# SIGNIFICANCE OF THE LENGTH OF THERAPY WITH NORFLOXACIN IN THE MANAGEMENT OF THE LOWER URINARY TRACT INFECTION

Bratislav Vasiljevic, Darko Laketic, Zvonimir Pesic, Jelena Stojiljkovic, Srdjan Mijatovic and Bojan Milosevic

The aim of the paper was to examine the significance of therapy with Norfloxacin as monotherapy in the treatment of the lower urinary tract infection and to examine the effectiveness of this antibiotic nowadays as it has not been used for a long time (it wasn't available on our market).

80 patients with the lower urinary tract infection were examined. Patients were divided in two groups according to the length of therapy and the age of patients. Before and after the therapy some examinations were done: clinical check – up, urine (general urine examination), KSL, SE, urea, creatinin, urine culture, urinary tract EHO.

There was no statistically significant difference in the number of patients with the lower urinary tract infections after 3 and 7 days of the Norfloxacin therapy. Often, the cause of this infection was *Escherichia coli*. There was no statistically significant difference in the number of the patients with the lower urinary tract infection after the therapy with Norfloxacin in respect to age.

There was no difference in the effects of the medicine in the group in which the therapy lasted for 3 days and the group in which the therapy lasted for 7 days. In addition, there was no difference in the effects of medicine in respect of the age of patients. *Acta Medica Medianae* 2008;47(4):5-8.

Key words: infection, Norfloxacin, urinary tract, uroantiseptic, lower urinary tract

Urology Department – Medical Centre "Toplica" in Prokuplje<sup>1</sup> Pharmaceutical House "Slaviamed "<sup>2</sup> Surgery Clinic,Clinical Centre Kragujevac<sup>3</sup>

Contact: Bratislav Vasiljevic

Urology Department – Medical Centre "Toplica"

Pasjačka nn. Street 18400 Prokuplje Tel.: 027/324000

### Introduction

In modern clinical practice, there is a dilemma about the length of antibiotic therapy in the treatment of the lower urinary tract infection (1).

In the past, the standard antibiotic treatment lasted 7 to 10 days, but nowadays it is considered that a three-day treatment is equally effective (2). Also, there occur the problems related to the efficiency of antibiotics in regard to the age of patient, as well as resistance of bacteria to antibiotics (3,4).

Norfloxacin is a peroral bacterial uroseptic from the hinoline group. It is very efficient against most gram – negative bacteria (*E. coli, Klebsiella, Proteus, Providentia, Enterobacter, Morganella, Citrobakter, Serratia, Pseudomonas*) and some gram – positive bacteria (stafilococcus).

After peroral use, Norfloxacin is quickly, but incompletely absorbed (30–40%). The highest most serum concentration is achieved 60 to 90

minutes after peroral use. The time of half – elimination is 2,5 to 4,5 hours.

#### **Aims**

The aim of the study was to examine the efficiency of Norfloxacin tablets as monotherapy in the treatment of the lower urinary tract infection related to the length of the treatment. In addition, a total efficiency of this antibiotic was examined, as medicine was not used on our market for a long time.

# **Material and methods**

The efficiency of Norfloxacin tablets was examined in the patients having the lower urinary tract infection, hospitalized in the Urology Department in Prokuplje. This investigation covered the period from the beginning to the 15<sup>th</sup> day of disease.

Mean age of the patients was 59 years.

The patients were divided in two groups in regard to the length of the therapy (the first group - 3 days and the second one - 7 days of therapy).

The patients were also divided in regard to the age (the first group up to 45 years and the second 46 years of age, and more). Mean age was 41 years in the first group and 64 years in the second group.

www.medfak.ni.ac.yu/amm

They were advised how to maintain an adequate hygiene – dietic regime, as resorption of this medicine depends on this parameter, too.

For statistical evaluation of the aims of the investigation, the Wilcoxon and Pearson coefficients of linear correlaton were used.

The following procedures were done: clinical examination, general urine examination, KSL, SE, urea, creatinine, examination of the middle stream urine, urinary tract EHO. To eliminate complicated urinary tract infections, in 9 patients the urinary tract Rtg was performed, and in 3 patients intravenous urography.

The finding of positive urine culture, and clinical and laboratory signs of the lower urinary tract infection were significant.

The investigations were performed at the beginning of disease and 3 – 5 days after the completion of therapy.

Norfloxacin tablets of 400 mg were used. The medicine was given orally, 400 mg twice a day during 3-7 days.

# **Results**

Graph 1 presents the patients with urinary infection after 3 to 7 days of therapy. After Norfloxacin therapy which lasted for 3 days, there were 5 (12,5%) patients with infection. Of that number, in one patient the number of isolated germs was up to 103/ml of urine, while in two patients the number of isolated germs was over 105/ml of urine. After a 7-day treatment, there were four patients with infection (10%). Of that number, in one patient the number of isolated germs was up to 103/ml of urine and in the range 103-105/ml of urine, while in two patients the number of the isolated germs was over 105/ml of urine.

Based on statistical analysis, it was established that there was no statistically significant difference in the number of patients with the lower urinary tract infection after 3 and 7 days with Norfloxacin therapy (p < 0.001).

Graph 2 presents the causes of infection of the lower urinary tract before the therapy with Norfloxacin in respect to the age of patients. In the group of 40 patients with mean age of 41 years, in 21 patients the infection of the lower urinary tract was caused by Escherichia Coli, in 8 patients by Pseudomonas, in 4 patients by Enterobacter, in two by Proteus, and in 5 patients by other causes. In the group of 40 patients, mean age 69 years, in 30 patients the infection was caused by Escherichia Coli, in 3 patients by Pseudomonas, Enterobacter and Proteus; in one patient it was some other cause. (5).

Clinical symptoms of the surinary tract infection after the therapy with Norfloxacin were reported in all the patients with a finding in urine.

Based on statistical analysis it was established that there was no statistically significant

difference in the number of patients with the lower urinary tract infection in the group with mean age of 41 years after the therapy with Norfloxacin in regard to the group with mean age 69 years (p < 0.001).

Some more patients with urinary tract infection after Norfloxacin therapy belonged to the group of elderly patients. The explanation probably lies in the fact that the urothelium of the elderly is convenient for developing infection because of the weakness of detrusor contractility and smaller local cell power to resist the microorganisms adhesion (6,7).

Graph 3 presents shows the causes of the lower urinary tract infection after the therapy with Norfloxacin in respect the age of the patients. There were 48 (60%) female patients and 32 (40%) male patients (8).

Graph 4 presents the most common causes of the lower urinary tract infection. The most frequent cause was Escherichia coli (9). This cause is especially prevalent in female population, probably because they have more adhesive urothelium for this bacterium (10,11).

# **Discussion**

The difference in efficiency between threeand seven-day therapy is not statistically significant. The reason in almost identical results is because the sterilization of urine is reached after the first day of therapy, so there is no essential difference in the length of therapy of 3 and 7 days (12). The most frequent cause was Escherichia coli which reacted well to Norfloxacin.

The highest frequency of urinary tract infection was noticed in the population aged 66-75 years. The reason is because the process of aging influences the lower urinary tract, causing fibrosis of the bladder wall and ultrastructural changes on detrusor (13), also associated with aging (14).

Higher frequency of infections is also noticed in the female population. The reasons could be found in the characteristic of the lower urinary tract anatomy in women, significantly shorter urethra, nearness of anus, habits of rare urination, etc. (15).

#### Conclusion

There is no difference in the effects of a medicine in the group in which the therapy lasted 3 days compared to the group with 7-day therapy. Also, there are no differences in the effects of a medicine in regard to the age of patients.

Three-day treatment could be taken as a standard length of management because of significant savings and identical post-therapeutic effects. It is also convenient to use this medicine in the elderly population due to good efficiency, minor side effects, and profile of administration.

### References

- Gobernado M, Valdes L, Alos JI, Garcia-Rey C, Dal-Re R, Garcia-de-Lomas J. Quinolone resistance in female outpatient urinary tract isolates of Escherichia coli: Age-related differences. Rev Esp Quimioterap 2007;20:206-10.
- Pippo T, Pitkjarvi T, Salo SA. Three-day versus sevenday treatment with norfloxacin in acute cystitis. Current therapeutic research 1990;47:644-53.
- Karlowsky JA, Hoban DJ, DeCorby MR, Laing NM, Zhanel G. Fluoroquinolone-Resistant Urinary Isolates of Escherichia coli from outpatients Are Frequently Multidrug Resistant: Results from the North American Urinary Tract Infection Collaborative Alliance-Quinolone Resistance Study. Antimicrob Agents Chemother 2006;50:2251-2.
- Vogel T, Verreault R, Gourdeau M, Morin M, Grenier-Gosselin L, Rochette L. Optimal duration of antibiotic therapy for uncomplicated urinary tract infection in older women; a double-blind randomized controlled trial. J Canad Medical Associat 2004;4:469-73.
- Nys S, Terporten PH, Hoogkamp-Korstanje JA, Stobberingh E. Trends in antimicrobial susceptibility of Escherichia coli isolates from urology services in The Netherlands. J Antimicrob Chemother 2005; 151:1-7.
- Hald T, Horn T. The human urinary bladder in ageing. Br J Urol 1998;82:59-64.
- Russo TA, Stapleton A, Wenderoth S, Hooton TM, Stamm WE. Chromosomal restriction fragment length polymorphism analysis of Escherichia coli strains causing recurrent urinary tract infections in young women. J Infect Dis 1995;172(2):440-5.

- 8. Mc Isaac WJ, Low DE, Biringer A, Pimlott N, Evans M, Glazier R. The impect of empirical menagement of acuta cystitis on unnecessary antibiotic use. Arch intern Med 2002;162:600-5.
- Truls E, Johansen B. Nosocomially acqired urinary tract infections in urology departments. Why an international prevalence study is needed in urology. J Antimicrob Chemoter 2004;1:30-4.
- Uzunovic-Kamberovic S. Antibiotic resistance of coliform organisms from community-acquired urinary tract infections in Zenica-Doboj Canton, Bosnia and Herzegovina. J Antimicrob Chemother 2006;58:344-8.
- Potić M. Korelacija između bakterioloških, laboratorijskih i kliničkih parametara nozokomijalnih infekcija urinarnog trakta. Acta Medica Medianae 2007; 46(2):5-8.
- 12. Drekonja DM, Johnson JR. Urinary Tract Infections. Primary Care. Clinics in Office Practice 2008; 35(2):345-67.
- Marković V. Uticaj starenja na detrusor i funkciju bešike u "Bolesti prostate" Savremena administracija 2000. str 47-8.
- Finer G, Landau D. Pathogenesis of urinary tract infections with normal female anatomy. Lancet Infect Dis 2004;4(10):631-5.
- Beyer I, Mergam A, Benoit F, Theunisson C, Pepersack T. Menagement of urinary tract infectiones in the elderly. Z Gerontol Geriat 2001; 34(2):153-7.
- 16. Sahm DF, Thornsberry C, Mayfield DC, Jones ME, Karlowsky JA. Multidrug-Resistant Urinary Tract Isolates of Escherichia coli:Prevalence and Patient Demographics in the United States in 2000. J Antimicrob Chemother 2001;45:1402-6.

# ZNAČAJ DUŽINE EMPIRIJSKE TERAPIJE NORFLOKSACINOM U LEČENJU NEKOMPLIKOVANIH INFEKCIJA DONJEG UROTRAKTA

Bratislav Vasiljević<sup>1</sup>, Darko Laketić<sup>1</sup>, Zvonimir Pešić<sup>1</sup>, Jelena Stojiljković<sup>2</sup>, Srđan Mijatović<sup>1</sup> i Bojan Milošević<sup>3</sup>

U radu je ispitivan značaj dužine terapije Norfloksacin-om kao monoterapije u lečenju infekcija donjeg urinarnog trakta i kolika je efikasnost ovog antibiotika u sadašnjem vremenu jer u dužem vremenskom periodu nije korišćen (bio je nedostupan na našem tržištu).

Ispitivano je 80 bolesnika sa infekcijom donjeg urotrakta. Bolesnicii su podeljeni na dve grupe u odnosu na dužinu terapije i godine starosti. Pre i nakon terapije bolesnici su podvrgnuti sledećim ispitivanjima: klinički pregled, urin (opšti nalaz), krvna slika, sedimentacija, urea, kreatinin, urinokultura, EHO urotrakta.

Ne postoji statistički značajna razlika u broju bolesnika sa infekcijom donjeg urotrakta nakon 3 i 7 dana terapije Norfloksacin-om. Najčešći uzročnik infekcije donjeg urotrakta je bila *Escherichia coli*. Ne postoji statistički značajna razlika u broju bolesnika sa infekcijom donjeg urotrakta nakon terapije Norfloksacin-om u odnosu na godine.

Nema razlike u efektima Norfloksacin-a kod grupe kod koje je terapija trajala tri u odnosu na grupu gde je terapija trajala sedam dana. Takođe, nema razlike u efektima Norfloksacin-a bez obzira na starost bolesnika. *Acta Medica Medianae 2008;47(4):5-8.* 

Ključne reči: infekcija, norfloksacin, urotrakt, uroantiseptik