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EFFLUX PUMP GENE EXPRESSION IN *PSEUDOMONAS AERUGINOSA* EXPOSED TO AZITHROMYCIN AND CLARITHROMYCIN

Background. One of the mechanisms of *P.aeruginosa* resistance to antimicrobial agents (AMAs) is the hyperactivity of efflux pumps, particularly MexAB-OprM and MexXY of the RND family, which are the determinants of resistance to aminoglycosides, fluoroquinolones and others [1]. It is known that drugs capable of affecting quorum sensing systems, in particular macrolides, can reduce *P.aeruginosa* resistance to host defense mechanisms [2], which may increase the susceptibility of this pathogen to AMAs. **Aim.** To determine the expression of efflux pump genes *mexR*, *mexY*, and *oprM* in *P.aeruginosa* under the influence of azithromycin and clarithromycin. **Methods.** Expression of the *mexR*, *mexY* and *oprM* genes in *P.aeruginosa* 449 at 0.5 MIC of azithromycin (25 µg/ml) and clarithromycin (100 µg/ml) was determined by RT-qPCR using SYBR Green dye. Amplification was performed under the following thermal cycling conditions: 20 s at 95 °C, followed by 40 cycles of 15 s at 95 °C and 60 s at 60 °C. The endogenous control was 16S rRNA gene. Statistical analysis of the results was carried out using the ANOVA method. **Results.** According to the obtained data, under the action of azithromycin the transcriptional activity of the *mexR*, *mexY* and *oprM* genes in the clinical isolate *P.aeruginosa* 449 decreased 3.2-fold, 7.8-fold and 5.3-fold, respectively. Under the influence of clarithromycin an increase in the expression of *mexR* and *mexY* genes was observed, by 1.6-fold and 7.8-fold, respectively, while the expression of the *oprM* gene decreased 2.8-fold compared to the control ($p < 0.05$). **Conclusions.** Thus, second – generation macrolide antibiotics azithromycin and clarithromycin affect the transport systems of *P.aeruginosa*. The decrease in the expression of *mexY* and *oprM* genes under azithromycin exposure may contribute to increased susceptibility of *P.aeruginosa* to aminoglycosides. Under the influence of clarithromycin activation of the *mexR* and *mexY* genes was observed, which may lead to the development of multidrug resistance, biofilm formation with chronic inflammation and alterations of *P. aeruginosa* virulence.

Keywords: *P. aeruginosa*, macrolides, gene expression, *mexR*, *mexY* and *oprM*

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