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## ANTIBIOTICS IN AMBULATORY PRACTICE IN THE TREATMENT OF DIFFUSE OTITIDES EXTERNA

DISEASES OF EXTERNAL EAR REMAIN AN UNSOLVED PROBLEM IN PRACTICAL OTORHINOLARYNGOLOGY.

ACCORDING TO VARIOUS AUTHORS, OTITIDSEXTERNA ARE COMMON AND MAKE UP 17 TO 23% OF ALL EAR LESIONS.

Seasonal increases of the incidence rate of otitidesexterna (often relapsing), the resistance to therapy, the development of complications determine the urgency of the problem and dictate the need for a more detailed study and improvement of methods of treatment.

The most common working classification of external otitides:

1. Limited otitidesexterna (furuncles).
2. Diffuse otitidesexterna.
3. Noncommunicable otitidesexterna.

Diffuse otitidesexterna—a common nosological form that includes a group of inflammatory diseases of bacterial or fungal origin. Due to the fact that in the pathogenesis one of the leading factors is bacterial, study of microflora with the aim to determine the degree of pathogenicity is of great importance when examining patients. However, microbiological examination takes three to five days, so prescription of antibiotics is carried out empirically, in order to achieve a positive result quickly and to prevent possible complications. When prescribing an antibacterial medicine, it is necessary to focus on the likely pathogen causing the disease, and the spectrum of its sensitivity to antibiotics.

According to the research carried out in Kharkiv region, the most common causative agents of diffuse otitidesexterna are Gram-positive microorganisms: *S. aureus*, *S. epidermidis*, *S. haemolyticus*, other representatives of the genus *Staphylococcus*, *S. pyogenes*, *S. viridans*, other representatives of the genus *Streptococcus* and Gram-negative microorganisms: *Escherichia coli*, *Enterobacter cloacae*, *Proteus vulgaris*, *Pseudomonas aeruginosa*. Given the wide pluricausal range of possible causative agents, there is the necessity to prescribe a medicine with a broad spectrum of antimicrobial action. Currently, the most common and frequently prescribed antibacterial medicines are semi-protected penicillins (amoxicillin / clavulanate), macrolides (azithromycin, clarithromycin), fluoroquinolones IV generation (gatifloxacin).

Important terms of clinical efficacy of the treatment of diffuse otitidesexterna in ambulatory practice are:

- rate of onset and persistence of the effect;
- multiplicity and ease of taking the drug [5];
- safety;
- financial costs of treatment.

The purpose of this randomized open comparative study was the investigation of the effectiveness of various groups of antibacterial drugs in complex treatment of diffuse otitidesexterna.

In conducting the researches as a basic therapy using fluoroquinolones Gatilin drug (gatifloxacin) 400 mg was used, on the market it is presented by Ananta Medicare (United Kingdom). Gatilin (gatifloxacin) is one of the most studied and effective antimicrobial drugs of IV generation fluoroquinolones [7]. The mechanism of its action is based on direct inhibition of DNA-Gyrase - the enzyme, responsible for genetic recombination and DNA repair, and inhibition of topoisomerase IV, which catalyzes the separation of two related strands of DNA after replication. Gatilin has a broad spectrum of antibacterial activity, it is sensitive to the Gram-positive flora (*S. aureus*, *S. epidermidis*, *S. haemolyticus*, *Staphylococcus* spp., *S. pyogenes*, *Enterococcus* spp.), Gram-negative flora (*E. coli*, *Proteus* spp., *P. aeruginosa*, *H. influenzae*, *M. catarrhalis*), atypical causative agents (*C. pneumoniae*, *L. pneumoniae*, *M. pneumoniae*).

A distinctive feature of Gatifloxacin is its bactericidal effect against the anaerobic flora (*Bacteroides fragilis*, *Clostridium perfringens*, *Peptococcus* spp.). Gatifloxacin is effective against the bacteria resistant to  $\beta$ -lactams and macrolides. After oral administration gatifloxacin is well absorbed from the gastrointestinal tract. Administration of this drug does not depend on the meal. The bioavailability of gatifloxacin is 96%. Maximum plasma concentration is achieved in 2 h after administration. Gatilin penetrates well into all tissues and organs, where it creates high inhibitory concentrations. It is primarily excreted by the kidneys in unchanged form, that's why there is no need to adjust the dose of the drug in case of liver pathology. The half-life makes up 12-14 hours. Due to the unique mechanism of action Gatilin has minimal risk of development of microbial resistance in comparison with antibiotics pertaining to other groups.

## Materials and methods

**The design of the study.** The open comparative randomized study was conducted in Kharkov municipal outpatient clinic №26.

Patients who met the criteria for inclusion into the study ( $n = 90$ ), were prescribed a standard treatment: antibacterial medicine, selective to COX-2 NSAIDs, antihistamines II-III generation, probiotics, medicines that improve blood rheology, local therapy (antiseptic compositions) [3].

The treatment lasted for 7-10 days. The patients were observed during 10-15 days. All the patients were divided into three groups depending on used antibacterial drug (see Table).

The design of the study did not assume the use of other drugs, but in case of low efficiency the treatment could be changed.

**The criteria for inclusion.** The study included the patients aged 18 to 60 years with acute diffuse otitis externa (bacterial etiology) of moderate severity. Classical approach was used in the selection of patients with diffuse otitis externa.

1. History: presence of a factor that caused the disease (mechanical damage of the skin, a dirty pond, etc.).
2. ENT examination: otoscopy - hyperemia, infiltration, maceration of the skin, concentric narrowing of the external auditory meatus, presence of a zone of perifocal inflammation, painfulness to palpation.
3. Laboratory studies: detailed clinical blood test, blood sugar test.
4. Bacteriological examination (smear from the external auditory meatus on the microflora and sensitivity).
5. Audiology researches.

## 6. X-ray (CT) study of mastoid bones (on indications).

Group (n)	Antibacterial medicine	Dose (mg)	Dosage frequency	Duration of application (days)
I (30)	Amoxicillin / clavulanate	875/125	2 times	7-10
II (30)	azithromycin	500	1 time	3-5
III (30)	Gatifloxacin (Gatilin)	400	1 time	5-7-10

**Exclusion criteria.** Otomycosis, presence of allergic reaction to the antibiotic in a medical history, exacerbation of chronic mesoattic disease in combination with otitis externa, patients with liver pathology (decrease of renal clearance below 40 ml / min).

**Evaluation of the results.** The clinical assessment of the patients' state was made on the 1<sup>st</sup> day (medical history, medical examination, laboratory and instrumental studies), on the 3<sup>rd</sup>, 5<sup>th</sup>, 7<sup>th</sup>, and 10<sup>th</sup> day according to five signs: degree of erythema, volume of infiltration of ear tissues, painfulness of an inflammation zone, degree of narrowing of external auditory canal, hearing loss.

The clinical effect of the treatment was assessed as follows:

Recovery - 0 points – absence of objective and subjective signs of otitis externa.

Significant improvement - 5 points - presence of two objective and / or subjective symptoms.

Lack of effect - 10 points – presence of 3-4 objective and / or subjective symptoms.

The changes in the patients' treatment regimens as well as the side effects of the medicines were recorded in the histories of the disease.

### Results and Discussion

The study involved 90 patients (34 men, 56 women) who met the inclusion criteria. The group of the participants were the most homogeneous by sex and age composition. Six participants did not complete the study as malignant otitis externa (caused by *P. aeruginosa*) was detected in one of these six cases, the patient was hospitalized in the clinic. The second patient admitted to the hospital on his own request. Four patients refused further treatment and observations due to the recovery.

Upon microbiological testing a mixed microflora was detected in the patients with acute diffuse otitis externa: Staphylococcus, streptococci, enterococci, Proteus, *Pseudomonas aeruginosa*, fungal flora (*Aspergillus* and *Candida albicans* in 15.1% of cases).

Negative results of bacteriological research were the recovery criterion. On the 10<sup>th</sup> day the treatment quality control was carried out by inoculation of medium of a swab from external auditory canals.

Bacteriological efficacy of therapy was as follows: in the first group – the complete eradication of causative agents 85.8% (26 people), in the second group - the total eradication of causative agents 79.2% (24 people), in the third group - 100% bacteriological efficacy (30 people).

Clinical evaluation of efficacy was performed on the basis of reduction of the severity degree of the external ear canal infiltration, erythema stiffness in the ear, increase of the clearance of external auditory canal, the severity of the subjective symptoms (Fig. 1 - 3).

Clinical efficacy of treatment made up:

- In the first group (amoxicillin / clavulanate) - 89.1% (27 people);
- In the second group (azithromycin) - 82.5% (25 people);
- In the third group (Gatilin) - 100% (30 people).

Thus, the application of Gatilin (gatifloxacin) as a representative of IV generation fluoroquinolones for the treatment of acute diffuse otitis externa is clinically justified because of its high bactericidal effect on Gram-positive, Gram-negative and anaerobic flora.



Fig. 1. Dynamics of the main symptoms in the course of treatment (a relative indicator: 0 % (0 points) – absence of symptoms of the disease, 100 % (10 points) – maximum expression of symptoms of the disease)



Fig. 2. Dynamics of the symptom of improvement of hearing (relative indicator: 0 % proper hearing, 100% –hearing loss)

## Conclusions

The research defined the high therapeutic efficiency and safety of Gatilindrug (gatifloxacin) of the Ananta Medicare company (Great Britain) in treatment of acute diffuse otitis externa in a dose of 400 mg, 1 time per day within 7-10 days.

Application of Gatilin together with antihistamine medicines of II-III generations, COX 2 selective NSAIDs, probiotics and local therapy allows achieving positive and stable dynamics in the treatment of diffuse otitis externa, with minimal financial expenses and as quickly as possible.

Gatilin is expedient for using for carrying out empirical therapy of bacterial infections in the area of external auditory canal under ambulatory- polyclinic conditions.