PHOTODYNAMIC THERAPY OF NONONCOLOGICAL DISEASES OF FEMALE GENITAL ORGANS

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Introduction. More than 50% of sexual active population are infected by human papilloma virus (HPV) during lifetime. Such diseases as genital condyloma, cervical intraepithelial neoplasia (CIN) and malignancies of cervix, vulva, vagina and perianal zone are considered as the consequences of HPV virus infection. Surgery, laser ablation and cryodestruction are usually applied for the treatment. Photodynamic therapy (PDT) is alternative and small invasive method in the treatment of HPV associated diseases.

The aim of this study was to estimate the clinical efficacy and safety of 5-ALA based medicinal formulation ALAsense in PDT treatment of HPV associated diseases of vulva and cervix. The kinetics of 5-ALA-induced Protoporphyrin (PPIX) accumulation in above tissue after oral application of ALAsense was studied by in vivo local fluorescence spectroscopy.

Materials and methods. The group of 34 patients included 28 cases with pointed condyloma and 13 cases with pathology of cervix uterus. The PDT sessions were carried out 3-6 h after oral administration of ALAsense at the dose of 25 mg per kg b.w. The emission of diode laser at 635 nm was used for tissue irradiation (Biospec Ltd, Russia). The average duration of PDT session was 27 min. The energy density varied from 30 to 150 J/cm² (90 J/cm² as average). We evaluated the clinical efficacy of PDT treatment visually and on the base of the data of PCR diagnosis, colposcopy, cytology and histology.

In vivo local fluorescence spectroscopy was applied in all patients before and every hour after oral administration of ALAsense. The fluorescence measurements were performed using a spectral fluorescence system Spectr-Cluster (Cluster Ltd, Russia) with a working range of 410-1000 nm and tissue fluorescence excitation at 405 and 532 nm.

Results. The fluorescence bands of 5-ALA-induced PPIX peaked at 635 and 705 nm were detected against the autofluorescence background in all spectra measured from the vaginal portion of cervix uterus in all patients. However the atypical epithelium generally exhibited more intensive 5-ALA-induced PPIX fluorescence then surrounding normal tissues. The fluorescence contrasts between pathological foci and healthy vulva were detectable as soon as one hour after Alasens administration and reached the maximum value 4 h after. It should be noted that 5-ALA-induced PPIX fluorescence from healthy skin of vulva was negligible in all period of the observation. According the data of PCR diagnosis performed three months after PDT the complete antiviral effect was confirmed in 18 cases (67%) with pointed condyloma and 6 cases (46%) with pathology of cervix uterus. HPV was confirmed in 9 cases (33%) with pointed condyloma and 7 cases (54%) with pathology of cervix uterus (no antiviral effect). The results of PDT treatment of HPV associated diseases are the following: 16 cases (59%) with pointed condyloma and 5 cases (38%) with pathology of cervix uterus had complete regression of lesions, 10 cases (37%) with pointed condyloma and 4 cases (31%) with pathology of cervix uterus had remarkable regression (about 60-95%) and 1 case (4%) with pointed condyloma and 4 cases (31%) with pathology of cervix uterus had no effect. It should be noted the realization of PDT effect was observed during up to three months after the treatment. As to concern the reparation process we observed the beginning of marginal epithelization at the 3rd or 4d day after PDT treatment. The epithelization was complete generally 2-4 weeks after the treatment.

Conclusion. In vivo fluorescence measurements revealed the fluorescence contrast between pathological lesions and surrounding healthy mucosa of vulva and cervix uterus that confirmed the increased induction of PPIX in pathological tissue after oral application of ALAsense. In vivo local fluorescence spectroscopy allowed to study the kinetic of 5-ALA induced of PPIX fluorescence and to determine the optimal time for PDT treatment. The selective induction of PPIX in epithelial layer of vulva and cervix uterus made it possible to preserve the structure of normal tissue and also to decrease the duration of post treatment tissue healing without erosions and scars formation.