Sparfloxacin in the Treatment of Purulent Sinusitis—A Multicentric Study in Indian Patients

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Sparfloxacin, a new quinolone antibacterial was used to treat one hundred and thirty two patients with acute purulent sinusitis, at a dosage of 400 mg on the first day followed by 200 mg once daily for a further four days. A clinically successful outcome (defined as disappearance of nasal discharge, fever, pain, tenderness over the sinuses and headache) was recorded in 122 (95.3%) patients. Sparfloxacin was well tolerated. Fourteen adverse experiences were reported in 7 patients (5.3%); they were mainly gastrointestinal and mild. No phototoxic or cardiological adverse events occurred. An unusual feature was that *Staphylococcus aureus* and *Pseudomonas* spp. were the most common bacterial species isolated from middle meatal wash of patients in this study.

Materials and methods

This was an open noncomparative study. Patients of either sex with acute suppurative sinusitis were included if the current episode was of less than 7 days duration. The diagnosis was made by the presence of purulent rhinorrhoea, pus in the middle meatus or on the posterior pharyngeal wall, pain and tenderness over the affected sinuses and headache. A sinus X-ray was performed and middle meatal wash was

subjected to bacteriological culture and susceptibility testing of isolates. All patients were aged above 18 years and gave written informed consent prior to enrollment in the study. Pregnant or breastfeeding women, patients requiring surgical management, patients with tumours of the nose or maxilla, history of allergy to quinolones or pre-study abnormalities in the ECG were excluded from the study. Also excluded were patients with uncontrolled hepatic, renal, cardiac, psychiatric, endocrinological or haematological disorders, or infections other than sinusitis requiring

antibacterial therapy. Drugs known to prolong the Q-T interval or inhibit the metabolism of sparfloxacin were not used during the study.

The study treatment was a 5 day course of sparfloxacin, with a loading dose of 400 mg on the first day followed by 200 mg once daily for the next four days.

Treatment efficacy was assessed as the rate of clinical success i. e., absence of nasal discharge, fever, tenderness over the sinuses and headache an relief of pain over the sinuses (persisting mild pain was not a criterion of "failure") 3-7 days after completion of therapy.

Results

The vast majority of patients had maxillary and or frontal sinusitis. One hundred and thirty two patients received the study drug and 128 patients completed the study per protocol. Three patients were lost to follow up. One patient who had taken a non-study medication in violation of the protocol was withdrawn from the study. The demographic characteristics of the patients are shown in Table I; predisposing factors

Table I Patient characteristics at baseline-intent to treat population (n=132)	
Total No. of patients (%)	132 (100%)
Sex	
Male (%)	82 (62%)
Female (%)	50 (38%)
Age (Yrs.)	
Mean $\pm$ SD	28.07 $\pm$ 7.84
Range	18-55
Height (cm)	
Mean $\pm$ SD	158.56 $\pm$ 9.47
Range	112-186
Weight (kg)	
Mean $\pm$ SD	56.62 $\pm$ 10.07
Range	38-84

and concomitant conditions are presented in Table II; radiographic and microbiological findings are shown in Tables III and IV respectively.

Table II Predisposing factors and concomitant conditions - intent to treat population (n=132)		
Predisposing Factors	No. of Patients	Percentage
Septal deviation	66	50
Coryza	53	40
Other structural abnormalities like turbinate hypertrophy	26	20
Diabetes	1	0.8
Concomitant conditions		
Pharyngitis	28	21
Cervical lymphadenopathy	18	14
Laryngitis	1	0.8
Allergy-dust	1	0.8
Allergy-smoke	1	0.8
Chronic suppurative otitis media	1	0.8

Table III Findings on sinus X-ray*		
Findings on Sinus X-ray	No. of patients	
	Pretherapy (n=122)	Post therapy (n=69)
Opacity	101	21
Mucosal swelling around the sinus	44	7
Air fluid level	3	0

* More than one of the above features was noted in many patients

Out of the 118 patients in whom pre-therapy cultures were performed, no pathogens were isolated in 46 patients. The organisms isolated were *S. aureus* (25 patients) *Pseudomonas* species (11 patients) *S. pneumoniae* (9 patients) and *H. influenzae* and *Klebsiella* species in 8 patients each . *M. catarrhalis* was isolated in one patient.

With sparfloxacin therapy there was a marked improvement in all signs and symptoms on the 5th day of treatment and further improvement at the final assessment 3-7 days after completion of therapy, as shown in Table V.

Therapy outcome was assessed as clinically successful

Table IV
Bacteria isolated at study admission (n=118)

Organism isolated	No. of patients	Percentage
No growth or commensals only	46	38.8
Staphylococcus aureus	25	20.4
Pseudomonas spp.	11	9.3
Streptococcus pneumoniae	9	7.6
Haemophilus influenzae	8	6.8
Klebsiella spp.	8	6.8
Proteus spp.	6	5
E. coli	3	2.5
Haemolytic streptococci	2	1.7
Moraxella catarrhalis	1	0.8
Enterococcus faecalis	1	0.8
Non-fermenting aerobes	1	0.8
Non-lactose fermenters	1	0.8

Table V
Signs and symptoms pre and post therapy

Signs & Symptoms	Baseline (n=132)	Day 5 or Visit 2 (n=131)	Day 8-12 or Visit 3 (n=129)
	No. of patients (%)		
Purulent rhinorrhoea	106 (80.3)	35 (26.5)	6 (4.5)
Pus in middle meatus	86 (65)	35 (26.5)	2 (1.5)
Pus on posterior pharyngeal wall	69 (52.3)	1 (9)	0
Pain over the sinuses			
none	17 (12.9)	80 (61.5)	120 (93)
mild	83 (62.9)	42 (32.3)	8 (6.2)
moderate	30 (22.7)	7 (5.4)	1 (0.8)
severe	2 (1.5)	1 (0.8)	0
Tenderness over the sinuses			
none mild	16 (12.1)	90 (68.7)	125 (94.7)
moderate	86 (65.1)	38 (29)	3 (2.1)
severe	5 (3.8)	2 (1.5)	0
Headache			
none	40 (30.3)	105 (80.7)	128 (99.2)
mild	71 (53.8)	21 (16)	0
moderate	20 (15.1)	4 (3)	1 (0.8)
severe	1 (0.8)	0	0

in 122 patients, a success rate of 95.3% in the 128 patients who completed the study according to protocol. Post therapy bacteriological examination was performed in 90 patients out of whom 10 were positive for a bacterial pathogen. Eight of these ten patients had a clinically successful outcome and two were failures. In two patients who failed to respond to sparfloxacin, the pre-therapy bacterial isolates were sparfloxacin resistant. Post-therapy X-rays showed resolution in all but 23 patients (opacity in 21 patients and mucosal swelling in 7 patients) (Table III); the clinical outcome was successful in all but one of these patients.

Discussion

To the best of our knowledge, this is the first study of sparfloxacin in Indian patients with acute purulent sinusitis.

It is unusual for *Staphylococcus aureus* and *Pseudomonas* species to be involved in community acquired acute sinusitis; *Staph. aureus* is often involved in chronic sinus disease and *Ps. aeruginosa* has been implicated in nosocomial sinusitis. In our study of patients with community acquired sinusitis these two organisms were isolated from 36 out of 118 patients (30.5%). All but one of the 36 patients had a successful outcome and this is consistent with the reported MIC⁹⁰ of sparfloxacin being 1.56 mcg/ml and 0.10 mcg/ml against *Pseudomonas aeruginosa* and *Staphylococcus aureus* respectively⁶.

The clinical success rate of 92.4% in the intention to treat population of patients with acute purulent sinusitis in the present study is comparable to the

82.6% success rate reported by Gehanno et al⁵, who employed the same dose and duration of therapy with sparfloxacin as in the present study, and used similar criteria for classifying outcomes as success or failure.

The persistence of radiological features of sinusitis in some patients despite successful therapy outcome is not surprising since radiological resolution may take upto three weeks after successful therapy.

Sparfloxacin resistant bacteria were involved in two patients not responding to therapy. In another non-responder no pathogen was isolated but deviated nasal septum was present and might have impacted on the negative outcome. Two other patients were declared as failures only because of persistent tenderness over the sinuses although they had improved in all other respects as per criteria for a successful outcome. In another non-responder, *Staphylococcus aureus* susceptible to sparfloxacin was grown in the pre-therapy culture; post-therapy, *Streptococcus pneumoniae*, *Haemophilus influenzae* and *Moraxella catarrhalis* were isolated. The antimicrobial susceptibility of the isolates was not determined. Symptomatic improvement was minimal.

The good efficacy of sparfloxacin observed in this study is of particular interest in the light of increasing bacterial resistance to conventional antibiotics used in the therapy of acute sinusitis. The results of this study indicate that the sparfloxacin dosage used in this study (loading dose of 400 mg followed by 200 mg daily for four more days) produces a high success rate and is well tolerated in Indian patients, and suggest sparfloxacin to be of suitable alternative for the therapy of acute sinusitis.

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