Comparison of minimum inhibitory concentration values for fluoroquinolones against *Escherichia coli* causing urinary tract infection in both hospitalized patients and outpatients

Mohamed Tayfour, PhD. A. Yuce, MD. N. Yulug, MD.

**ABSTRACT**

**Objective:** To determine the resistance among *Escherichia coli* isolates causing urinary tract infections in hospitalized patients and outpatients.

**Methods:** This study was carried out in the Department of Microbiology, Dokuz Eylul University, Medical Faculty Hospital, Inciralti, Ismir, Turkey, from February 1997 through to June 1998. A total of 300 *Escherichia coli* strains were isolated from urine specimens of 111 hospitalized and 189 elderly outpatients (more than 20 years of age). We determined the minimum inhibitory concentrations of the test drugs nalidixic acid, pefloxacin, ofloxacin, norfloxacin and ciprofloxacin by the microdilution method, recommended by the National Committee for Clinical Laboratory Standards.

**Results:** Minimum inhibitory concentrations and minimum inhibitory concentrations of strains tested against fluoroquinolones, pefloxacin and nalidixic acid were the same for strains isolated from hospitalized and outpatients (0.125µg/ml outpatients 0.03µg/ml). Twenty-six (9%) of 300 *Escherichia coli* strains were resistant to all drugs used. Twenty (77%) of these 26 strains were isolated from hospitalized patients. We found that the resistance to nalidixic acid is much higher than other fluoroquinolones. At the same time, the resistance in the strains that were isolated from hospitalized patients is again higher than outpatient strains (46%).

**Conclusion:** Resistance among *Escherichia coli* isolates from patients to quinolones used in the treatment of urinary tract infections was rare during this period. Our study, like many other reports showed the increased resistance to fluoroquinolones for clinical isolates. However the appearance of multi resistant clones and the elevated prevalence of quinolones resistance in the hospital studied are warning signals for an increase in resistant strains as seen in many other countries. Therefore, it is important for physicians to use fluoroquinolones carefully so as to prevent, or delay, the emergence of resistant strains.

**Keywords:** *Escherichia coli*, minimum inhibitory concentration, fluoroquinolone, urinary tract infection.


Quinolones are bactericidal antibiotics that inhibit bacterial deoxyribonucleic acid (DNA) replication. The quinolone nalidixic acid (NA), was developed initially as a urinary antiseptic. A new

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class of quinolones, also known as fluoroquinolones, have been synthesized by modifying the original 2 ring quinolone nucleus with different side chain substitution.1 Fluoroquinolones are bactericidal antibiotics that bind to the b-subunit of DNA gyrase, an essential enzyme for DNA replication.2 Deoxyribonucleic acid gyrase, an A,B, tetrameric enzyme and the target of the quinolones, is a Type II topoisomerase that is essential for replication and gene expression and is also involved in recombination and conjugation.3,4 Quinolone antibiotics are highly active against gram negative bacilli, gram positive species and other microorganisms like Legionella, Mycoplasma, Chlamydia, Plasmodium and intracellular bacterial species such as Mycobacteria and Rickettsia.5-14 Since 1962, when the first quinolone NA was used in treatment and since 1984 when the first fluoroquinolone norfloxacin (NOR) was marketed in Europe, there has been a marked increase in the usage of this class of drugs. The widespread use of fluoroquinolones has increased resistance to these drugs in clinical isolates of many bacteria such as E.coli.5 Different mechanisms of resistance to fluoroquinolones are known: 1. Decrease in membrane permeability or reduction of the quinolone accumulation and 2. Alteration of the molecular target of quinolone action DNA gyrase, and 3. Increased efflux of quinolones.3,5,15-21 Escherichia coli is the most common agent in urinary tract infections (UTIs) especially in hospitalized patients.22-24 In this study, in vitro activities of fluoroquinolones were investigated in 300 E.coli strains isolated from UTI cases both in hospitalized patients and outpatients.

Methods. Microorganisms. A total of 300 E.coli strains were isolated from urine specimens of 111 hospitalized patients and 189 outpatients submitted to our Microbiology Department, Dokuz Eylul University, Medical Faculty Hospital, Inciralti, Ismir, Turkey, from February 1997 to June 1998. The isolated strains were collected randomly from both male and female elderly patients. The identification of all isolates was confirmed by using standard biochemical methods.1,22 Escherichia coli American Type Culture Collection (ATCC) 25922 was used as a control strain

Drugs. All drugs were purchased from the appropriate pharmaceutical companies and were in powder form. Nalidixic acid was dissolved with sodium hydroxide (NaOH) and than diluted with Muller-Hinton (MH) broth. Other fluoroquinolones; pefloxacin (PEF), ofloxacin (OFX), NOR and ciprofloxacin (CIP) were dissolved in distilled water and diluted with MH broth as described previously.26

Inoculum. A standard inoculum of the microorganism used was 10^8 cfu/ml as described previously.26

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<table>
<thead>
<tr>
<th>Drugs</th>
<th>Sensitive</th>
<th>Resistant</th>
<th>Intermediate</th>
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<tr>
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<td>4 µg/ml &lt;</td>
<td>2 µg/ml &lt;</td>
<td>1 µg/ml &gt;</td>
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<tr>
<td>Ofloxacin</td>
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<td>4 µg/ml &lt;</td>
<td>2 µg/ml &gt;</td>
</tr>
<tr>
<td>Norfloxacin</td>
<td>16 µg/ml &lt;</td>
<td>8 µg/ml &lt;</td>
<td>4 µg/ml &gt;</td>
</tr>
<tr>
<td>Ciprofloxacin</td>
<td>4 µg/ml &lt;</td>
<td>2 µg/ml &lt;</td>
<td>1 µg/ml &gt;</td>
</tr>
<tr>
<td>Nalidixic acid</td>
<td>32 µg/ml &lt;</td>
<td>- µg/ml &lt;</td>
<td>16 µg/ml &gt;</td>
</tr>
</tbody>
</table>

Table 1 - Interpretation of sensitivity tests according to minimum inhibitory concentration (MIC) values (µg/ml).
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Whereas usage of fluoroquinolones without any antibiotic coverage was very high. Like our study, many other reports have shown increased resistance to fluoroquinolones by various clinical isolates.10,11,30,31 Aydin et al11 found resistance rates of 46% and in outpatient strains 21% as shown in Table 3.

**Discussion.** Fluoroquinolones are commonly used for the treatment of outpatients and nosocomial infections caused by gram-negative bacilli and gram-positive species.3,11,15,27-29 The size of the antibiotic market in developing countries is double than that seen in a developed country.20 In developing countries the resistance to quinolones has been increasing yearly.30 Our study showed that the resistance for quinolones to *E. coli* strains isolated from urine specimens is higher for hospitalized patients and outpatients as compared to outpatients. Twenty-six (9%) of 300 strains were resistant to all used quinolones, and 20 (77%) of these strains were isolated from hospitalized patients (n=111). On the other hand, we observed that the resistance rate to NA in *E. coli* strains isolated both in hospitalized patients and outpatients was very high. Like our study, other reports have shown increased resistance to fluoroquinolones by various clinical isolates.20,21,24,25,29 Özkan et al10 found the resistance rate to quinolones OFX as 8%, CIP as 7%, NOR as 8%, and PEF as 10%. Çöplü et al31 studied 100 *E. coli* strains isolated from urine specimens of hospitalized patients and found 13-18% resistance rate to various quinolones. Aydin et al24 found resistance rates of *E. coli* strains to various quinolones as following: NA 9-15%, NOR 0-6%, OFX 0-15%, PEF 12-17% and CIP 4-14%. Perez-Trallero et al26 found in a prospectively study between 1989 and 1992 that uropathogen *E. coli* resistance to CIP increased from 1%-7%. It is known that antibiotic resistance differs depending on the country, region, the patients from whom they are isolated and the antibiotic policy of that place. Widespread usage of fluoroquinolones without any national antibiotic usage program in Turkey, the clinical diagnosis of patients, a history of patients like previous infection or immunsupression may have influenced our finding of a high rate of resistance in hospitalized patient strains. Therefore, it is important for physicians to use fluoroquinolones carefully so as to prevent or delay the emergence of resistant strains.

**References**

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