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Management of acute bacterial sinusitis: a prospective observational, multicenter study focusing on the safety and efficacy of Moxifloxacin

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Abstract

Objective: To observe the efficacy, safety & tolerability of moxifloxacin in patients with Acute Bacterial Sinusitis across Pakistan.

Material & Methods: This was the prospective, observational multicenter study in patients diagnosed with Acute Bacterial Sinusitis treated with Moxifloxacin therapy. The convenient sampling technique was used to select the patients. The ethical approval was taken by the institutional research forum of Rawalpindi Medical College. Patient data originating from assessments and evaluations performed according to the physician's routine practice was collected in a well-designed proforma. SPSS version 20.0 was used to analyze the data.

Results: The most common reason for change of medication was failure of the previous therapy in 139 (81%) patients.The comparison of symptoms at 3rd and 14th day period revealed that they were absent in 152 (88.4%) patients at 14th day, while mild and severs symptoms were reduced to 17(9.9%) and 3(1.7%) patients with a significant p value of 0.004. The most common adverse effect was dizziness that was found in 30% of the cases followed by nausea and vomiting, others like palpitation, body ache and gastric upsets and dry mouth in 7%, 6% and 4% cases respectively.

Conclusion: Moxifloxacin is effective in resolving the symptoms of acute bacterial sinusitis. It is more effective than other antibiotics because of its efficacy and least side effects. The medicating of simple once daily dosage offer benefits over many existing agents in terms of compliance as well.

Keywords: Management of Acute Bacterial Sinusitis; Safety and Efficacy of Moxifloxacin;

Introduction

A well predictable and common health problem is acute sinusitis which primarily affects the maxillary sinuses but its disease burden is often considered insignificant. The bacteria most often responsible for acute sinusitis include *Haemophilus influenzae*, *Streptococcus pneumoniae* and *Moraxella catarrhalis.* Otherbacterial pathogens, such as *Staphylococcus aureus*, Enterobacteriaceae and anaerobic bacteria are the rare causative agents [1]. Sinus involvement is frequently associated with the common cold. Thus, the condition probably is well pronounced as viral rhino sinusitis (VRS) rather than sinusitis. An estimated 1 billion of such cases of VRS occur each year in the United States. However, around 0.5% to 2% of VRS cases in the United States are complicated by secondary bacterial infections of the sinuses [2]. It was estimates that over 25% of the population suffer from rhinosinusitis with significant associated comorbidities which considerable effects on quality of life and educational performance [3]. An acute viral or bacterial infection categorized by inflammation of the nose mucosa and paranasal sinuses is considered as Acute Rhinosinusitis (ARS) [4]. An acute bacterial rhinosinusitis is equally communal in incidence; however most cases are of viral basis. There is a prompt improvement in most of patients without antibiotic therapy but it must be considered in patients with extended or more severe indications. Rhinosinusitis is considered to be acute (viral or non-viral origin) if it lasts less than 12 weeks, and chronic when it exceeds more

than 12 weeks. However, if it occurs with three or more episodes in one year, then is considered as recurrent. In 40% of the cases its symptoms disappear spontaneously without and therapy. However, medical treatment is specified to reduce the symptoms, hasten the improvement of the clinical features and avoid apparent complications [5]. The signs and symptoms of Acute Bacterial Sinusitis (ABS) include nasal obstruction or stuffiness, mucopurulent nasal expulsion or postnasal dribble, facial pain, headache, and decrease or loss of smell and observation of bad smell (cacosmia). Signs include erythematous nasal turbinate, mucopurulent nasal discharge of meatus and post nasal drip [6].

Antimicrobial agents and local nasal decongestant like corticosteroids used in combination or as a solitarytreatment have verified theraupatic utility in controlled experimental trials [7, 8].

Accumulative resistance of organisms to regularlyemployed antibiotics presents a challenge in the treatment of sinusitis. However, Fluoroquinolones are not demolished by beta-lactamase-producing organisms and are therefore used as substitute treatment operative against gram-negative pathogens, such as H. influenzae and M. catarrhalis. Some quinolones also have activity against S. pneumoniae, including multidrug resistant strains Moxifloxacin is a new 8-methoxy-fluoroquinolone antibacterial agent [9, 10, 11, 12]. Moxifloxacin has a extended half life with high capacity of dissemination. It is

Table 1: Clinical features of Acute Bacterial Sinusitis

Variable		Yes	No
Cheek Tenderness	n	151	21
	%	88	12
Forehead Tenderness	n	143	29
	%	83	17
Fever	n	156	16
	%	91	9
Purulent Nasal Discharge	n	147	25
	%	85	15
Headache	n	163	9
	%	95	5
Facial Pain	n	93	79
	%	54	46
Upper Alveolus	n	142	30
	%	83	17
Diminished or Absent Sense of Smell	n	128	44
	%	74	26
Bad Breath	n	124	48
	%	72	28
Fatigue	n	138	34
	%	80	20
Ear Pain	n	119	53
	%	69	31

Table 2: Symptoms of ABS on 3rd Day and 7th day

Variable	3rd Day		7th Day		
	Frequency	Percent	Frequency	Percent	P-Value
Totally Relieved	17	9.9	113	65.7	0.007
Partially Relieved	137	79.7	57	33.1	
Not Relieved	18	10.5	2	1.2	
Total	172	100.0	172	100.0	

*Kendall's tau-b test applied to see the significance

The Symptoms was compared at 3rd and 7th day of treatment. It was noticed that symptoms were absent in 113 (65.7%) respondents at 7th day. Mild symptoms were decreased to 57 (33.1%) and sever symptoms were reduced to 2 (1.2%) . A significant difference was found with p value of 0.007 (Table 2, Figure 2)

Table 3: Symptoms of ABS 3rd Day vs 14th day

Variable	3rd Day		14th Day		
	Frequency	Percent	Frequency	Percent	P-Value
Totally Relieved	17	9.9	152	88.4	0.004
Partially Relieved	137	79.7	17	9.9	
Not Relieved	18	10.5	3	1.7	
Total	172	100.0	172	100.0	

*Kendall's tau-b test applied to see the significance

The comparison of symptoms at 3rd and 14th day period revealed that they were absent in 152 (88.4%) patients at 14th day, while mild and severs symptoms were reduced to 17(9.9%) and 3(1.7%) patients with a significant p value of 0.004. (Details are given in Table 3, Figure 3)

Table 4: Symptoms of ABS 7th Day vs 14th day

Variable	7th Day		14th Day		
	Frequency	Percent	Frequency	Percent	P-Value
Totally Relieved	113	65.7	152	88.4	0.000
Partially Relieved	57	33.1	17	9.9	
Not Relieved	2	1.2	3	1.7	
Total	172	100.0	172	100.0	

*Kendall's tau-b test applied to see the significance

The symptoms were compared at 7th and 14th day period. It was noticed that symptoms were absent in 152 (88.4%) patients at 14th day. Mild symptoms were decreased to 17 (9.9%) and sever symptoms were reduced to 3(1.7%) patients with a p-value of 0.000 (Table 4, Figure 4)

Table 5: Patient Condition 3rd day vs 7th day

	Frequency	Percent	Frequency	Percent	P-value
Cured	9	5.2	96	55.8	0.047
Improved	163	94.8	66	38.4	
Unchanged	0	0.0	5	2.9	
Worse	0	0.0	5	2.9	
Total	172	100.0	172	100.0	

*Chi square test applied to see the significance

It was noticed that on 7th day as compared to the 3rd day the patients were cured and improved in 96 (55.8%) and 66 (38.4%) respectively with a significant p value of 0.047. (Table5)

well absorbed orally and recent studies have shown that it has predominantly good activity against S.pneumoniae, H. infuenzae and M. catarrhalis. These organisms are important causative agents of respiratory and sinus infections [13, 14]. The high concentration of moxifloxacin at the site of infection is due to its good tissue penetration, that becomes progressively significant with the range of antibiotic-resistant strains [15].

This study was intended to recognize the usefulness of moxifloxacin in patients with acute bacterial sinusitis in Pakistani population. The purpose ofthis study was to observe the efficacy, safety in terms of adverse events other than side effects & tolerability of moxifloxacin in patients with Acute Bacterial Sinusitis across Pakistan.

Table 6: Patient Condition 3rd day vs 14th day

	Frequency	Percent	Frequency	Percent	P-value
Cured	9	5.2	146	84.9	
Improved	163	94.8	17	9.9	
Unchanged	0	0.0	4	2.3	0.034
Worse	0	0.0	5	2.9	
Total	172	100.0	172	100.0	

*Chi square test applied to see the significance
It was noticed that on 14th day as compared to the 3rd day the patients were cured and improved in 146 (84.9%) and 17 (9.9%) respectively with a significant p value of 0.034. (Table 6)

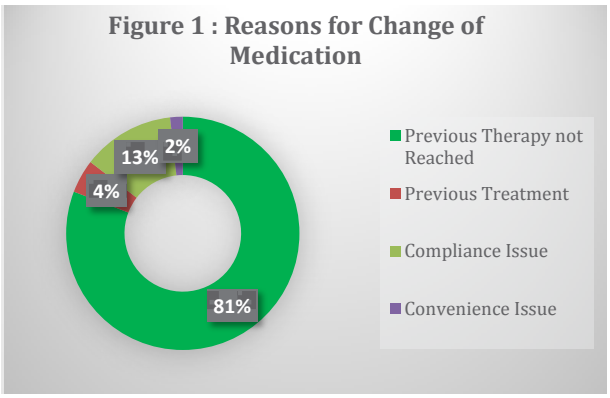

Figure 1: The most common reason for change of medication was failure of the previous therapy in 139 (81%) patients. (Figure 1)

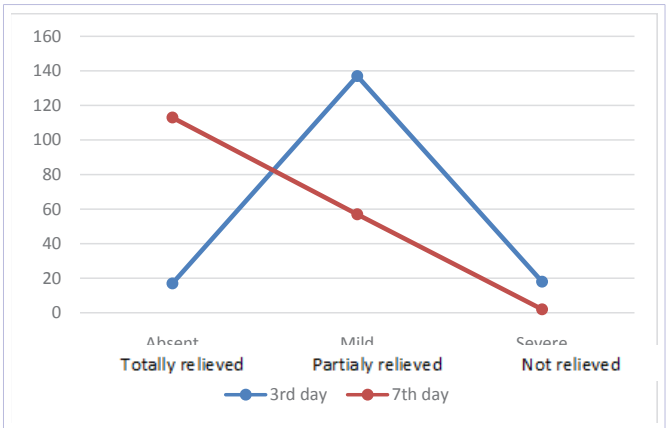

Figure 2: Symptoms of ABS 3rd Day vs 7th day

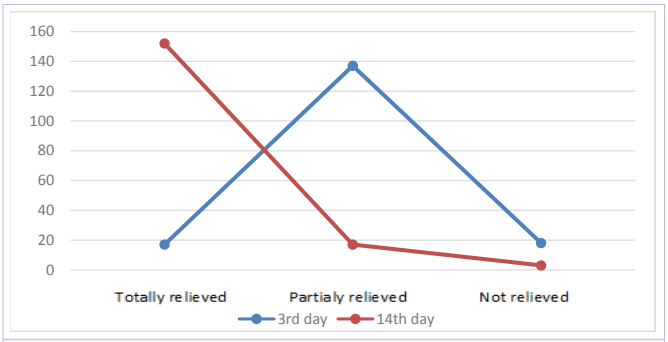

Figure 3: Symptoms of ABS 3rd Day vs 14th day

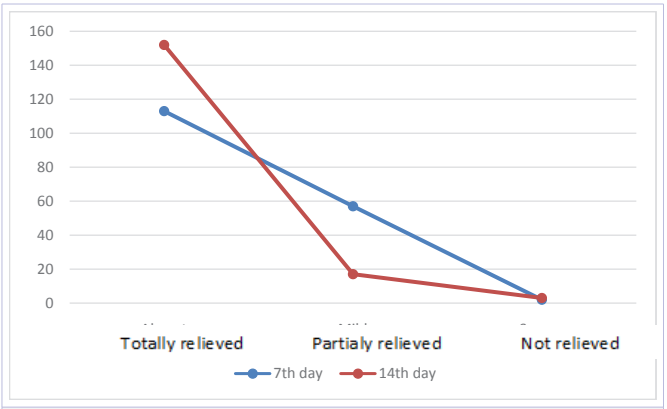

Figure 4: Symptoms of ABS 7th Day vs 14th day

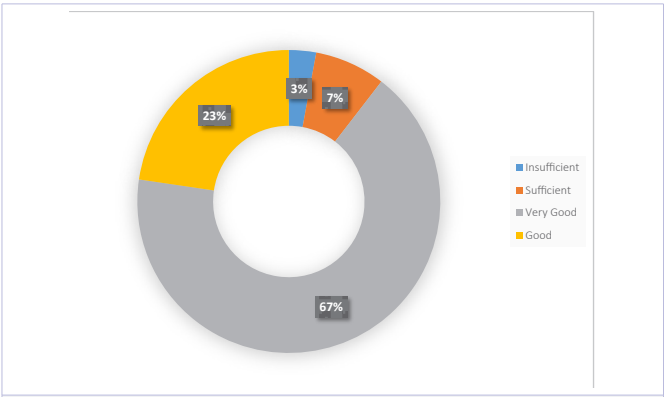

Figure 5: Patient Satisfaction with Moxifloxacin (14 Days)
The patient satisfaction was good and very good in 23% and 67% cases respectively. This was noticed as the end of the fourteen day treatment. (Figure: 5)

Materials and methods

This was the prospective, observational multicenter study in patients diagnosed with Acute Bacterial Sinusitis treated with Moxifloxacin therapy. The convenient sampling technique was used to select the patients. The ethical approval was taken by the institutional research forum of Rawalpindi Medical College. The study population comprised of approximately 200

male and female patients with a diagnosis of acute bacterial sinusitis on clinical basis for whom fourth-generation synthetic fluoroquinolone antibacterial agent Moxifloxacin daily is recommended by the treating physician. The dose of Moxifloxacin is 400 mg once every 24 hours. Out of 200 patients 28 were excluded from the study due to incomplete proforma and lost to follow ups.

Patient data originating from assessments and estimations executed according to the physician's routine practice was composed. As per discretion of doctor Moxifloxacin therapy was prescribed to the newly diagnosed & known patients of Sinusitis. All patients were screened as per inclusion & exclusion criteria. The patients who were willing to participate, had give informed consent, were having the age of greater than 18 years with signs and symptoms of acute bacterial rhinosinusitis including nasal blockage or stuffiness, mucopurulent nasal discharge or postnasal drip, facial pain, headache, and reduction or loss of smell or perception of bad smell and has never been treated with the moxifloxacin were included in the study. The patients were diagnosed on clinical basis. The patients having known hypersensitivity to moxifloxacin previously were excluded from the study.

The observational period comprised of four 04 visits. An initial visit and third day follow-up visits was recognized, followed by a visit on seventh day and fourteenth day at the end of therapy.

Symptoms of Acute Bacterial Sinusitis (fever, cough, nasal obstruction, nasal secretion, facial pain with feeling of fullness and headache) were assessed at baseline and at follow-up visits, and classified as 'absent', 'mild' or 'severe' by the attending physician.

The course of symptoms during moxifloxacin therapy was analyzed in terms of the categories 'cured', 'improved', 'unchanged' or 'worse'. The patient's satisfaction with moxifloxacin therapy was assessed on a 4-point scale from 'insufficient' to very good.

All patients were treated with 400 mg/day of moxifloxacin orally for fourteen days in combination with anti-inflammatory and anti-allergic medicine. Patients were instructed to take each dose of moxifloxacin at the same time every day, while anti-inflammatory and anti-allergic medicine was prescribes thrice and twice a day respectively.

The safety assessments consisted of observing and recording all adverse events AEs) and serious adverse events (SAEs).

Data analysis

Data analysis was done through the software SPSS version 20.0. For continuous variables, summary statistics included mean, standard deviation, median, minimum and maximum values, as well as frequencies and percentages for categorical variables are presented. Kendall's tau-b test and Chi square test was to see the significance at different levels of treatment at 3rd day, 7th day and 14th day period. P-values of< 0.05 are considered to be significant.

Results

A total of 172 patients were includedwithAcute Bacterial Sinusitis. Mean age of the patient was found to be 33.51± 9.6 years. Male were found to be 108 (63%) while rest were female 64 (37 %).

Cheek tenderness was noticed in 151 (88%) patients. Forehead tenderness was observed in 143 (83%) subjects. Fever was found in 156 (91%) whereas purulent nasal discharge was seen in 147 (85%) cases. Headache was observed in 163 (95%) patients. Facial pain was seen in 93 (54%) subjects. Upper Alveolus was found in 142 (83%) cases. Diminished or absent sense of smell was noticed in 128 (74%) patients. Bad breath was observed in 124 (72%) patients. Fatigue and ear pain were found in 138 (80%), 119 (69%) of the cases respectively. (Table 1) Multiple symptoms were observed in a single patient with the combination of cheek and forehead tenderness in 132 cases (77 %).

The most common adverse effect was dizziness that was found in 30% of the cases followed by nausea and vomiting, others like palpitation, body ache and gastric upsets and dry mouth in 7%, 6% and 4% cases respectively. There was no report of the serious adverse events.

Discussion

The aim of antibiotic remedy is to eliminate bacterial pathogens at the site of infection. It has been established that the failure of antibiotic to achieve this goal increases the potential for clinical failure, adds further costs, and may be due to selection of antibiotic with bacteria were resistant [16].

The common symptom was nasal discharge (98.3%) followed by nasal obstruction or stuffiness, postnasal drip, headache, facial pain, reduced smell and cacosmia [17]. This is inconsistent with our study in which headache (95%) and fever (91%) are the commonest symptoms followed by cheek tenderness (88%) and purulent discharge in 85% of cases.

There was no phototoxicity in patients treated with moxifloxacin as it is believed that the methoxy group at the 8-position on moxifloxacin confers decreased photo toxicity which is in accordance to our study which did not reveal any of the phototoxic effect of moxifloxacin.

In one of the study the most common adverse events reported were vomiting (4.35%) and nausea (4.35%). Whereas in our study vomiting was found in 7% of the cases and dizziness was the most common side effect found in 30% of patients. Dizziness and headache are the common clinical presentation of acute bacterial sinusitis hence further studies are needed to identify the relationship of this side effect with moxifloxacin.

It was suggested by a worldwide assessment of response to treatment with moxifloxacin that the electrocardiogram records after treatment did not show any evidence of increate QT intervals which reflects the complete valuation on the collective parameters of efficacy and safety that is consistent with our study in which clinically no cardiac toxicity is reported.

In one of the study physician's overall assessment showed that 91.31% of patients treated with moxifloxacin group had excellent-to-good response to treatment which is balanced with our study in which 85 % of the patients were completely cured and 10 % were improved [18]. There was no occurrence of any serious adverseconsequence during the study.

The assistances of this study are that our suitable collection methodology has qualified that we have sampled the accounts of extensive range of physician and patients perspectives and their proficiencies of treating the patients of acute bacterial sinusitis. Furthermore, it delivers wide extractions of the practitioner's perceptions. However, there are some detriments found in this study such as observer and recall bias. Reflecting the opinions of patients and experience and to what range they are reliable with those of the general physicians would be enlightening and valuable to standardize the misapprehensions about the treatment of the disease.

Conclusion

Moxifloxacin is effective in resolving the symptoms of acute bacterial sinusitis. It is more effective than other antibiotics because of its efficacy and least side effects.The medicating of simple once daily dosage offer benefits over many existing agents in terms of compliance as well.

Conflict of interest

The authors declare no conflict of interest. Ahson Siddiqi & Neeta Maheshwary are employees of Hilton Pharma Pvt Ltd. Dr.Adnan Anwar has received honorarium for data analysis, editorial assistance, preparation of figures and styling of the manuscript for journal submission. In this study, the integrity of the study was not compromised by any financial interests. The investigators were paid for the data filling and the examination of patient during the study period. Since this was a non-interventional study, patients were observed in real-life setting, and no support for any laboratory test or drug supply was provided to the investigators.

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