Spectrum of activity of Sparfioxacin against local Isolates

Saleem Hafiz,Shehla Naseem (Mid East Medical Center, Karachi.)

Abstract

Objective: Determine the sensitivity pattern of local isolates to a new fluoroquinolone and MIC 90 of the isolates. Method: Four hundred clinical isolates belonging to 21 genera were included in the study Sensitivity was determined by disc difussion method and MIC by agar dilution method.
Results: The in-vitro study of the sensitivity pattern of local isolates indicates that the isolates are susceptible to Sparfioxacin and the MIC 90 for common clinical isolates from various sites is lower than those achieved by the drug. The international data available also suggests that the drug could be very effective in difficult-to-treat infections.
Conclusion: It could be concluded from the study that Sparfioxacin is a useful drug for treating respiratory, entero and urinary pathogens due to its unique pharmacological profile (JPMA 50:211, 2000).

Introduction

The pace at which resistance to antimicrobial agents is developing is cause for concern worldwide. Multi-drug resistant strains further complicate the problem[1]. The introduction in 1980s of fluoroquinolones, a class of synthetic antibiotics with a broad spectrum of antimicrobial activity provided an effective new approach to the treatment of urinary tract infections, skin and skin structure infectiOns, diarrheal illnesses and sexually transmitted diseases[2]. The fact that available fluoroquinolones have many therapeutic benefits and only a few marked shortcomings has spurred development of new compounds in this class[1]. Sparfioxacin is a newer fluoroqinolone with several pharmacokinetic and microbiologic advantages compared to the older members of its class[2]. Sparfioxacin has a wide spectrum range. Hence it is particularly suited for infections under investigation when etiology is not known. Concentrations of Sparfioxacin achieved in the lower respiratory tract are higher than those detected after administration of certain other fluoroquinolones such as Ciprofloxacin[2] . The post antibiotic effect of sparfioxacin when measured against a variety of pathogens ranged from 0 to >8 hours as compared to 0-2.4 hours for Amoxycillin-ca/vulanale. The PAE may be an important parameter in preventing the emergenc of quinolone resistane'. Patient compliance for multidose and multidrug therapy is usually low. The cost issues also play an important role. The once daily therapy of Sparfioxacin should make compliance better and would definitely come out to be useful for reducing hospitalization costs. The chief attributes of Sparfioxacin are its expanded activity against gram positive pathogens, once daily dosage and relatively low incidence of interactions with other drugs[2]. The interesting pharmacokinetic and pharmacodynamic profiles of Sparfioxacin prompted us to conduct the in-vitro study of
Sparfioxacin against the local isolates causing infections in different systems.

Material and Methods

Four hundred and forty clinical isolates belonging to 21 Genera i.e., Staphylococcus aureus, coagulase negative staphylocci, Streptococcus pyogenes, Streptococcus pneumoniae, Entercoccus, Neisseria gonorrhoeae, Moraxella catarrhalis, Haemophilus influenzae, Pseudomonas aeruginosa, Eschrichia coli, Kiebsiella spp., Acinetobacter spp., Morganella morganii and Bacteroides spp., were collected from different sites. Sixty isolates of Salmonella typhi, Salmonella paratyphi A and Salmonella paratyphi B were collected, identified and confirmed by the methods recommended by Manual of clinical microbiology[4]. Their sensitivity and minimum inhibitory concentration were determined by sensitivity discs (DIFCO USA)[5] and agar dilution method[6].

The isolates were mainly from urine, stool, pus, taken from cases of septicemia, urinary tract infections, gastrointestinal tract infections, lower respiratory tract infections and surgical wound infections.

Results

Table 1. In vitro activity of sparfloxacin against clinical isolates by Kirby Bauer method using 5 μg disks.

Organisms	Total tested	Susceptible		Intermediate		Resistant	
		Total	%	Total	%	Total	%
Staphylococcus aureus	20	16	80	1	5	3	15
Coag. Neg. Staphylococcus	20	17	85	1	5	2	10
Strep. pyogenes (GpA)	20	19	95	1	5	nil	nil
Streptococcus pneumoniae	20	18	90	1	5	1	5
Enterococcus	20	16	80	2	10	2	10
Neisseria gonorrhoeae	20	20	100	nil	nil	nil	nil
Moraxella catarrhalis	20	19	95	1	5	nil	nil
Haemophilus influezae	20	20	100	nil	nil	nil	nil
Pseudomonas aeruginosa	20	14	70	3	15	3	15
Escherichia coli	20	12	60	4	20	4	20
Klebsiella spp.	20	17	85	2	10	1	5
Shigella spp.	20	20	100	nil	nil	nil	nil
Enterobacter spp.	20	16	80	2	10	2	10
Citrobacter spp.	20	15	75	2	10	3	15
Seratia spp.	20	14	70	3	15	3	15
Proteus spp.	20	17	85	1	5	2	10
Acinetobacter spp.	20	18	90	nil	nil	2	10
Morganella morganii	20	17	85	2	10	1	5
Bacteroides spp.	20	13	65	3	15	3	15
Salmonella typhi	20	19	95	1	5	nil	nil
Salmonella paratyphi A	20	19	95	1	5	nil	nil
Salmonella paratyphi B	20	18	90	2	10	nil	nil
Cumulative results							
Genera 22	440	374	85	33	7.5	32	7

Table I records the cumulative results of disc sensitivity test against local isolates and almost all of the common pathogens encountered in routine infections are susceptible to Sparfioxacin and the sensitivity ranges from 80-100% and cumulative sensitivity in 85% while about 7% are resistant.

Table 2. MIC Sparfloxacin in local isolates in mg/ml or mg/l.

Organisms	Total	Range	MIC 50	MIC 90
E.coli	20	0.062-2.0	0.062	0.5
E.aerogenes	20	0.25-4.0	0.5	1
E.cloacae	20	0.25-4.0	0.5	1
K. pneumoniae	20	0.125-4.0	0.25	0.5
S. marcescences	20	0.125-2.0	0.25	0.5
Shigella spp.	20	0.062-0.5	0.062	0.25
Y. enterocolitica	15	0.062-0.5	0.125	0.25
P. mirabilis	20	0.5-8.0	0.5	1
P. vulgaris	20	0.5-8.0	0.5	1
M. morganii	20	0.5-4.0	0.5	1
P. aerugenosa	30	1.0-8.0	1	2
H. influenzae	20	0.062-0.25	0.062	0.25
M. catarhalis	24	0.062-0.5	0.062	0.25
Staph. aureus	20	0.5-2.0	0.5	1
Coagulase negative Staph.	20	0.5-2.0	0.5	1
Enterococcus	25	1.0-8.0	2	4
Strep. pyogenes	30	1.0-4.0	1	2
Strep. pneumoniae	40	0.25-1.0	0.5	1
Strep. viridans	30	1.0-4.0	1	2
Salmonella typhi	20	0.062-0.5	0.125	0.25
Salmonella paratyphi A	20	0.062-1.0	0.125	0.5
Salmonella paratyphi B	20	0.062-2.0	0.062	1

Table 2 lists the M.l.C. 50 and M.I.C. 90 for most of the clinical isolates. M.l.C. 50 for most of the pathogens ranges between 0.062-1.0 mg/mI and M.l.C. 90 being 0.5-2.0 mg/mI, which is adequate to cover most of the pathogens.

Table 3. Sensitivity of clinical isolates against commonly used antimicrobial agents.

Organism	Total tested	Sparfloxacin		Ofloxacin		Ciprofloxacin		p value
		No.	%	No.	%	No.	%	
Staphylococcus aureus	20	*17	85	9	45	14	70	<0.05
Coag. Neg. Staphylococcus	20	*18	90	10	50	17	85	<0.05
Strep. pyogenes (GpA)	20	*19	95	12	60	19	95	<0.05
Streptococcus pneumoniae	20	*19	95	13	65	19	95	<0.05
Entercococcus	20	#18	90	6	30	8	40	<0.01
Neisseria gonorrhoeae	20	20	100	20	100	20	100	@
Moraxella catarrhalis	20	20	100	19	95	20	100	@
Haemophilus influenzae	20	20	100	20	100	20	100	@
Pseudomonas aeruginosa	20	*17	85	11	55	14	70	<0.05
Eschrichia coli	20	15	75	14	70	15	75	@
Klebsiella spp.	20	18	90	18	90	19	95	@
Shigella spp	20	20	100	20	100	20	100	@
Enterobacter spp.	20	18	90	18	90	18	90	@
Citrobacter spp.	20	16	80	15	75	15	75	@
Seratia spp.	20	3	25	nil	nil	nil	nil	@
Proteus spp.	20	17	85	17	85	17	85	@
Acinetobacter spp.	20	18	90	16	80	16	80	@
Morganella morganii	20	17	85	17	85	18	90	@
Bacteroides spp	20	13	65	12	60	13	65	@
Aeromonas hydrophilia	20	20	100	20	100	20	100	@
Ples. Shigelloides	20	20	100	20	100	20	100	@
Yersinia enterocolitica	20	20	100	20	100	20	100	@

* Significant difference between *Sparfloxacin* and *Ofloxacin* only.

Significant difference between *Sparfloxacin* and *Ofloxacin* and *Ciprofloxacin*.

@ No significant difference.

Organism	Sparfloxacin	Ofloxacin	Ciprofloxacin	p-value
Staphylococcus aureus	*85%	45%	70%	<0.05
Coag. Neg. Staphylococcus	*90%	50%	85%	<0.05
Strep.pyogenes (GpA)	*95%	60%	95%	<0.05
Strtep. Pneumoniae	*95%	65%	95%	<0.05
Entercococcus	#*90%	30%	40%	<0.01

Table 3 compares sensitivity of clinical isolates against commonly used antimicrobial agents. Sparfioxacin showed significantly better activity against local isolates of Staph. aureus (85%) as compared to Ofloxacin (45%) while activity against Ciprofloxacin (70%) was slightly better but not statistically significant. Sparfioxacin showed statistically significant activity against Staphylococcus aureus, Coagulase negative staph, Streptococcus pyogenes, Pseudomonas aerugenosa, Streptococcus pneumoniae and Entercoccus as compared to Ofloxacin. Ciprofloxacin, activity against Streptococcus pneumoniae, is also very good as compared to Ofloxacin. Sparfioxacin showed significantly better activity against Enterococcus as compared to Ciprofloxacin.

Discussion

Recognition of a worldwide increase of penicillin resistant Streptococcus pneumoniae and cross resistance to other classes of antimicrobials has placed a great urgency on the need for new antimicrobial agents. Sparfioxacin is one of the newly introduced antimicrobial agents belonging to fluoroquinolone group. Fluroquinolones are a relatively new class of antibiotics with broad spectrum activity against infections of urinary tract, skin and soft tissues and respiratory tract as well as some gram positive pathogens[1]. Certain quinolones for example Ciprofloxacin and ()floxacin are limited or less potent against clinically important gram positive pathogens[1]. Compared with Cipro/loxacin all of the new fluoroquinolones exhibit improved coverage against streptococci and enterococci[1]. Compared to Ciprofloxacin their pharmacokinetic profile demonstrate equivalent or greater bio-availability, higher plasma concentrations and increased tissue penetrations reflected in greater volume of distribution[1]. Sparfioxacin has enhanced activity and a broader spectrum, due to an amino group at C-5 position in its molecular structure. The amino group confers additional in-vitro activity against gram positive cocci, including Streptococcus pneumoniae[7,8]. Coupled with a cyclopropyl group at N-i and a fluorine group at C-8, this molecular group provides increased activity against mycoplasma and chalmydia[9,10]. Sparfioxacin attains higher than the required levels for treating pathogens encountered in the lower respiratory tract, Gl tract and urinary tract, as most of the local isolates are presently susceptible to the drug. Sparfioxacin is more active against gram positive respiratory pathogens as compared to Levofloxacin which is also a fluoroquinolone[2].

Photosensitivity reactions are a class effect of fluoroquinolones[2]. These have been reported with Sparfioxacin but are rare and the incidence is 0.03%. The highest rates of photosensitivity reactions have been reported with Lornejioxacin and Flerofloxacin[2]. Sparfioxacin was associated with lower rates of gastrointestinal and central nervous system side effects, the types of adverse reaction seen most frequently with other fluoroquinolones[2].

The drug is excreted 66% through entero-hepatic cycle while 33% is excreted through urine thus making it a very suitable drug for treating entero and urinary pathogens. The efficacy of Sparfioxacin has been evaluated in treating urinary tract infection and has been found to be very successful[7]. The data also suggests that a once daily, 3 day regimen of Sparfioxacin is effective and generally well tolerated in the treatment of acute uncomplicated urinary tract infections. Salmonella sensitivity to SparJloxacin in vitro is very encouraging.

Sparfioxacin shows higher concentrations in the bronchial mucosa, epithelial lining and alveolar macrophages as compared with other fluroquinolones[3]. Concomitant use of Sparfioxacin with theophylline is safe for patients of chronic obstructive pulmonary disease and lower respiratory

tract infections[5,9,10]. The pulmonary distribution after 12 hours is adequate for treating most of the respiratory pathogens. Sparfioxacin has shown good activity against S. pneumoniae and other respiratory pathogens, which supports its use in the lower respiratory infections, particularly community acquired pneumonia.

References

1.Joseph MB. Expanded Activity and utility of the new Fluoroquinolones: A Review. Cl in. Tbcr., 1 999:21:29-31.
2.,Lipsky BA. Safety profile of Sparfioxacin, a New FIouroquinlone Antibiotic, Clin. Ther., 1 999;21 :148-57.
3.Schuler P, Zeniper K, Bonier K, et al. Penetration of Sparfloxacin and Ciprofloxacin into alveolar macrophages, epithet ial lining fluid and polymorphonuclear leucocytes, Fur. Respir. J., 1997:10:1130-36.
4.Editors: Murray PR, Baron EJ, Pfaller MA, et at. Manual of Clin. Microbial., 46th Edition, Washington DC, Amer. Soc. Micro., 1995.
5.Bauer AW, Kirby WMM, Sherris JC, et al. Antibiotic susceptibility testing by standarized single disc method. Am. J. Clin. Pathol., 1996:45:493-96.
6.National Committee for Clinical Laboratory Standards. Methods for dilution Antimicrobial Susceptibility Tests for bacteria that grown Aerobically. Approved standard M7-A3, Villanova, Pa. National Committee for Clinical Laboratory Standards, 1993.
7.Wolfson JS, Hooper DC. The Fluoroquinolones: structures, mechanism of action and resistance and spectra of activity in vitro. Antimicrob. Agent. Chemother., 1985:28:581-86.
8.Hooper DC, Wolfson JS. Mode of action of the quinolone antimicrobial agents. Review of recent information. Rev. Infect. Dis., 1989;11(suppl. 5):s902-s911.
9.HenryD, Ellison W, Sullivan J, et al Treatment of community acquired acute uncomplicated urinary tract infection with Sparfioxacin Multicenter UUTI Study group. Antimicrob. Agents, Chemother., 1998:42:2262-66.
10.Niro 0, Masaru 5, Chikara N, et at. Effect of Sparflaxaein on plasma concentration of slow release theophylline. Sparfioxacin, 3rd International Symposium on new Quinotones, Vancouver, Canada, July, 1990.