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The experience in application of Gatifloxacin in the therapy of urogenital ureaplasmatic and mycoplasmatic infections

Recently the specialists have been preoccupied by a steady growth of the number of sexually transmitted infections (STIs), especially of so called masked infections: chlamydia, ureaplasmosis, mycoplasmosis.

On the one hand, the reason for that is the change of sexual stereotypes and behavior patterns; on the other hand, we observe an increased resistance to medicines, traditionally applied in clinics. Thus, more attention is paid to new antibacterial medicines, towards which microbial resistance is minimal.

Disorders affecting the organs of the genitourinary system that are of mycoplasmatic and ureaplasmatic etiology have recently become more frequent and make up about 40% of all cases of inflammatory diseases of the urinary system. These infections often recur and are associated with the development of complications. In healthy individuals M. hominisand U. urealyticum exude from the urethra in 9,4% of cases.

Treatment of urogenital mycoplasmosis and ureaplasmosis is an urgent and difficult task of modern venereology. There is a range of problems in treatment of these infections: a high rate of relapses (up to 40%), the occurrence of microbial resistance to the existing antibacterial medicines, the immune deficiencyand the necessity to apply large doses of antibiotics.

The introduction of modern diagnostic and medical technologies allowed to achieve positive dynamics as to mycoplasmatic and ureaplasmatic infections. Nevertheless, with the growth of the demonstrative data new aspects of this problem are opened. Thereby, the development and bringing of innovative medicines to market are urgent.

Fluoroquinolones (FQs) isone of the most important classes of antimicrobial medicines (AMM), which are in demand in modern clinical practice. The evolution of FQs is accompanied with the expansion of their activity spectrum as to some Gram-positive causative agents (in particular S. pneumoniae), and subsequently to anaerobic microorganisms, including Bacteroidesfragilis, which role in the development of mixed infections is proved.

Initially FQs were used for treatment of the diseases caused by Gram-negative agents; at present they are used for the therapy of respiratory infections (RIs), skin and soft tissues infections (SSTIs), as well as urinary tract infections (UTIs), including chlamydia, ureaplasmosis and mycoplasmosis.

Absence of the mechanisms of development of the cross-resistance with other classes of AMMs makes it possible to apply the fourth generation FQs for the therapy of infections caused by resistant causative agents, for instance, RIs that are induced by pneumococci, and resistant to penicillin and macrolides; or UTIs induced by enterobacteria, and resistant to β-lactams. Due to the improved pharmacokinetic and pharmacodynamic characteristics (high bioavailability and a long half-life) the application of the fourth generation FQs is also possible in cases with accompanying pathology.

The results of a range of clinical researches show a high efficiency of new FQs, economic advantages of oral or graded (in case of a grave infection) therapy, using the medicines related to this class, as well as the possibility to take a single dose of these medicines a day considerably increases patients' commitment to the therapy.

It is important to notice that the similarity of FQs' chemical structure andtheir mechanism of action makes it possible to unify the results of certain clinical studies and the epidemiological observations of causative agents' resistance and the extrapolation of given data onto the representatives of the FQs class, including the medicines that are active against anaerobes (Moxifloxacin, Gatifloxacin).

The spectrum of antibacterial activity of the fourth generation FQs Gatifloxacin includes Gram-positive and Gram-negative, anaerobic and atypical microorganisms. An ultra-broad spectrum of action of Gatifloxacin is determined by inhibition of DNA gyrase (an essential enzyme that takes part in replication, transcription and reparation of bacterial DNA) and topoisomerase IV (an enzyme that plays a key role in decomposition of chromosomal DNA during a bacterial cell division). Gatifloxacin absorbs well from the digestive tract following oral ingestion and may be administered withoutregardtotimingoffoodingestion. Absolute bioavailability of Gatifloxacin constitutes 96%, its maximum concentration in the blood plasma is observed in 1-2 hours after an oral administration. Oral and intravenous ways of introduction of Gatifloxacin are considered to be interchangeable, as the pharmacokinetics of the medicine in an hour after an intravenous introduction corresponds to its pharmacokinetics after an oral ingestion of the same dose.Gatifloxacin is distributed well in the tissues of the body, thus, providing higher concentrations in the majority of tissues and organs in comparison with the concentration in the blood plasma. The medicine is mainly excreted intact by the kidneys (more than 70% during 48 hours after oral or intravenous administration).

One of the medicines of Gatifloxacin, presented at Ukrainian pharmaceutical market, is Gatilin (200 mg and 400 mg tablets) of "Ananta Medicare" company.

The aim of the work was the estimation of therapeutical effectiveness and tolerance of FQ Gatilin in treatment of uncomplicated and complicated forms of ureaplasmetic and mycoplasmatic infections.

Materials and methods

The research involved 50 patients (25 men and 25 women) from 21 to 41 years old with a history of the disease from 2 month to 2 years and more, who were hospitalized in the STI department of theInstituteofDermatologyandVenereologyof theAcademyofMedicalScienceofUkraine. Mycoplasmatic infection was diagnosed in 20 cases (9 men and 11 women),ureaplasmatic infection – in 20 cases (11 men and 9 women), mixed ureaplasmatic and mycoplasmatic infection – in 10 cases (5 men and 5 women).

The smears of the vaginal, cervical, urethral and prostate discharge served as the material for the laboratory studies.

The diagnostics of the infection were conducted using method of enzymemultipliedimmunoassay for Mycoplasma hominis and Ureaplasmaurealyticum; the identification of such causative agents as Mycoplasma genitalium, Mycolpasmahominis and Ureaplasmaurealyticumby method of DNA polymerase chain reaction. The intensity of signs was estimated in points (0-3).

Table. The dynamics of clinical laboratory tests against the background of Galin drug administration	Symptom	Initially	In 5 days	In 10 days	

abs.	%	abs.	Presence of discharge from the pudenda	48	96	18	

Subjective sensations (itch, burning)	27	54	17
Hyperemia of sponges of the urethra	21	42	14
Urination disorder	18	36	11
Pain in the lower part of abdomen	27	54	19

The patients got the prescription to take Gatilin tablets once a day (provided that creatinine clearance is more than 40 ml/min)withoutregardtotimingoffoodingestion:

- with body weight < 50 kg – 200 mg/day;
- with body weight 50-80 kg – 400 mg/day;
- >80 kg – 600 mg/day.

The course of treatment constituted 10 days.

During the clinical studies together with the test preparation the patients receivedthe antifungal drug Fluconazole at a dose 150 mg once in 5 days, hepatoprotectors and probiotics. The assessment of effectiveness of the test preparation was carried out according to the next scale:

- high effectiveness (3 points) – complete clinical remission;
- moderate effectiveness (2 points) – reduction of clinical manifestations by 50-75%;
- low effectiveness (1 point) – reduction of clinical manifestations<50%;
- no effectiveness (0 points) – absence of changes of test indices.

Results and discussion

The patients complained on burning sensation, itch, discomfort and discharge from the pudenda, frequent urination, and pain in the lower abdomen. The manifestations of urethritis, vaginitis,endocervicitis, and salpingo-oophoritis prevailed among the women, and those of urethritis and prostatitis prevailed among the men. Rarely, the cases of epididymitis and vesiculitis were observed.

Among the men at the time of the 2d visit (in 5 days after the beginning of the treatment) the manifestations of urethritis decreased in 7 cases (28%); on the 3d visit (in 10 days after the beginning of the treatment) those of urethritis and balanitis decreased in 10 cases (40%); the manifestations of prostatitis – in 10 cases (40%); after the 4th visit the improvement was observed in 23 cases (92%) and only in 2 cases (8%) the manifestations of prostatitis remained.

Among the women at the time of the 2d visit the intensity of symptoms of urethritis decreased in 7 cases (28%), of vaginitis – in 15 cases (60%); on the 3d visit the manifestations of cervicitis decreased in 8 cases (32%), of salpingo-oophoritis – in 12 (48%) cases; by the 4th visit the main pathology wasn't observed in 22 cases (88%) and only 3 (12%) female patients still had the manifestations of salpingo-oophoritis (Table).

The majority of the patients noted the decrease of itch, burning sensation, hyperemia of sponges of the urethra and the amount of discharges already by the end of the 1st week of treatment, herewith in 5 days of the therapy the amount of discharges reduced by 62,5%, the intensity of pain in the lower abdomen – by 29,6%; in 10 days – by 79,2 and 55,6%, respectively. By the 3d visit there was a notice of significant decrease in total subjective signs by 48,2%, of total objective ones – by 57,2% in comparison with the 1st and 2d visits.

High therapeutic effectiveness of the Gatilin drug (2,5±0,3 points) was detected in the overwhelming majority of cases of the patients with ureaplasmatic and mycoplasmatic infections, moreover there was a notice of the reduction of total subjective manifestations by 85,2%, objective ones – by 88,9%. Microbiological

effectiveness was confirmed in 45 cases (90%); in 2 cases (4%) laboratory studies detected mycoplasmas in the analysis and in 3 cases (6%) – ureaplasmatic infection was detected. An additional course of treatment was recommended to these patients.

The comparative assessment of the dynamics of the results of the clinical laboratory examination of the patients registered an apparent trend to the reduction of erythrocytesedimentationrate from 18,6±4,4 to 9,8±2,7 mm/h.

The drug tolerance was assessed during all the period of treatment on the basis of subjective indices and objective data, received in the course of therapy, as well as the dynamics of laboratory tests and it was defined as a good one.

During the treatment none of the patients complained on changes in general condition; there was no notice of any cases of variation of arterial tension or heart rate.

In 10 cases (5 patients) there were slight dyspepsic events in the form of epigastric discomfort, nausea, and diarrhea, but all this didn't require the drug withdrawal.

There was a tendency to increase of the level of aspartatetransaminase from 0,400±0,027 to 0,459±0,037 mmole/l×h^{-1} andalanineaminotransferase from 0,409±0,039 to 0,440±0,040 mmole/ l×h^{-1}, however these changes were inaccurate, and the indices didn't exceed the level of the referential values. There was no evident difference in the other biochemical tested parameters, if we compare them before and after the treatment.

Conclusion

An apparent therapeutic effectiveness and a good tolerance of the drug Gatilin ("Ananta Medicare") were determined. The obtained results allow to recommendGatilin for application in a complex treatment of patients with urogenital ureaplasmatic and mycoplasmatic infections.