According to the sources, vaginal candidiasis develops on the background of papillomavirus infection in 36–41% of cases. The violation of the vaginal biocenosis decreases the immunological potential of the epithelium, and creates favourable conditions for the carcinogenic effect of the human papillomavirus. We have examined 100 patients (18–40 years old) in order to evaluate the efficiency and safeness of Fluzamed (active ingredient: Fluconazole-150 mg) usage in treatment of vulvovaginal candidiasis with cervical dysplasia caused by papillomavirus infection. The treatment control was performed three times: after the first course of treatment, in 3 and 6 months. The study has shown that due to Fluconazole-150 mg treatment, the disease recurrences at 3 and 6 months were occurred significantly rarely as compared to the cases of Butoconazole-20 mg/g application. The complete eradication of PVI was clinically and laboratory confirmed after 3 and 6 months of treatment. In our study, we have confirmed the safety of a systemic drug Fluzamed (active ingredient: Fluconazole-150 mg) usage by the lack of adverse reactions after its administration.

Key words: vaginal candidiasis, papillomavirus infection, Fluzamed.

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**Efficiency of using antifungal drugs in women with vaginal candidiasis on the background of papillomavirus infection**

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**Key words:** vaginal candidiasis, papillomavirus infection, Fluzamed.
More than 290 million of women in the world are infected with papilloma viruses [3].

Based on the recent medical research, 50–70% of sexually active adults in the world are infected with PVI. At the same time, only 1–2% has the clinical signs. The largest annual increase of PVI rate is observed among young people aged from 14 to 24 years [3].

Abnormal vaginal biocenosis reduces the immune potential of the epithelium, and creates conditions for the carcinogenic effect of the human papillomavirus (PVI) [6].

According to the sources, vaginal candidiasis develops on the background of papillomavirus infection in 36–41% of cases, but the problem of combination of these two infections is not fully investigated yet. That is why we decided to study the possibilities of modern medical therapy of vaginal candidiasis caused by papillomavirus infection.

The key aim of the study is to evaluate the efficiency and safety of the agent Fluzamed (active substance: Fluconazole) in the treatment of women at the stage of preconception care suffering from vulvovaginal candidiasis combined with cervical dysplasia caused by papillomavirus infection.

We have defined the next tasks:
1. To study the etiological agent of vaginal candidiasis in women with cervical dysplasia caused by papillomavirus infection.
2. To study the clinical efficiency of Fluzamed (active substance: Fluconazole-150 mg) as compared to Butoconazole-20 mg/g during follow-up monitoring in 3 and 6 months.
3. To evaluate the safety of systemic drug Fluzamed as compared to locally acting Butoconazole-20 mg/g.

According to our key aim and tasks, in total 100 women aged 18–40 years were examined, suffering from colpitis of fungal etiology combined with cervical dysplasia caused by papillomavirus infection. The treatment included administration of Fluzamed (active substance: Fluconazole-150 mg) compared to the locally acting Butoconazole-20 mg/g.

All patients were divided into two groups: group I (basic) that comprised 50 women who were treated for colpitis of fungal etiology combined with cervical dysplasia caused by papillomavirus infection with Fluconazole-150 mg; and group II (comparison) included 50 women who were treated for candidal colpitis combined with dysplasia of the cervix caused by papillomavirus infection with Butoconazole-20 mg/g.

Exclusion criteria: existence of severe extragenital pathology, which was as follows:
- diabetes;
- uncompensated pathological conditions of the liver;
- chronic and acute renal failure;
- hypersensitivity to fluconazole or other azole compounds, or to any excipients of the drug.

Research duration: 6 months.

During the first visit, the next diagnostic procedures were carried out, including:
- assessment of the nature of vaginal discharge, duration of symptoms, concomitant symptoms, sexual contacts during the last 12 months, contraceptive methods, results of the last preventive examination;
- history taking (anamnesis vitae, gynecological, reproductive, family, allergic history, hereditary background);
- objective clinical and laboratory examination.

Laboratory diagnostics included comprehensive evaluation of vaginal microbiocenosis: the microscopy of Gram-stained vaginal smears, bacteriological examination of the type of fungus and sensitivity to antimycotic drugs; liquid cytology and quantification of PVI after the disappearance of clinical and laboratory signs of candidiasis.

It is important to mention that it is still problematic to identify the etiology of the disease and to detect a significant number of infected people without laboratory diagnostics.

Diagnostic procedures during the follow-up visits included:
- control of the clinical symptoms in dynamics;
- control of bacterioscopic examination;
- simple and extended colposcopy;
- cervical biopsy based on medical indications;
- cytological research;
- quantitative determination of high-oncogenic genotypes of PVI.

In our study, we have used the syndromic approach that is scientifically substantiated, and offers affordable, immediate and effective treatment.

Treatment control was conducted 3 times: after the first course of treatment, in 3 and 6 months.

Treatment efficiency criteria:
- positive clinical effect — absence of symptoms and clinical signs of the disease;
- positive microbiological effect — the absence of the causative agent.
Clinical efficiency included the next terms:
1. **Recovery** — the absence of complaints and clinical signs of the disease with negative laboratory results.
2. **Improvement** — reduction or disappearance of complaints when the microbiological changes remain the same.
3. **No changes** — the constancy of clinical and laboratory signs after the treatment course.
4. **Relapse of the disease** — the restoration of clinical and laboratory signs of vaginal candidiasis after a full recovery within the period of 1–6 months since the onset of therapy.

The safety of drugs was evaluated based upon the presence of adverse reactions.

**Results and discussion.** The average age of the examined women was 24.6 ± 1.2 years. In most women (85.0%), menstruation began at the age of 13–14 and was regular. Only 15.0% of patients reported a history of menstrual irregularities. Anamnestic data showed that in the structure of inflammatory diseases of female genital organs prevailed the following: colpitis (70.0%), salpingo-oophoritis (30.0%), endometritis (10.0%). In 14.0% of patients, infertility was noted.

In the reproductive anamnesis of patients, there was noted:
- pregnancy — in 65.0% cases;
- woman who has given birth once — in 28.0% of cases;
- among those who have given birth, threatened miscarriage in 60.0% of patients and spontaneous abortion in 14.0%;
- stillbirth — in 2.0% of patients.

The dissonance between microbiological and clinical signs of vaginal candidiasis caught our attention. Ninety percent of patients presented with vaginal discharge. However, during the objective examination the excessiveness of the discharge was confirmed only in 75.0% of patients. In 60.0% of women from two groups were noted hyperemia and swollen vaginal mucosa. However, the microscopic examination revealed the increase of white blood cells in 100.0% of the examined women.

The obtained data showed that the mild or moderate dysplasia of cylindrical epithelium (according to the Bethesda system, ASC-US ‘Atypical Squamous Cells of Undetermined Significance’, squamous cell anemia of unknown genesis) was more often observed in women aged 18 to 25 years (61.0%). The PVI test found a predominance of the 16th, 18th, 31st and 52nd types.

Table 1

<table>
<thead>
<tr>
<th><strong>Table 1</strong></th>
<th><strong>Candida spp. Sensitivity to Antimycotic Drugs</strong></th>
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<tbody>
<tr>
<td><strong>Candida</strong></td>
<td></td>
</tr>
<tr>
<td><strong>species</strong></td>
<td><strong>Sensitive to</strong></td>
</tr>
<tr>
<td>C. albicans</td>
<td>98.8</td>
</tr>
<tr>
<td>C. krusei</td>
<td>75.0</td>
</tr>
<tr>
<td>C. tropicalis+C. albicans</td>
<td>100.0</td>
</tr>
</tbody>
</table>

According to the histological examination, CIN-I was diagnosed in 86.0% of women; CIN-II — in 14.0% of examined patients.

In our study, the types of *Candida spp.* were as follows:
- *C. albicans* — 90.0%;
- *C. krusei* — 8.0%;
- combination of *C. albicans* with other types — 2.0%.

The assessment of the sensitivity to antymycotic drugs is shown in Table 1.

Prior to initiating therapy, women participating in our study noted the following symptoms:
- vaginal discharge — 75.0%;
- hyperemia and swollen vaginal mucosa — 60.0%;
- dysuria — 15.0%.

We have estimated the rate of clinical symptoms disappearance during the first 72 hours (Fig. 1).

Despite the fact that the clinical effect when using topical antifungal agent developed faster as compared to systemic drug administration, in our study the disease recurrences at 3 and
6 months were occurred significantly rarely with Fluconazole-150 mg than Butoconazole-20 mg/g.

After vaginal candidiasis treatment completion, we have pointed out the full eradication of PVI. It was also clinically and laboratory proved in 27.0% of cases in group I and 17.0% of cases in group II after 3 months of treatment, and after 6 months of treatment in 58.0% of cases in group I and in 49.0% of cases in group II.

Side effects with Fluconazole-150 mg were not found, while with Butoconazole-20 mg/g, a local allergic reaction occurred in 1 case (2.0%).

Conclusions

1. In our study, the most common pathogens of vaginal candidiasis were commensals Candida spp., which were as follows: C. albicans — 90.0%; C. krusei — 8.0%; combination of C. albicans with other types — 2.0%.

2. The clinical effect of antifungal drug of local action Butoconazole-20 mg/g developed faster. However, the clinical effect with Fluconazole-150 mg treatment was manifested in the significantly rare disease recurrences at 3 and 6 months than after the using of Butoconazole-20 mg/g. The full eradication of PVI was clinically and laboratory confirmed after 3 months treatment in 27.0% of patients in group I and 17.0% of patients in group II; after 6 months in 58.0% of patients in group I and 49.0% of patients in group II.

3. The safety in the use of systematic agent Fluzamed (active substance: Fluconazole-150 mg) was confirmed by the lack of adverse reactions after its administration in our study, while Butoconazole-20 mg/g application caused a local allergic reaction in 1 patient (2.0%).

Conflict of Interest: No conflict of interest was declared by the authors.
Флузамед

ГРИБОК ТУРБУЄ – ФЛУЗАМЕД ЛІКУЄ

- Протигрибковий засіб системного застосування
- Показаний при генітальному кандидозі
- Разове застосування при неускладненому кандидозі

ЛІМЕНДА

Метронідазол 750 мг / Міконазол 200 мг

- Протигрибкова дія
- Антибактеріальний та антитрихомонадний ефект
- Можливість застосування з 2-го триместру вагітності

1 Інструкція для медичного застосування препарату Лімента.
2 Інструкція для медичного застосування препарату Флузамед.