Time to abandon Ofloxacin?

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Letter to the Editor

Time to abandon Ofloxacin?

Madam, Ofloxacin is a DNA gyrase inhibitor and a member of the Fluoroquinolone family which are popular and effective outpatient antibiotics. It is a racemic mixture of which Levofloxacin is the active component. The more than 30 formulations available in Pakistan all contain 200 mg of Ofloaxacin (although formulations with up to 400 mg are available internationally) which is insufficient to treat many common infections. The usual 200 mg single oral dose yields a serum concentration of 1.5 µg/mL, 2 hours after administration and a steady state level (after >4 doses) of 2.2 µg /ml. This compares with a single 500 mg dose (usual dose) of Levofloxacin (the active ingredient of Ofloxacin) yielding levels of 4.5 - 6.2 µg/mL at 2 hours and a steady state concentration of 5.7 µg/ml.

Correlation between the serum concentration of an antibiotic, the minimum concentrations required to inhibit either 50% (MIC50) or 90% (MIC90) of all organisms in the culture[1,2] and the clinical response of these infections is well known.[3,4] While serum drug concentrations must always exceed the MIC50 of the organisms, increasing drug concentrations further enhance bactericidal activity. This effect levels off at around 10 fold the MIC50.[3] Table depicts MIC50 and MIC90 of some common bacteria from inpatient and outpatient clinical practice. This depiction of the World literature also highlights the markedly higher MICs for some bacteria such as E. coli (a common urinary pathogen) in certain situations.

As can be seen, the standard dose of Ofloxacin yields drug levels at or below the therapeutic threshold for many organisms, particularly all skin pathogens and many that cause pneumonia, suggesting Ofloxacin's potential ineffectiveness in these situations. That many patients improve clinically with such sub-standard therapy reflects antibiotic use for viral infections and the human body's ability to heal itself. Beyond clinical ineffectiveness, such sub-therapeutic dosing lead to widespread resistance to Levofloxacin, other Fluoroquinolone and even other classes of antibiotics rendering these potent antibiotics ineffective in clinical

Table. Ofloxacin MIC50s and MIC90s of various common organisms in international literature.

	United States*		Turkey**	
	MIC_{50} (mg/ml)	MIC_{90} (mg/ml)	MIC_{50} (mg/ml)	MIC_{90} (mg/ml)
Gram positive organisms				
Streptococcus pneumoniae (Penicillin Sensitive)	2	2	2	2
Streptococcus pneumoniae (Penicillin Resistant)	2	2	2	4
Streptococcus pyogenes	1	2		
Streptococcus agalactiae	2	2		
Viridans Streptococci	2	4		
Enterococcus faecalis	2	>64	2	64
Enterococcus faecium	>64	>64		
Staphylococcus aureus (Methicillin Resistant)	32	>64	8	16
Staphylococcus aureus (Methicillin Sensitive)	0.5	2	0.5	1
Staphylococcus epidermidis	4	>32		
Staphylococcus haemolyticus	1	64		
Staphylococcus saprophyticus	1	1		
Gram negative organisms				
Acinetobacter baumannii	0.25	16	8	16
Burkholderia cepacia	.64	64		
Haemophilus influenzae	0.03	0.06	0.03	0.06
Haemophilus parainfluenzae	0.06	0.12		
Moraxella catarrhalis	0.06	0.12	0.03	0.03
Pseudomonas aeruginosa	1	32	4	32
Stenotrophomonas maltophilia	2	16		
Citrobacter freundii	0.12	8		
Enterobacter aerogenes	0.12	1	0.12	16
Eneterobacter cloacae	0.06	1		
Escherichia coli	0.06	0.5	16	64
Klebsiella oxytoca	0.06	1		
Klebsiella pneumoniae	0.12	2	0.12	1
Morganella morganii	0.12	0.25		
Proteus mirabilis	0.12	1		
Proteus vulgaris	0.12	1		
Serratia marcescens	0.25	4		

* Hoban DJ, Bouchillon SK, Johnson JL et al. Comparative in vitro potency of gemifloxacin and fluoroquinolones against recent European clinical isolates from a global surveillance study. Eur J Clin Microbiol Infect Dis 2001; 20:814-819.

** Gonullu N, Aktas Z, Salcioglu M, Bal C, Ang O. Comparative in vitro activities of five quinolone antibiotics, including gemifloxacin, against clinical isolates. Clin Microbiol Infect 2001; 7:499-503.

practice.[5] Such antibiotic resistance has become a major problem worldwide.

Enhancing Ofloxacin dose to match Levofloxacin 250/500 mg bio-equivalency is inadvisable due to lack of experience with safety of this dose. As Levofloxacin (the active ingredient in Ofloxacin) is available in the market in 250 and 500 mg formulations and is very safe, we recommend that clinicians abandon prescribing sub-therapeutic formulations of Ofloxacin and use either Levofloxacin or other antibiotics instead.

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References

1. Craig WA, Ebert SC. Killing and regrowth of bacteria in vitro: a review. Scand J Infect Dis (Suppl) 1990; 74:63-70.
2. Craig WA. Pharmacokinetic/pharmacodynamic parameters: rationale for antibacterial dosing of mice and men. Clin Infect Dis 1998; 26:1-10.
3. Moore RD, Lietman PS, Smith CR. Clinical response to aminoglycoside therapy: importance of the ratio of peak concentration to minimal inhibitory concentration. J Infect Dis 1987; 155:93-9.
4. Drusano GL, Johnson DE, Rosen M, Standiford HC. Pharmacodynamics of a fluoroquinolone antimicrobial agent in a neutropenic rat model of Pseudomonas sepsis. Antimicrob Agents Chemother 1993; 37:483-90.
5. Graffunder EM, Venezia RA. Risk factors associated with nosocomial methicillin-resistant Staphylococcus aureus (MRSA) infection including previous use of antimicrobials. J Antimicrob Chemother 2002; 49:999-1005.