Trakia Journal of Sciences, Vol. 8, Suppl. 2, pp 171-173, 2010

Available online at:
http://www.uni-sz.bg

ISSN 1313-7050 (print)
ISSN 1313-3551 (online)

SENSIBILITY OF CLINICAL ISOLATES TO LEVOFLOXACIN UNDER THE CONDITIONS OF INCREASING ANTIMICROBIAL RESISTANCE

D. Rukanova* , G. Lazarova , K. Rachkova , M. Boicheva , H. Djeneva , M. Teneva

Department of Microbiology, Medical Faculty, Trakia University, Stara Zagora, Bulgaria

ABSTRACT

The appearance of comparatively new diseases, caused by multi-resistant microbial species and their toxins, as well as the increase in the population of patients at risk imposes the application of contemporary approach when choosing antimicrobial therapy. Suitable medicine which meets the modern needs of antimicrobial therapy is Levofloxacin. The purpose of this recent investigation is to determine the antimicrobial resistance of the most frequent clinical isolates to Levofloxacin. The resistance of 183 isolates of Gram (+) and Gram (-) bacteria (S. aureus , S. pneumoniae , S. agalactiae , Enterococcus spp. , family Enterobacteriaceae , P. aeruginosa and Acinetobacter spp.) has been investigated , using DDM and BDM . One of the 25 investigated S. aureus strains has shown resistance to Levofloxacin ,while S. pneumoniae and S. agalactiae have not.The half of the tested Enterococcus spp. strains have been levofloxacin resistant. Among 119 investigated Gram (-) bacteria, 41 have shown resistance to Levofloxacin, (mainly due to Enterobacteriaceae, producing Extended Spectrum Beta Lactamases and multi –resistant Acinetibacter spp.)

Key words: Levofloxacin ,Gram (+) cocci, Enterobacteriaceae, P. aeruginosa, Acinetobacter spp.

INTRODUCTION

Despite the serious success in antibiotic treatment of the infections, the antimicrobial therapy is still of great challenge for medicine. The application of contemporary approach in the choice of antimicrobial medicaments depends on various factors:

1. The appearance of new diseases, caused by new bacterial species and their toxins: Legionellosis, caused by L. pneumophila; Lime Borreliosis, caused by B. burgdorferi; necrotising fasciitis, caused by S. pyogenes; TSS - Toxic Shock Syndrome, caused by toxigenic S. aureus, producing TSST-1 (Toxic Shock Syndrome Toxine 1); antibiotic associated colitis due to C. difficile-enterotoxin.
2. The wider spreading of multi-resistant microbial species such as: S. aures-vancomycin – intermediate; S.pneumoniae - penicillin-resitant; Enterococcus faecium-oxazolidinones- and vancomycin-resistant, Gram (+) cocci with MLS (macrolides-lincosamides-streptogramins)-types of resistance, members of the family Enterobacteriaceae producing Extended Spectrum Beta Lactamases ($ESBL_s$), Gram (-) nonfermentative bacteria with multi-resistance.
3. The increase in the number of the patients at risk predisposes on the one hand to infections with multi-resistant microorganisms, on the other to sevierer course and higher mortality rate.
4. Medical practice has to dispose with appropriate peroral and parenteral drugs for empirical therapy, as well as with such for the continuing treatment.
5. For the treatment of infections, caused by multi-resistant microbial species, there are only a few numbers of antimicrobial medicaments.

- Against G ram (+) species: glycopeptides, oxazolidinones ,streptogramins etc.
- Against Gram (–) species : cephalosporins, aminoglycosides etc.

Modern antimicrobial medicine, which meets the requirements of contemporary approach in antimicrobial therapy, is Levoflixacin. It has powerful bactericidic effect, wide antibacterial spectrum, exellent penetration in pulmonary

***Correspondence to:** *Dr.Rukanova, , Department of Microbiology, Medical Faculty, Trakia University, Stara Zagora, Bulgaria, 042/664272, 0887 877 450, rukanova58@yahoo.com*

tissue and sinuses, high intercellular concentrations.The chemical formula of Levofloxacin is with low potential for developing resistance in bacterial species.

Levofloxacin inhibits the enzymes which catalyse the process of replication of DNA - deoxyribonucleic acid - gyrase and topoisomerase IV. The inhibition of these enzymes leads to bacterial death.

The spectrum of activity of Levofloxacin includes a great number of Gram (+) and Gram (-) microorganisms such as *Haemophilus influenzae ,Moraxella catarrhalis, Enterobacter* spp., *Escherichia coli, Klebsiella* spp ., *Proteus* spp. , *Serratia* spp. , *Pseudomonas aeruginosa , Stenotrophomonas maltophilia, Acinetobacter* spp.

The medicine is suitable for the treatment of widely spread intercellular (atypical) microorganisms: Chlamydophila pneumoniae, Micoplasma pneumoniae, Ureaplasma urealyticum, Legoinella spp. (1-3).

Levofloxacin is the first choice drug of empirical therapy of patients at risk with pulmonary infections (smokers, immunosupressed and other), urogenital infections, wound infections and etc. Thereby this medicine is one of the most appropriate and often used antimicrobial drug in medical practice (4-7).

PURPOSE

The aim of this recent investigation is to determine the antimicrobial resistance of the most frequent clinical isolates to Levofloxacin during one year period.

MATERIALS AND METHODS

There were investigated totally 183 strains; 64 Gram (+) and 119 Gram (-) bacteria, isolated from infections of upper and lower respiratory tract, urogenital and surgical infections. The antimicrobial susceptibility of the isolates was determined via DDM (Disk Diffusion Method) and BDM (Broth Dilution Method). The interpretation of the results was done according to CLSI (Clinical Laboratory Standard Institute) 2009.

RESULTS

The results of the antimicrobial resistance of Gram (+) isolates is shown on **Table 1.**

From all of the investigated 65 Gram (+) isolates, 15 were resistant to Levofloxacin. Resistant to Levofloxacin was only 1 singular isolate of S. aureus, the same was also multi-resistant -MRSA and MLS. Among the isolates of S. pneumoniae and S. agalactiae there were not resistant to Levofloxacin, although some strains were multi-resistant among them: five isolates PNSSP, three isolates of S. pneumoniae and two of S. agalactiae with MLS-resistance. The most of the tested Enterococcus species (eight from fifteen), were resistant to Levofloxacin, which is usual for Enterococci. Among Levofloxacin resistant isolates of Enterococci, two were multi- resistant, while the others were resistant only to fluoroquinolones.

Among Gram (-) bacteria there was considerably higher resistance to Levofloxacin **(Table 2)**. Among 119 isolates, being tested, 41 were Levofloxacin resistant. These resistant strains were mainly multi-drug resistant P.aeruginosa and Acinetobacter spp. and Enterobacteriaceae, producing $ESBL_s$.

Table 1. *Resistance to Levofloxacin of Gram (+) isolates of different phenotypes:*

	N	Levofloxacin-R
S. aureus-Total	25	1
S. aureus-MSSA	24	0
S.aureus-MRSA	1	1
S. aureus-MLS	4	1
S. pneumoniae-Total	15	0
S. pneumoniae PNSSP	5	0
S. pneumoniae-MLS	3	0
S. agalactiae-Total	10	0
S. agalactiae-MLS	2	0
Enterococcus spp.	15	8
Enterococcus spp.-MDR	2	2

MSSA-methicillin- sensitive S. aureus
MRSA- methicillin-resistant S. aureus
MLS – resistance to macrolides, lincosamides and streptogramins
PNSSP – penicillin-nonsensitive S. pneumoniae
MDR- multi-drug resistant

CONCLUSIONS

- Under the conditions of constantly increasing antimicrobial resistance Levofloxacin keeps its activity against the most of the clinically significant Gram (+) microorganisms such as S. aureus, S. agalactiae, S. pneumoniae (including PNSSP, MLS) and family Enterobacteriaceae.
- Resistance to Levofloxacin more often display bacteria with multi-drug resistrance such as Enterococcus spp. , Enterobacteriaceae – $ESBL_s$ (+), P. aeruginosa, Acinetobacter spp.

Table 2. *Resistance to Levofloxacine of Gram (-) isolates of different phenotypes of resistance*

Mechanism/phenotype of resistance	N	Levofloxacin-R
Enterobacteriaceae - total	84	22
Enterobacteriaceae $ESBL_s$(+)	19	11
P. aeruginosa - total	20	10
P. aeruginosa - MDR	7	7
Acinetobacter spp.	15	12
Acinetobacter spp. - MDR	12	11

$ESBL_s$ – Extended spectrum β-lactamase
MDR - Multi-drug resistant

REFERENCES

1. Bradley, J.S., Arguedas, A., Blumer, .L., Saez-Llorens,X., Melkote, R., Noel,G.J., Comparative study of levofloxacin in the treatment of children with community-acquired pneumonia. Pediatr Infect Dis J, 26 (10):865-867, 2007.
2. Mikamo, H., Sato, Y., Hayasaki, Y., Hua, Y. X., Tamaya, T., Adequate levofloxacin treatment schedules for uterine cervicitis caused by Chlamydia trachomatis. Chemotherapy, 46 (2):150-152, 2000.
3. Yu, V. L., Greenberg, R. N., Zadeikis, N., Stout, J. E., Khashab, M. M., Olson, W.H., Tennenberg, A. M., Levofloxacin efficacy in the treatment of communiti-aquired legionellosis. Chestjournal,125,6,2004
4. Burgess, D.S., Use of pharmacokinetics and pharmacodynamics to optimise antimicrobial treatment of Pseudomonas aeruginoas infections. Clin Infect Dis, 15;40 Suppl 2:99-104, 2005.
5. Frei, C. R., Burgess, D.S., Pharmacodynamic analysis df ceftriaxone, gatifloxacin, and levofloxacin against Streptococcus pneumoniae with the use of Monte Carlo simulation. Pharmacotherapy,25 (9): 1161-1167, 2005.
6. Obrtsch, M. D., Fish, D. N., MacLaren, R., Jung, R.,Nosocomial infections due to multidrug-resistant Pseudomonas aeruginosa: epidemiology and treatment options. Pharmacotherapy, 25 (10): 1353-1364, 2005.
7. Smith, H. J., Noreddin, A. M., Siemens, C. G., Schurek, K. N., Greisman, J., Hoban, C. J., Hoban, D. J., Zhanel, G. G., Designing fluoroquinolone breakpoints for Streptococcus pneumoniae by using genetics instead of pharmacokinetics-pharmacodynamics. Antimicrob Agents Chemother, 48 (9):3630-3635, 2004.