DRUG & THERAPEUTICS LETTER

A quarterly bulletin from
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Vol. 11 No. 1 October-December 2004

The Newer Fluoroquinolones

? Fluoroquinolones are a widely used class of antimicrobial agents. They are bactericidal drugs that act by disrupting the bacterial DNA replication and transcription. Their unique mechanism of action, wide tissue distribution and relative safety has led to their emergence as useful antimicrobial agents.

? The quinolones can be grouped on basis of their antimicrobial spectrum. The initial quinolones like nalidixic acid lack fluorine substituent and have a limited spectrum of activity, short half-life, poor tissue and serum concentrations that restrict their utility. In contrast the fluoroquinolones such as ciprofloxacin, ofloxacin and norfloxacin exhibit good activity against gram negative aerobic bacilli including *Pseudomonas aeruginosa,* and moderate to good activity against gram positive bacteria and atypical organisms like mycoplasma, chlamydia and legionella.

? Ciprofloxacin and ofloxacin are used to treat serious infections like enteric fever and septicaemia due to gram negative bacilli whereas the use of norfloxacin has been restricted to urinary tract infections. Ofloxacin has also been used to treat skin and soft-tissue infections as well as respiratory tract infections.

? The newer fluoroquinolones includes levofloxacin, sparfloxacin, gatifloxacin, moxifloxacin, trovafloxacin & clinafloxacin. which are more effective against gram positive organisms. They provide reliable coverage against *Streptococci pneumoniae* including penicillin resistant & multidrug resistant strains. Activity against other respiratory pathogens like *Haemophilus influenzae, Moraxella catarrhalis, Legionella pneumophila, Chlamydia pneumoniae* and *Mycoplasma pneumoniae* is also high. Thus these agents are useful in treating community

acquired pneumonia, exacerbations of chronic bronchitis and paranasal sinus infections

? The newer agents are less reliable than ciprofloxacin against gram negative bacteria, especially *P. aeruginosa*, an organism common in nosocomial pneumonia. Trovafloxacin, clinafloxacin and to some extent moxifloxacin and gatifloxacin also provide significant anaerobic coverage.

? Most of the newer fluoroquinolones have a long half-life that allows once daily dosage. Overall these fluoroquinolones are well absorbed after oral administration, food may decrease the rate, but not the extent of absorption. Sucralfate and antacids containing Mg^{2+} or Al^{3+} ions can markedly impair their absorption.

? The newer fluoroquinolones achieve high concentrations in various tissues and have excellent penetration into respiratory tissues, including the epithelial lining fluid and alveolar macrophages.

? Levofloxacin and gatifloxacin are eliminated by the kidney whereas sparfloxacin, moxifloxacin and trovafloxacin undergo extensive hepatic metabolism.

? Common side effects of the newer fluoroquinolones include gastrointestinal disturbance and phototoxicity. Neurological manifestations such as headache, dizziness and seizures have been reported, and rupture of tendons may also occur.

? The use of trovafloxacin has been restricted because of hepatotoxicity, and QTc prolongation has been observed with sparfloxacin and moxifloxacin. The safety of the newer fluoroquinolones remains uncertain during pregnancy or in the pediatric population.

The newer fluoroquinolones offer important therapeutic advantages and have emerged as important alternatives in the empirical treatment of community-acquired respiratory infections. As with other antibiotics, the development of resistance is a potential problem associated with their increased use. Rational and thoughtful prescribing, and continuous monitoring of antibiotic resistance levels would help sustain their antibacterial efficacy.

Sources:

☞ British National Formulary, September 2003. In Antibiotics: Quinolones,288-291.

☞DE King, R Malone, SH Lilley. New Classification and Update on the Quinolone Antibiotics. Am Fam Physician 2000;61: 2741-2748.

☞HF Chambers. Sulfonamides, Trimethoprim, & Quinolones. In Katzung BG, Basic & Clinical Pharmacology. 8th edition. New York: Lange Medical Books/ Mcgraw-Hill. 2001: 793-802.

Brief Information:

Pilot Study on Prescribing Practices & Pharmacy Services of TUTH

The study was conducted in the hospital by the Drug Committee of TUTH. The findings of the study of prescriptions collected from OPDs of three departments in the hospital are as follows:

Prescribing Practice	Medical OPD	Gynae OPD	Surgical OPD
Total Prescriptions	40	30	20
Prescriptions by prescriber (%)			
a) Consultant	7.5	-	30.0
b) Resident	7.5	-	-
c) House Officer	65.0	-	-
d) Not ascertained	20.0	100.0	70.0
Number of drugs prescribed per patient	2.4	2.5	1.7
Prescriptions with diagnosis (%)	82.5	86.7	90.0
Patients informed about dosing by the prescriber (%)	80.0	63.3	65.0
Patients with correct knowledge of prescribed drugs (%)			
a) When (frequency)	65.9	42.1	41.1
b) How much (dose)	47.4	34.2	38.2
c) How long (duration)	45.3	44.7	44.1
d) Precautions	2.1	0.0	5.8
e) Side-effects	0.0	0.0	0.0
Drugs prescribed from the hospital formulary (%)	82.5	90.8	64.8
Prescriptions with one or more antibiotics (%)	37.5	26.7	50.0
Patients with knowledge of hospital pharmacy services (%)	65.0	50.0	65.0

Some reasons given by patients for not buying drugs from the hospital pharmacy include, non-availability of the drugs or the particular brand prescribed, preference for buying drugs from a familiar shop & drugs costlier in hospital pharmacy.

Merck Withdraws Rofecoxib from Market

? Merck announced the withdrawal of its rofecoxib from the U.S. and worldwide markets due to safety concerns, in September 2004. Rofecoxib is a nonsteroidal anti-inflammatory drug (NSAID) which selectively inhibits cyclooxygenase-2 (COX-2). Selective COX-2 inhibitors were approved by US FDA for the management of osteoarthritis and acute pain in adults, menstrual symptoms, and rheumatoid arthritis in adults and children.

? Recently the long-term study APPROVe [Adenomatous Polyp Prevention On Vioxx (Rofecoxib)], was halted early when patients receiving rofecoxib showed an increased risk of cardiovascular events compared with placebo. A significant increase in the incidence of cardiovascular events, such as myocardial infarction and thrombo-embolic stroke was observed in the rofecoxib treatment group.

? FDA has cautioned against the possibility of similar adverse effects with other selective COX-2 inhibitors, such as celecoxib, valdecoxib and parecoxib.

Potential Vaccine for SARS

? In the late 2002, cases of life threatening respiratory disease with unidentifiable cause were reported from Guangdong province of China. Soon there were reports of similar febrile respiratory illness from Vietnam, Canada and Hongkong. The syndrome was designated as Severe Acute Respiratory Syndrome(SARS).

? Yang and colleagues have recently reported the efficacy of the prototype vaccine in a mouse model of the infection. The study has shown some hope and promise for development of a candidate vaccine for this life threatening illness.

The Drug & Therapeutics Letter, a publication from the Drug Information Unit (DIU), TUTH, is being restarted with this issue. The format of the information has also been changed. It will include details about a drug or a group and other section will include brief information including findings from studies. It will be published quarterly to highlight topics related to recent and relevant developments in Clinical Pharmacology & Therapeutics. Suggestions and comments are welcome. For more information please contact DIU.

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