



Bioavailability of Fluoroquinolones in Human Aqueous Humor

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Abstract

Endophthalmitis is an intraocular bacterial infection, may lead to irreversible loss of vision. Antimicrobial chemotherapy is prescribed prior to ocular surgical procedures to avoid endophthalmitis. Fluoroquinolones are the most commonly prescribed and used antibiotics during such procedures. However, the selection of single entity and the proper regimen are not specified in medical guidelines.

This thesis explores the bioavailability of four fluoroquinolones (Ciprofloxacin, Gatifloxacin, Moxifloxacin and Ofloxacin) in aqueous humor after antibiotic topical administration using simultaneous validated High Performance Liquid Chromatography- tandem Mass Spectroscopy (HPLC-MS/MS) bioanalytical method according to EMA and FDA Bioanalytical Method Validation guidelines.

Method validation showed an accurate, precise and selective simultaneous analysis of the four antibiotics in human aqueous humor samples.

Human Research Ethics Committee of Royal Medical Services, Jordan Armed Forces has approved to conduct the clinical part on patients undergoing cataract surgery in the Ophthalmology Department. Sixty- seven patients were divided into four groups; one antibiotic was assigned for each group. Before surgery, each group received 4 drops of one of the antimicrobial agent over one hour separated by 15 minutes time interval.

Consultants collected approximately 50-100 μL . of aqueous humor by paracentesis using a 30-gauge needle on a tuberculin syringe.

We have reported for the first time the employment of HPLC-MS/MS in simultaneous separation of the four fluoroquinolones agents using Gemifloxacin as Internal Standard.

The newly developed and validated method was capable of accurately and precisely quantify each antibiotic at the lowest reported lower limit of detection, 10 ng/mL.

Furthermore, it operates on very low pipetting volume 15 μl comparing with other reported methods; indicating a reliable quantitation of the analyte using very small quantity of the aqueous humor.

Concentration of the four analytes were measured in patient's aqueous humor samples applying the validated method; the descending order for bioavailability was, Moxifloxacin, Gatifloxacin, Ofloxacin then Ciprofloxacin. Moxifloxacin average concentration was higher than the Minimum Inhibitory Concentration (MIC) for the common endophthalmitis pathogens; Susceptible *Staphylococcus aureus*, *Streptococcus pneumoniae*, Bacilli species and Enterococci species. While Gatifloxacin average concentration was higher than the MIC for susceptible *Staphylococcus aureus* *Streptococcus pneumoniae* and Bacilli species, however, it didn't reach the MIC for Enterococci species. On the other hand, the average concentration of Ciprofloxacin and Ofloxacin didn't reach Minimum Inhibitory Concentration (MIC) for any of the common endophthalmitis pathogens.

All antibiotics were well tolerated by the patients, No adverse event were reported by the ophthalmologist nor the patients.

It could be concluded that among the four antibiotics, Moxifloxacin is the most effective antibiotic for endophthalmitis inhibition after the administration of four drops over one hour separated by 15 minutes time interval before cataract surgery.