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Fluoroquinolones- A maligned class being re-discovered?

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Background: Fluoroquinolones were discovered in the early 1980's with norfloxacin and ciprofloxacin being early class members. In the intervening 30 years the group has expanded and contracted mainly due to a series of adverse events. The class was "cutting edge" due to the breadth of activity, the oral and IV formulations and significant tissue distribution. Indeed these characteristics enabled courses of therapy to be shortened with all those attendant benefits. In the past decade no further quinolones have been approved, why? A combination of safety worries association with *Clostridium difficile* infection and emergence of resistance among the pathogens for which the class was developed.

Current status: The current global situation of antibiotic resistance among many pathogens is alarming and alternative agents are being sought, these include new members of the quinolone class. These agents are being developed based on either a novel mode of action or an expanded spectrum of activity. The local environment in an infected lesion or space is approximately pH 5 which can have adverse effect on some conventional antibiotics including current quinolones. The fluoroquinolones, delafloxacin and finafloxacin have better activity at the lower pH compared with MICs at pH 7.0. These two agents are being developed based on their enhanced activity against gram-positive and gram-negative pathogens, e.g. delafloxacin [MIC MRSA 0.5 mg/l] and finafloxacin [*E. coli* MIC 0.12 mg/l]. Thus these are being developed for acute bacterial skin and skin structure and complicated urinary tract infections respectively. The respiratory fluoroquinolones were vanguards of the shorter course therapy in respiratory infections based on many characteristics, most of which are harnessed by zabofloxacin which is highly active against an array of *Streptococcus pneumoniae* strains and penetrates lung compartments very well. Thus this drug is being examined for mild-moderate community acquired bacterial pneumonia with a 3 day course. This presentation will review the three new fluoroquinolones from microbiological, pharmacological and clinical perspectives with regard to the 3 different indications being studied.

Biography

Glenn Tillotson has 30+ years pharmaceutical experience in early pre-clinical and clinical research, commercialization, medical affairs, scientific communications including publication planning strategic drug development, life cycle management and global launch programs. Dr Tillotson has been instrumental in the development and launch of ciprofloxacin, moxifloxacin, gemifloxacin and other antibacterials. Glenn has held several key committee positions at the American College of Chest Physicians, he is on the Scientific Steering Committee for the GTCBio. Annual Summit on Anti-infective Partnering. Currently Dr Tillotson has published >140 peer-reviewed manuscripts, presented >270 scientific posters and is on several journal Editorial Advisory Boards including the Lancet Infectious Disease, eBioMedicine and F1000.

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