

Are Fluoroquinolones, Macrolides, or Oxazolidinones Preferable Medicines in Management of Leprosy? Laboratory and Clinical Evidence

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Fluoroquinolones are group of antimicrobials that killed the microorganisms by inhibiting the deoxyribonucleic acid (DNA)-topoisomerases enzymes. Ofloxacin is recommended to treat multidrug-resistant cases with low percentage of resistance compared with the dapson (1.3% versus 8.1%, respectively) [1]. One study showed that combination of rifampicin and ofloxacin is a preferable combination without resistance [2]. Mutations of *gyrA*, and *gyrB* genes are the causes of ofloxacin-resistance in leprosy [3]. Moxifloxacin is recommended as a prophylactic agent for contacts of leprosy patients in an enhanced regimen included three doses of rifampicin (600 mg) and moxifloxacin (400 mg) at four week interval [4]. In the murine model of rifampicin resistant leprosy, a combination of Moxifloxacin, minocycline and clarithromycin is useful regimen, and a combination of rifapentine with moxifloxacin is an alternative regimen in this situation [5]. In animal study, gatifloxacin (300 mg/kg) has a bactericidal activity against *M. leprae* infected mice [6]. *In vitro* study, the bactericidal activity of fluoroquinolones against *M. leprae* are in the following orders; moxifloxacin > sparfloxacin > gatifloxacin > levofloxacin [7].

Clarithromycin is a macrolide member with a bactericidal activity against microbes by a mechanism related to the inhibition of the ribosomal 50 subunit (RNA-dependent synthesis of protein). Its efficacy against multidrug-resistant leprosy patients in a dose of 2g daily for three months is comparable to the 600 mg daily of rifam-

picin when combined with dapson and clofazimine [8]. Linezolid is a member of oxazolidinone derivatives acts by inhibiting the protein synthesis in the microbe. High doses of linezolid (at $\geq 50\text{mg/kg}$) acts as potent bactericidal agent against rapidly multiplying *M. leprae* in infected mice [6]. Minocycline is a second generation of tetracycline-related drugs with a pleiotropic effect that used in different pathological conditions including disorders of peripheral and central nervous system. Its neuroprotective effect is observed against recent-onset nerve damage that occurred in leprosy [9]. There is no evidence shows that minocycline has a bacteriostatic or bactericidal against *M. leprae*. Table 1 shows that the variability in the bioavailability, elimination half-life and pharmacological actions of antimicrobials that act against *M. leprae* in comparison with the reference anti-leprosy agents including dapson, rifampicin and clofazimine lead to suggest that there is no specific pharmacological characteristics that fulfill the ideal anti-leprosy. It concludes that the anti-leprosy agent acts specifically against *M. leprae* whatever it is bactericidal or bacteriostatic or pharmacokinetics profile. This could explain that why clarithromycin has anti-leprosy while azithromycin lacks such effect, and the same with linezolid and streptogramins. Therefore, it is necessary to test a wide panel of antimicrobials against *M. leprae* in order to discover or to identify which medicine is effective against *M. leprae* or to look for drugs acting on the DNA via several pathways.

Antimicrobials	Bioavailability	Elimination half-life	Anti-bacterial category
Ofloxacin	85-95%	8 - 9hour	Bactericidal
Moxifloxacin	86%	12.1hour	Bactericidal
Gatifloxacin	96%	7 - 14hour	Bactericidal
Sparfloxacin	92%	16 - 30hour	Bactericidal
Clarithromycin	50%	3 - 4hour	Bacteriostatic
Linezolid	100%	3 - 7hour	Bacteriostatic, Bactericidal
Minocycline	100%	11 - 22hour	Bacteriostatic
Dapson	70 - 80%	20 - 30hour	Bacteriostatic, weak bactericidal
Rifampicin	90 - 95%	3 - 4hour	Bactericidal
Clofazimine	&0%	70dour	Bactericidal (delayed)

Table 1: Pharmacological properties of drugs tested or acted as anti-leprosy.

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