tab Moxifloxacin 400 mg OD for 7 days

Patients in group I and group III were given tablets for 3 days initially and then asked to report to the hospital, clinical assessment was done following which they were given tablets for 4 more days. Patients were then followed up after completing the treatment, 7 days in case of amoxicillin, moxifloxacin and 3 days in case of azithromycin for recording of any improvement in signs and symptoms, any adverse effects of the treatment and to repeat the investigations. The patients in all the groups were instructed not to take any medicine other than the medicines provided to them during the study period. They were also told to stop the medication if they notice any major undesirable effects and to inform the same to the doctors at the ENT OPD. In assessing the improvements of symptoms after treatment, the patients were told to express his or her improvement as 25%, 50%, 75% or 100% of the initial intensity of the symptoms. Patient's response to treatment was monitored by assessing clinical parameters at baseline and on days 4 and 8 of the study (±1). If there was no improvement in patient's opinion, it was recorded as 0%. If the patient was totally relieved of the symptoms, the improvement was recorded as 100%. Along with patient's opinion, the investigator's assessment of symptoms and signs was also recorded. Similarly the investigation parameters before and after the treatment were recorded in tabular form. The data collected was analyzed using Microsoft Excel.

RESULTS

Of the 60 patients included in this open label study, four patients each in amoxicillin and azithromycin group were dropped out from the study owing to non compliance. One patient in moxifloxacin group withdrew as she developed insomnia, anxiety and nausea. Another patient in the same group was excluded since he did not turn up for the follow up. The efficacy data for this study is therefore based on a total of 50 evaluable patients, 16 each in amoxicillin and azithromycin group and 18 in moxifloxacin group. The demographic data of the included patients is presented in the table 1 and the incidence of various symptoms of acute sinusitis in these patients in table 2.

Table 1: Demographic data

Drug	No if Males	No of Females	Age(Year) Mean±SD
Amoxicillin	9(45%)	11(50%)	35.2±10.87
Azithromycin	12(60%)	8(40%)	32.95±12.95
Moxifloxacin	11(50%)	9(45%)	32.1±10.16

Table 1: Incidence of various symptoms in the patients (n= 60)

S.No	Symptom	No. of Cases
1	Headache	42 (70)
2	Facial pain	33 (55)
3	Nasal discharge	28 (80)
	Watery	3
	Mucoid	12
	Mucopurulent	13
4	Nasal blocking	40 (66.6)
5	Sinus tenderness	42 (70)
6	Anosmia	4 (6.66)
7	Epistaxis	2 (3.33)
8	Fever	12 (20)
9	Pus in the middle meatus	6 (10)
10	Nasal allergy	24 (40)

The percentage improvement in symptoms like Headache, facial pain, Nasal discharge, nasal block and sinus tenderness was almost similar in all the three groups (Table 3). Other associated symptoms like fever, anosmia,

cough, epistaxis, earache and post nasal discharge decreased by 100% in all the groups.

Table 2: Percentage overall improvement in symptoms in each group

Symptom	Amoxicillin	Azithromycin	Moxifloxacin
Headache	81.25	82.50	88.46
Facial Pain	80.55	87.50	90.00
Nasal discharge	80.76	87.50	88.33
Nasal Block	84.09	88.88	88.46
Sinus tenderness	95.83	97.50	96.15

The investigators opinion of clinical response at the end of the therapy in the evaluable group of patients was done. The results in the groups treated with azithromycin and moxifloxacin were virtually identical and that in the amoxicillin group was slightly less. The clinical cure rate measured after day 8 but after only 3 days treatment of azithromycin once daily dosing was 75% compared to 77.77% with moxifloxacin once daily dosing and 68.75% with amoxicillin three times a day dosing (Fig 1).

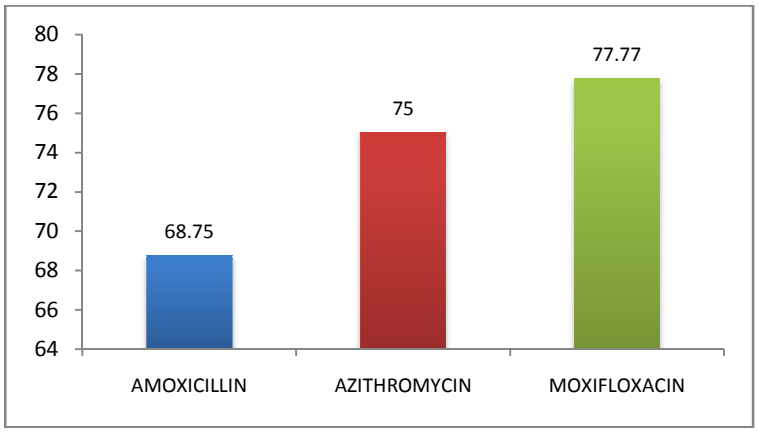

Figure 1: Percentage of patients showing clinical cure at the end of the study

Physical signs of acute sinusitis as seen by rhinoscopy improved better with azithromycin, 66.66% patients showing normal appearance of nasal cavity after treatment as compared to 50% with amoxicillin and 55.55% with moxifloxacin (table 4). Two patients in amoxicillin group showed concha bullosa (a large pneumatised middle turbinate get secondarily infected giving rise to chronic nasal symptoms) on rhinoscopy.

Table 3: Rhinoscopy findings

Drug	Before treatment	After treatment		
	No of patients showing any features of acute sinusitis*	No. (%) of patients showing		
		No improvement	Partial improvement	Normal appearance
Amoxicillin	14	3 (21.43%)	4 (28.57%)	7 (50%)
Azithromycin	15	2 (13.33%)	3 (20%)	10 (66.66%)
Moxifloxacin	18	2 (11.11%)	3 (16.66%)	13 (72.33%)

Regarding the blood parameters, significant reduction was observed in neutrophil count in all the three groups. (fig 2).

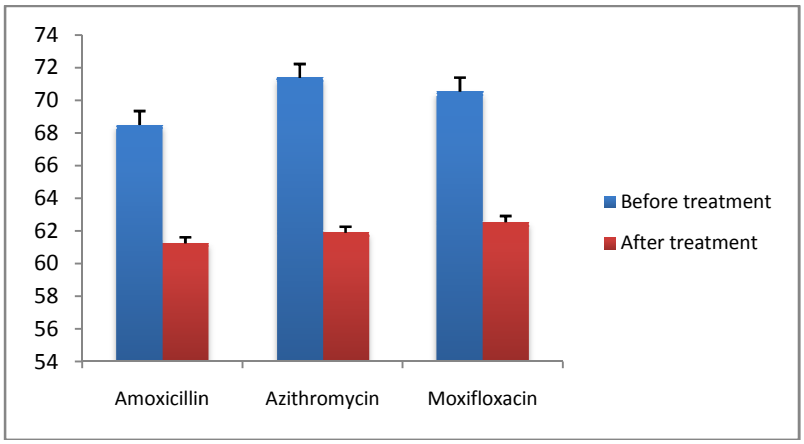

Figure 2: Graphical representation of neutrophil count (Mean + SEM)

X-ray paranasal sinuses were suggestive of acute sinusitis in all the cases before starting the treatment, which were read by a radiologist. Complete clearing of the sinuses was observed in 15 sinuses (55.55%) in amoxicillin group, 17 (58.62%) in azithromycin group and 20 (62.50%) in moxifloxacin group. Persistence of mucous membrane thickening was observed in 4 (44.44%) in amoxicillin group, 6 sinuses (60%) in azithromycin group and 4 sinuses (33.33%) in moxifloxacin group. The mucosal thickening can be taken as intermediate radiological sign during the resolution of sinus inflammation. Out of the 6 cases showing air fluid level before treatment, it was observed that it persisted only in 2 cases (33.33%) after treatment. Three out of 6 opaque antra turned normal. Further evaluation and treatment are needed for the remaining three cases that did not turn normal.

Patients of the three groups reported adverse effects. Four out of 50 patients reported a total of six side effects. In the amoxicillin group, two (12.5%) patients reported gastro intestinal disturbances namely loose stools and dyspepsia while one (6.25%) in azithromycin group complained of nausea. One patient in moxifloxacin group (5.56%) complained of nausea. Another one patient in the moxifloxacin group complained of insomnia, anxiety and giddiness withdrew from the study.

DISCUSSION

Sinusitis is the one of the most commonly acquired respiratory tract infections encountered in large number of patients attending Ear, Nose, Throat clinics who seek advice with variable complaints ranging from mild nasal congestion to debilitating pain. It is the result of impaired mucociliary clearance, obstruction of the osteomeatal complex with secondary bacteria infection. Acute bacterial sinusitis(ABS) is primarily treated empirically in family physician's clinic with first line antibiotic like amoxicillin with or without clavulanic acid. Other antibiotics that are also effective are third generation cephalosporins, macrolides and fluoroquinolones.[2]

In the present study, safety and efficacy of amoxicillin, azithromycin and moxifloxacin in the treatment of acute bacterial sinusitis was compared. The results indicated virtually identical symptomatic improvement in all the treatment groups. However overall clinical improvement is more pronounced in moxifloxacin group (77.77%) followed by azithromycin group (75%) when compared to amoxicillin (68.75%).

Azithromycin is a semisynthetic derivative of macrolide erythromycin. It has unique pharmacokinetic properties, which includes extensive tissue distribution and high drug concentrations in within the cells (phagocytes), resulting in much greater concentrations of drugs in tissue or secretions compared to simultaneous serum concentrations.[3] The clinical cure rate with Azithromycin in the patients of ABS was found to be 95.83%[4], faster than that with amoxicillin/Clavulanate[5]. A study comparing 500mg Azithromycin 3 days, 5 days regimes to 10 days course of Amoxicillin/ clavulante showed that the clinical efficacy to be equal.[6.7] Another study from Iran comparing efficacy of coamoxiclav and azithromycin reported faster cure rate with azithromycin with no difference in the incidence of side effects.[8]

Moxifloxacin is a respiratory fluoroquinolone known to have high cure rate (89.4%)[9] and low incidence of adverse effects in patients of acute bacterial sinusitis. It is found to be effective even in Penicillin resistant strains of Staphylococcus aureus.[10] A study comparing the moxifloxacin and Amoxicillin/ clavulanate in ABS showed that both the drugs are similar in their clinical and bacteriological cure rates.[11] The main advantage with moxifloxacin is its rapid cure rate and relief of symptoms compared to β-lactum antibiotics.[12] This may be attributed to the greater penetration of moxifloxacin in the sinus mucosal tissues.[13]

CONCLUSION

This study of patients with radiologically documented acute bacterial sinusitis has shown that only 3 doses of azithromycin over 3 days was as effective as 7 days course of once daily dose of moxifloxacin. Though symptomatic improvement in all the three groups was virtually identical, clinical cure rate was slightly lower with 7 days course of amoxicillin given 3 times a day.Improvement in physical science is also more or less identical with all the three antibiotics. The improvement in radiological (x-ray) appearance was equal in the azithromycin, moxifloxacin groups but it was slightly lower in the amoxicillin group.

The clinical efficacy was found to be equal with all the three drugs. Adverse effects shown by patients of all the three groups were mild and subsided after treatment. Patient compliance is likely to be better with moxifloxacin due to its once daily dosing with moxifloxacin as compared to thrice daily dosing of amoxicillin. Patient compliance would be much better with azithromycin as the course of treatment is only for 3 days with once daily dosage.

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