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Modern aspects of management of benign cervical disease associated with papillomavirus infection

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Summary: The objective of this research work was to evaluate the clinical efficacy of Proteflazid, an immunomodulating and antiviral drug, in the treatment of underlying cervical disease in a setting of viral infectious contamination. As one of the results of the assessment in the study population of women, the sequence and the prevalence of human papillomavirus have been determined. The resulting findings provide evidence for the high efficacy of immunological therapy with Proteflazid and support the expediency of testing women for human papillomavirus, which is aimed at prevention of malignant disease.

Key words: antiviral therapy, Proteflazid, underlying cervical disease.

Introduction.

Infectious urogenital disease caused by viral or bacterial agents is an important medico-social problem due to the potential development of severe complications and substantial prevalence. A unique position within the morbidity patterns of sexually transmitted disease belongs to papillomavirus infection.

More than 100 types of specific DNA sequences of human papillomavirus (HPV) have been identified. As informed by the results of assessments using *in situ* hybridization technique, the signs of papillomavirus infection are detectable in 3-38 % females; the results of polymerase chain reaction (PCR) inform detection rates within the range of 26–46 % [5, 7]. The literature also reports other data on the prevalence of papillomavirus infection (PVI). According to some reports [3], highly carcinogenic HPV types are found in 54 % of female patients assessed at women's health clinics and centers.

According to a number of researchers [4, 6], there is an inverse relationship between the prevalence of PVI and age, which may be attributable to the immunity against the infection, which develops in the course of life. Despite the high potential hazards, HPV is an opportunistic pathogen. This is confirmed by detection of papillomaviruses in 10–30 % of women without gynecological disease [6]. In 50 % of HPV–infected females, spontaneous elimination of the virus occurs within a year and in 85 % of HPV–infected females it occurs over a span of 4 years [2].

The presence of papillomavirus in cervical tissues does not cause cervical cancer directly. However, the significant changes in epithelial proliferation activity in a setting of viral infection can be viewed as one of the factors included in the overall specter of carcinogenesis.

Modern therapeutic modalities used in the management of HPV-associated cervical disease include systemic and local treatments.

Local treatments include drug therapy with cytotoxic agents (Podophyllin, 5-fluorouracil, Condylin), local chemical agents (Solkoderm, resorcin) and surgical removal of lesions (cryoablation, diathermy/electrocoagulation and CO_2-laser vaporization). When various types of surgical interventions are used (which are basically directed at removal of local lesions), relapses of the disease may develop within a short time, since these methods lack systemic antiviral influence on intracellular mechanisms of viral replication.

The objective of this research work was to evaluate the systemic use of Proteflazid, an antiviral product, and to study its therapeutic efficacy in benign cervical disease associated with papillomavirus infection.

Materials and methods.

The study enrolled 120 women with the benign cervical disease. The age of the patients was 25.8 ± 2.3 years on the average.

For identification of HPV types 6–11, 16–35, 18–59 and 52–66, the study site used PCR diagnosis (with reagents manufactured by Amplisens). Test material included scrapings from cervical mucosa, from cervical canal and from the lesion, obtained with Cytobrush® cell collectors.

The schedule of clinical assessments included patient's history, pelvic exam, colposcopy and bacteriological/cytological testing.

As an antiviral agent, the study employed Proteflazid (manufactured by Scientific & Manufacturing Company Ecopharm Ltd.), an herbal product containing flavonoid glycosides [1]. Proteflazid was used orally according to the following regimen: Week 1: 5 drops daily 3 times daily; Week 2–3: 10 drops daily 3 times daily; Week 4: 8 drops daily 3 times daily. The product was also used locally as vaginal tampons soaked in a 1:4 solution of Proteflazid (diluted with 0.9 % NaCl) 2 times daily, daily for 10 days.

Results and discussion.

After assessment of 120 female subjects, HPV was detected in 45 subjects (37.5 %).

The most common type of papillomavirus is type 18 (28.5 %), followed by type 16 (23.7 %), type 56 (12.8 %), type 33 (9.8 %) and type 66 (9.7 %). In addition to that, most patients had associations of two HPV types. Based on these investigations, it is possible to conclude that highly carcinogenic HPV types are predominant even in benign cervical disease.

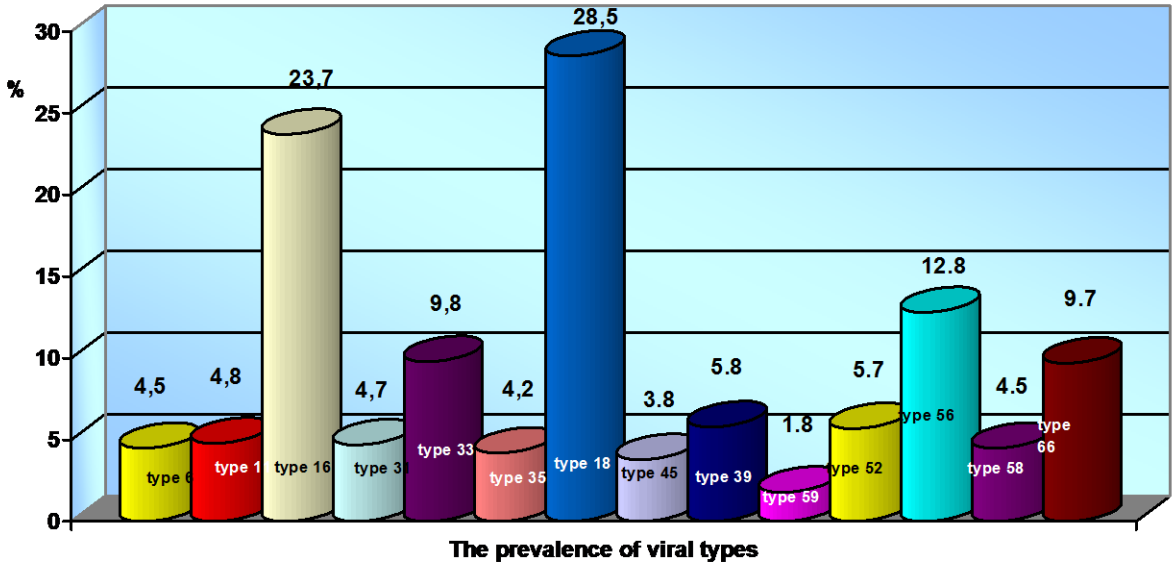

Figure 1. Detection rates of the main HPV types (%).

In a vast majority of cases, HPV was diagnosed as a part of bacterial/viral associations, which had a significant impact on the vaginal microbiome and contributed to the progress of the underlying cervical disease.

All of the women were sexually active; the mean age of the onset of sexual activity was 17.8 ± 1.2 years. History of pregnancy and delivery was positive in 48.7 % women; 28.5 % of these women had abortions. As many as 42.5 % of the women had a history of the extragenital disease (pyelonephritis, peptic ulcer disease, gastritis, hepatitis and chronic tonsillitis).

The main patient complaints included the following: various types of genital discharge (58 %), lower abdominal pain (34.8 %), contact spotting (8.7 %) and vaginal discomfort/itching (12.5 %).

Colposcopic assessment detected the following: cervicitis (70.8 %), ectopy of cylindrical epithelium (61.4 %), incomplete transformation zone (6.8 %), ectropion (4.5 %) and polyps in the cervical canal (2.4 %). The cytological assessment found signs of viral infection (dyskeratosis, parakeratosis and koilocytes) in 30.7 % of the assessed women. Positive changes of clinical presentation were seen with a time of treatment: the improved well-being of the patients, reduced pain and reduced amount of vaginal discharge. Colposcopic follow-up has demonstrated reductions of the area affected by the disease and the severity of inflammation.

Drug therapy contributed to the improvement of colposcopic presentation in 62.4 % of the patients. It is possible to state that the highest therapeutic efficacy was achieved in patients with a small area of the cervical lesion(s), with a moderately pronounced topography and in patients without extragenital disease.

In 8–10 weeks after completion of the antiviral treatment regimen, follow-up of papillomavirus infection with a PCR technique was performed; test reports were negative in 85.8 % of the patients.

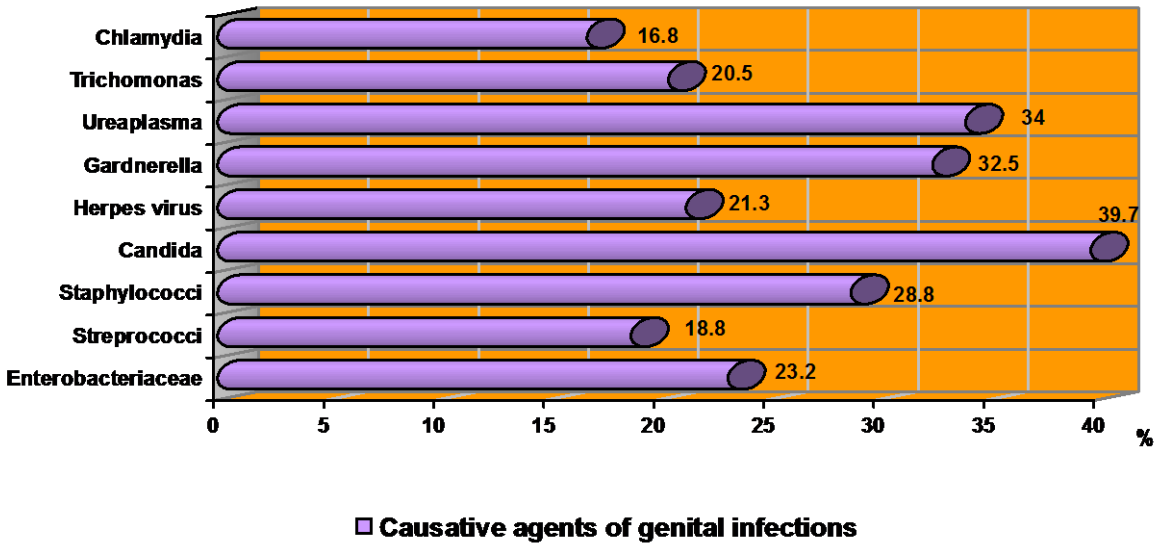

Figure 2. Detection rates of genital infection (%).

Conclusions:

1. Human papillomavirus is diagnosed in 37.5 % of women with the benign cervical disease.
2. Most women are diagnosed with associations of sexually transmitted pathogens.
3. The diagnosis of underlying cervical disease must involve both cytology and colposcopy with a mandatory molecular biology assessment for HPV.
4. A timely and full assessment of women and elimination of abnormal cervical changes (while taking into account all causative agents and pathogens) contribute to a reduction in lesion areas and improvement of disease severity, allowing to manage this disease conservatively in 62.4 % of the patients.
5. Using Proteflazid is an antiviral component of multimodality therapy for underlying cervical disease associated with papillomavirus infection is effective. This allows reversing clinical and laboratory findings to normal and eliminating human papillomavirus in 85.8 % of the patients, as confirmed by PCR.

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