

FEATURES OF ENDOMETRIAL RESTRUCTURING IN HIV INFECTION

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Abstract

The purpose of our study was to evaluate the features of endometrial restructuring when infected with the human immunodeficiency virus. **Materials and methods:** The study involved sectional material taken from 60 women of reproductive age from 20 to 40 years. Group 1 (30 women) consisted of women who were diagnosed with HIV infection. The control group comprised women (30) without concomitant HIV infection. **Results.** An average diameter of the endometrial glands (proliferative type) was 8% smaller in HIV infection than in the comparison group. The minimum diameter of the endometrial glands (proliferative type) decreased by 1.73 %, the maximum was 5.24 % less in the HIV-infected group than in the comparison group. The wall thickness was reduced by 0.5 % in HIV infection. The relative volume of the epithelium decreased by 2.4 % (proliferative type). There were also significant changes in the structure of the glands and endometrium in secretory phase, as in the proliferative type. Thus, the average diameter of the glands decreased by 5%, the minimum volume of the glands by 5.01 %, the maximum by 11.2 %, the wall thickness by 1.5 %, the relative volume of the epithelium by 9.5 %, less in the group HIV-infected than in the comparison group. The thickness of the epithelium increased by 4.5 % in the HIV-infected group compared with the comparison group. **Conclusion.** The study evaluated features of endometrial restructuring in the presence of concomitant HIV infection in women.

Keywords: uterus, endometrium, HIV, glands.

Introduction

Many different studies have investigated the immunological and hormonal aspects of hyperplastic diseases of the uterus (HDU) [1–3]. Many authors have shown a violation of the supervisory functions of the immune system, which regulate the processes of cell proliferation [4–7]. These changes can be both hereditary and acquired during the expression or mutations of the corresponding genes during life [8]. The results of other studies have suggested that there is a genetic predisposition to the development of HDU, and genetic determinants are the main risk factors triggering pathogenic mechanisms of proliferative processes in the uterus [9, 10].

HIV (AIDS) today occupies a leading position among the causes of death of women of reproductive age all over the world. The

disproportionate impact of HIV on young women may be due not only to social inequality, but also to biological patterns of heterosexual transmission of the virus [11–13]. HIV infection is a disease that affects all organs and systems of a patient. Approximately 60–90 % of HIV transmission occurs through sexual contact.

Globally, women make up more than half of the population living with HIV. The majority of women become infected during sexual intercourse, when the mucous membrane is most vulnerable to HIV infection [14, 15]. It has a special effect on the human reproductive system. Being an entrance gate, this pathological condition starts a cascade of pathological reactions, causing various changes in all organs of the reproductive system.

The first line of defense against HIV infection in the female genital tract is the mucous membrane of the epithelial barrier [14]. Consequently, the expected maximum pronounced changes can occur precisely in the endometrium.

2. Purpose, subjects and methods:

2.1. The purpose of our study was to evaluate the features of endometrial restructuring when infected with the human immunodeficiency virus.

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2.2. Subjects & Methods

The study involved the sectional material taken from 60 women of reproductive age from 20 to 40 years. All the subjects were divided into two groups. Group 1 (30 women) consisted of women who were diagnosed with HIV infection.

The control group comprised women (30) who died from diseases not associated with reproductive disorders without concomitant HIV infection (deaths as a result of traffic and other accidents).

The material was fixed in 10 % neutral buffered formalin, after which the selected samples were embedded in paraffin. At the next stage, sections with a thickness of 5×10^{-6} m were made from the prepared paraffin blocks. Subsequently, staining with hematoxylin and eosin was performed. Microscopic examination was carried out on an Olympus BX41 microscope, followed by morphometric examination using the Olympus DP-soft 3.12 software.

The following indicators were determined: average diameter of the endometrial glands (proliferative type), minimum diameter of the endometrial glands (proliferative type), maximum diameter of the endometrial glands (proliferative type), wall thickness (proliferative type), relative volume of the epithelium (proliferative type), average diameter of the glands (secretory type), minimum diameter of the glands (secretory type), maximum diameter of the glands (secretory type), relative volume of the epithelium (secretory type), thickness of the epithelium.

Statistical processing was performed using the methods of variation statistics. Correspondence

of the distribution to normal was determined by Shapiro-Wilk's test, which showed that the samples were close to the normal distribution. Statistical indicators are presented in the format $M \pm \sigma$, where M is the arithmetic mean, σ is the standard deviation. Student's t-test was used. Correlation analysis was carried out using Spearman's rank correlation coefficient. The statistical difference between the studied parameters was considered significant at p less than 0.05.

The procedure was done strictly in compliance with the Helsinki Declaration after approval from the Regional Ethical Review Board at Odessa National Medical University, protocol No. 3 dated 17th October 2011.

Conflict of interests

The authors of the article declare no conflict of interest.

3. Results & discussion

Results of performed morphometric study are shown in the *table*.

Thus, the study showed that the average diameter of the endometrial glands (proliferative type) was 8 % smaller in HIV infection than in the comparison group. The minimum diameter of the endometrial glands (proliferative type) decreased by 1.73 %, the maximum was 5.24 % less in the HIV-infected group than in the comparison group. The wall thickness was reduced by only 0.5 % in HIV infection.

The relative volume of the epithelium decreased by 2.4 % (proliferative type) in the HIV-infected group compared with the comparison group.

Indicators of the structure of endometrium in HIV infection and in the comparison group

| Parameter under study | Comparison group | HIV-infected women |
|---|-------------------|--------------------|
| The average diameter of the endometrial glands (proliferative type), $\times 10^{-6}$ m | 51.71 \pm 2.90 | 47.62 \pm 2.29 |
| The minimum diameter of the endometrial glands (proliferative type), $\times 10^{-6}$ m | 32.47 \pm 1.83 | 31.88 \pm 1.92 |
| The maximum diameter of the endometrial glands (proliferative type), $\times 10^{-6}$ m | 72.14 \pm 2.21 | 68.36 \pm 3.15 |
| Wall thickness (proliferative type), $\times 10^{-6}$ m | 15.18 \pm 1.60 | 15.10 \pm 1.04 |
| The relative volume of the epithelium (proliferative type), % | 54.43 \pm 1.79 | 53.12 \pm 2.41 |
| The average diameter of the glands (secretory type), $\times 10^{-6}$ m | 101.55 \pm 3.12 | 96.34 \pm 4.26 |
| Minimum diameter of glands (secretory type), $\times 10^{-6}$ m | 33.86 \pm 1.17 | 32.14 \pm 1.67 |
| Maximum diameter of glands (secretory type), $\times 10^{-6}$ m | 127.98 \pm 2.10 | 113.64 \pm 3.51 |
| Wall thickness (secretory type), $\times 10^{-6}$ m | 13.02 \pm 1.36 | 12.82 \pm 1.26 |
| The relative volume of the epithelium (secretory type), % | 61.24 \pm 1.11 | 55.43 \pm 1.70 |
| Epithelial thickness, $\times 10^{-6}$ m | 49.14 \pm 1.44 | 51.33 \pm 1.23 |

At the next stage the indicated indicators (secretory type) were investigated.

There were also significant changes in the structure of the glands and endometrium, as in the proliferative type. Thus, the average diameter of the glands decreased by 5 %, the minimum volume of the glands by 5.01 %, the maximum by 11.2 %, the wall thickness by 1.5 %, the relative volume of the epithelium by 9.5 %, less in the group HIV-infected than in the comparison group.

The thickness of the epithelium increased by 4.5 % in the HIV-infected group compared with the comparison group. Our study identified the changes in the endometrium due to the presence of concomitant HIV infection in women. Based on the data obtained, it can be assumed that concomitant HIV infection stimulates the development of hyperplastic changes in the endometrium.

There are reports in the literature on the "inflammatory" origin of HDU [16–18]. It is known that in the presence of long-term [19, 20], often exacerbated inflammatory processes of the genital organs, the risk of endometrial cancer increases 20 times, and against a background of HDU – 15 times [21–22]. Long-term persistent infection of the genital organs leads to a change in the receptors of estradiol and progesterone in the tissue of the endo- and myometrium.

Nevertheless, it is probably fair to consider the fact that in the development of hyperplastic processes, the main role is traditionally assigned to an increase in the concentration of estrogens [23].

Changes of the HER (human epidermal growth factor receptor) expression should be considered the most frequent problem of the state of the endometrium and as a consequence of the actual problem in the female population and oncological alertness due to its high prevalence [24, 25]. Today HDU is officially recognized to be one of the most important and potentially health-damaging medical problems that challenge doctors around the world. The steady increase in the number of patients with HDU, unclear etiology, variable clinical manifestations and a high relapse rate and risk of malignancy, as well as low treatment efficacy have led to a significant increase in scientific interest in this problem in recent years [26].

In Ukraine, the HIV-infected population is growing every year with the overwhelming majority (77.6% of people of young, reproductive and working age, i.e. 15–49 years), the number of HIV-infected pregnant women is increasing [27], which is explained by the high proportion of women of reproductive age among the patients with HIV infection.

Currently, HDU is defined as a pathological process affecting the epithelial and stromal components of the endometrium and manifested by an increase in the total number of glands, as well as various changes in the phenotypic characteristics of cells [28]. Endometrioid, intraepithelial neoplasia is currently considered as a variant of atypical hyperplasia, a feature of which is the formation of foci more than 2 mm in diameter with a predominance of the parenchyma over the stroma, with pronounced atypia of the crowded gland cells and with loss of PTEN (phosphatase and tensin homolog) expression [29].

Currently, interesting and at the same time contradictory statistical data are given in relation to the combined pathological processes of the endo- and myometrium, which, to some extent, can be explained by a fairly frequent asymptomatic course [30]. HDU occupies 15–40 % in the structure of all gynecological diseases, and up to 80 %, when combined with adenomyosis. Contradictory data in the literature are also given in relation to the combination of HDU and uterine leiomyoma, the frequency of which ranges from 13 to 80 %. In the asymptomatic course of uterine leiomyoma in postmenopausal women, every sixth patient has HDU, at the same time, when uterine bleeding appears, concomitant development of HDU is determined in every second patient [30].

It should be noted that the least reliably ($p < 0.05$) variable indicator is the thickness of the endometrial wall (proliferative type), which significantly is decreased by only 8 mm on average in the presence of HIV infection.

The most pronounced significant changes affected the glands, especially the secretory type. Thus, at the same time the maximum volume of the glands changed at $14 \times 10^6 \text{ m}$. Subsequently, these findings can be confirmed by other additional studies.

Consequently, our study gives grounds to assume the possible development of hyperplastic processes in the endometrium in HIV-infected patients, which cannot but affect the peculiarities of the presentation, diagnosis and treatment of inflammatory and non-inflammatory processes of the reproductive system.

Conclusions

The study evaluated the features of endometrial restructuring in the presence of concomitant HIV infection in women. These changes are manifested by hyperplastic changes in the mucous membrane. The most pronounced changes were revealed in the endometrial glands (secretory type).

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