DIAGNOSTIC AND TREATMENT METHODS

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LIQUID CYTOLOGY IN COMPARISON WITH TRADITIONAL IN THE DIAGNOSIS OF CERVICAL DISEASES

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This paper presents the results of a cytological study of patients with pathology of the cervix uteri (CU) based on traditional cytology (TC) and on liquid-based cytology (LBC).

It was found that the combined use of liquid-based cytology and conventional cytology can improve the effectiveness of CU pathology diagnostics. It is recommended to complete the cytological study with testing for human papillomavirus (HPV). The use of these screening methods (cytological and HPV tests) contribute to improving the early diagnosis, monitoring, and prognosis of CU cancer.

Keywords: cervical cancer, diagnostics, liquid-based cytology, screening.

The problem of cervix uteri (CU) diseases is one of the most urgent in modern gynecology and has great importance for preventing the occurrence and development of malignant neoplasms. CU pathology is the background for the development of precancerous changes and cervical cancer (CC) among gynecological disorders that occur in women of reproductive age [7]. The time of active, rapid development and use of new technologies in medicine dictates the need and shows the importance of changes in traditionally used methods. The question of improving and optimizing the quality of cytological diagnostics is the most prevalent issue. Liquid-based cytology (LBC) plays an important role in solving this issue. LBC is introduced in order to overcome the disadvantages of traditional methods and thereby to increase the effectiveness of cytological diagnostics [1]. The main feature of the LBC is the production of thin-layer (monolayer) preparations (in which cells are located almost in one layer) from a liquid cell suspension using special cytospins. The difference between this method and the traditional one is that the substance is not applied directly to the glass, but it is placed in a bottle with a stabilizing solution. Rapid conservation of the substance allows preventing the bacterial contamination of the sample, and the damage of the cells due to their drying that preserves the sample in optimal conditions for further transportation to the laboratory and research. The stabilizing solution ensures the preservation of morphological, immunocytochemical and genetic properties of cells [4]. The sensitivity of the cytological method in using LBC increases to 85% [5]. A feature of the LBC is also that up to 6 "serial" smears can be obtained from a single sample of the substance, that is, identical in cell composition, which makes it possible to use additional research methods, for example, HPV testing, immunocytochemical determination of cancer markers [6].The LBC with a high specificity should be supplemented with molecular diagnostic methods. Currently, it is considered proven that the main etiological factor of CU cancer is papillomavirus infection [2, 3, 8]. Two major meta-analyses of data from European and American studies have found that the human papillomavirus (HPV) test is more sensitive than cytological screening [11,15]. The combination of the HPV test and the cytological method has a higher predictive value for detecting CIN (cervical intraepithelial neoplasia) compared to a single HPV test [9, 10, 13] which makes it possible to detect precancerous changes in CU early and, consequently, reduces the risk of developing CC [12,14].

Purpose of research: to study the frequency of background and precancerous pathology of CU by conventional cytology and LBC, and compare their results. Evaluate the effectiveness of TC and LBC, as well as establish the HPV genotype in the examined women.

Materials and methods. The study was conducted in the clinical laboratory of pathomorphology, histology, and cytology on the basis of North-Eastern Federal University named after M.K.Ammosov, Federal State Autonomous Educational Institution of Higher Education. The material was taken from CU and cervical canal scraping from the patients (100 people aged 22-60) after examination and extended colposcopy in the OOO "Malex" clinic (Yakutsk, Russia). The sample was obtained from every patient was conducted by traditional cytology and liquid-based cytology on the automated system CellPrep Plus (Korea), as an independent highly informative method that contributes improvement and standardization of cytological examination of all stages. The Romanovskiy - Gimza stain method was used. The presence of endocervical, flat, and metaplastic epithelium cells makes the material adequate for the study. It is very important to take into account that such material should be obtained from the transformation zone – the area-where the tumor most often occurs. If the material is represented by a very small number of cells, a large number of blood elements, mucus, and the presence of artifacts, which makes impossible to properly assess the cytological picture, it is considered inadequate.

Cytological decision was made in accordance with the clinicopathologic classification of J. V. Bokhman (1976), and with the commonly accepted

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criteria for assessing the state of the epithelium by Bethesda System (2015) [16]. It is based on the introduction of the term SIL (Squamous Interaepithelial Lesion) - squamous intraepithelial lesion. The main categories of the Bethesda classification: NILM- intraepithelial lesions and malignant processes are absent. LSIL- Low Grade Squamous Intraepithelial Lesions. (Mild changes in squamous epithelial cells corresponding to a low risk of cancer), the group covers changes typical of HPV infection and mild dysplasia CINI. HSIL-High Grade Squamous Intraepithelial Lesions (marked changes in squamous epithelial cells corresponding to a high risk of cancer), the group involves moderate and severe dysplasia - CIN-II, CINIII and CIS. The Bethesda classification separately identifies the following categories: • "atypical squamous cells of undetermined significant"- ASC-US-cell changes that are more significant than reactive, but quantitatively or qualitatively insufficient to establish a diagnosis of CIN. • Non-exclusive HSIL (ASC-H) — a category that takes middle position between ASC-US and HSIL.

Detection, typing (co-testing) of human papilloma virus (HPV) (6, 11, 44, 16, 18, 26, 31, 33, 35, 39, 45, 51, 52, 53, 56, 58, 59, 66, 68, 73, 82 serotypes) by PCR was performed on the basis of microbiological laboratory of the Medical Institute clinic based on NEFU.

Results and discussion. The comparative analysis of cytological samples of 100 women was conducted to evaluate the effectiveness of the liquid-based cytology and traditional cytological screening in the early diagnosis of CU cancer. The patients were aged from 23 to 60 years. The average age of all women surveyed was 38.9+9.2 years.. The percentage of detected background and precancerous pathology was estimated (Fig. 1).

By TC method the absence of intracellular damage (no findings cytogram) was detected in 16 samples (16%). By LBC method (NILM - intraepithelial changes and malignant processes are absent) it was detected in 66 (66% of the entire group) samples, and among all of the samples 26 (26%) have no pathology and 40 (40%) have reactive (background) changes (squamous metaplasia, inflammation, moderate hyperplasia). Generally, according to these data cervical pathologies during routine cytology were detected in 84% of cases, and during liquid-based cytology – in 74 %. Reactive (background) changes in the TC are 53% of cases, while the LBC are 40% of cases. Cervical dysplasia of varying severity in TC was detected in 31 cases, which was 31% of the total number of samples. Among it, 23 women (74.1% of the total number of samples with detected cervical dysplasia of various severity) had I grade dysplasia (mild), 7 women (22.5%) had II grade dysplasia (moderate) and III grade (severe) dysplasia was diagnosed in 1 woman, which was 3.2% of all cervical dysplasia in the study group. Among it, 23 women (74.1% of the total number of samples with detected cervical dysplasia of various severity) had I grade dysplasia (mild), 7 women (22.5%) had II grade dysplasia (moderate) and III grade (severe) dysplasia was found in 1 woman, which was 3.2% of all cervical dysplasia in the study group. LSIL was detected in 27 cases (79.4%), of which CINI – 20 (58.8%) cases, CINI with coilocytes – 7 (20.6%) cases. HSIL was found in 6 cases and accounted for 17.6% of the total number of dysplasias in the study group In 1 (2.9%) case was diagnosed atypia of unknown origin (ASCUS) (Fig.2).

As seen, even a small difference in the cytological diagnosis in traditional smears compared to smears obtained by LBC indicates that each of these methods showed effectiveness depending on the type of CU pathology.

47 (47%) women were tested for HPV, among them, 19(40%) women were confirmed to have HPV. The presence of oncogenic types of high-risk HPV was detected in 17 women (89.4%), of which 26.3% (5 women) were diagnosed with LSIL, 15.8% (3 women) with HSIL, 5.2% (1 woman) with ASCUS, and 42.1% (8 women) with NILM. HPV type 16 was found in 7 patients (36.8%), the next most common type was HPV type 51 – 4 women (21%). The frequency of other genotypes distribution (39, 68, 31, 52, 73, 58, 18) varies from 4.2-2.1%. 3 negative cases of LSIL and 2 negative cases in HSIL which were detected in the diagnosis can indicate the beginning of viral damage or other causes of dysplasia.

In conclusion, based on our results, we would like to note that each stage of morphological research has not only certain opportunities but also limitations. This requires the use of complex diagnostic methods. We recommend using the method of liquid-based cytology with traditional cytology obtained with the analysis of HPV to compare the results. This will significantly increase the value of diagnostic measures, including cytological studies, and will determine

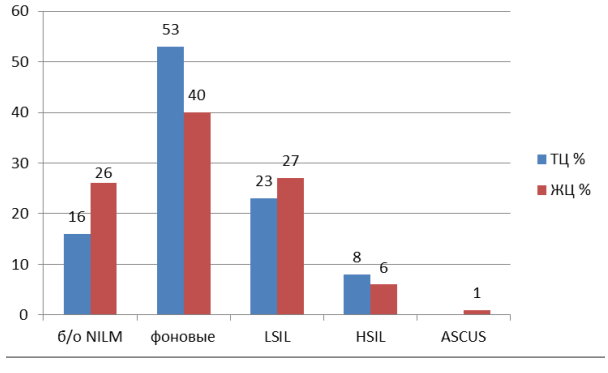

Fig.1. Comparative characteristics of the diagnosis of cervix uteri diseases by traditional and liquid-based cytology

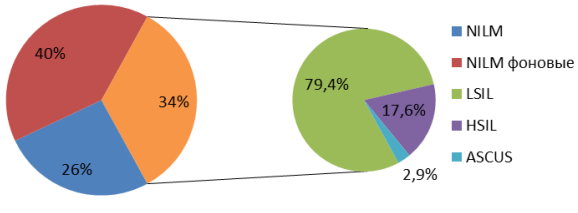

Fig.2. Structure of detected precancerous lesions of the cervix uteri by liquid-based cytology.

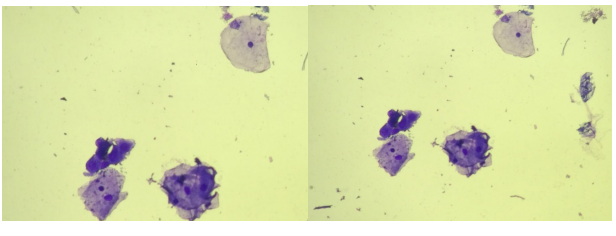

Fig.3. HSIL (CIN III): severe dysplasia. The group of small cells with large hyperchromic nuclei on the background of flat epithelium surface cells (Romanovsky-Gimza staining method), X400

the most effective therapy for detected cervical pathology.

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