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Research Article

THE ROLE OF CIN-DIAG RAPID TEST IN SCREENING FOR CERVICAL EPITHELIUM PATHOLOGY

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ABSTRACT

This article is aimed at identifying the pathology of the cervical epithelium in the early diagnosis of cervical cancer using an express test. During the study 10716 women aged 25-65 years were examined (mean age 43.28±3.82 years). To increase the specificity and sensitivity of screening, local express tests were used, in particular, a modified CIN-Diag test. As a result, the use of the proposed algorithm for screening CC made it possible to detect metaplasia of the CC epithelium in the early stages (precancer) and reduce the need for colposcopy by 4.65 times.

KEYWORDS

Cervical cancer, screening, CIN-DIAG test.

INTRODUCTION

Cervical cancer (CC) is a pathology for which the possibility of effective prevention has been proven. Preventive topical treatment of preinvasive cervical lesions (so-called high-grade cervical intraepithelial neoplasia, HG CIN) is an established strategy that has proven its clinical relevance [3,6]. Progression from human papillomavirus infection (HPVI) to CC can take 15–20 years [13]. Such a long precancerous phase provides opportunities for early diagnosis and timely therapy, and also makes it possible to express the imperative about the advisability of population screening. Despite the introduction of population screening, invasive cervical cancer remains one of the most common malignant diseases - the fourth most common among malignant neoplasms in women, according to world statistics [14].In 2018, cervical cancer was diagnosed in 570,000 women and caused death in 311,000. At the same time, 84% of cases and 88% of deaths from cervical cancer occur in developing countries [4].

To increase the specificity and sensitivity of screening, it is possible to use local express tests, in particular, a modified CIN-Diag test (Anhui Deepblue Medical Technology Co., LTD., China). The test, being local, is not cytological. It is based on determining the concentration of active oxygen radicals in epithelial cells. Active oxygen ions stain the colorless dye contained in the swab in a dark color. The color intensity correlates with the severity of the lesion. In the affected cells, a large amount of active oxygen ions accumulates, which is accompanied by an increase in the expression of folic acid receptors on the cell membrane. Folic acid contained on the surface of the test swab penetrates into the cytoplasm of the cell along with the dye and the buffer solution of glacial acetic acid. According to the manufacturer, the sensitivity of the test for the detection of HSIL is 98%, the specificity is 95%. The test allows you to detect inflammatory changes (light green or green indicator, CIN 1 (dark green), CIN 2 (blue green or emerald), CIN 3 (blue), cervical cancer (dark gray or black).

This technology is based on the detection of changes in cell biochemistry and is not pathogenetically associated with oncogenesis, so its place in the cervical cancer screening program remains uncertain.However, the ability to detect lesions of the CMM epithelium in the early stages and calibrate the degree of damage sets the direction for trail studies [3,7].

MATERIALS AND METHODS

In the course of this study during 2020-2021 10,716 women aged 25-65 years (mean age - 43.28 ± 3.82 years) were examined, who did not present complaints, indicating gynecological pathology and did not have a history of erosive lesions of the cervix. All examined women underwent a PCR test to detect HPV DTCs in the cells of the cervical mucosa. Cells were obtained by taking with a special brush. As a result, groups of HPV-positive (HPV+) and HPV-negative (HPV-) women were identified. Also, all the subjects underwent an examination of the cervix in gynecological mirrors to visually determine the state of the mucosal epithelium and cytological

examination by the Papanicolaou method. During the examination, all examined women were divided into a group with unchanged cervical mucosa (PAP-) and a group with erosive changes in the cervical mucosa.

All women of these groups underwent a rapid CIN-DIAG test, in case of detection of LSIL, electrocoagulation of the affected area of the cervical mucosa was performed, HSIL - electroconization, carcinomas - hysterectomy.

During the study, the number of women with indications for various treatment options for cervical pathology was recorded, depending on the algorithm of diagnostic tactics.

At the first stage today is a cytological examination of the cervix, thanks to which malignant processes can be detected in the early stages. According to the author E.G. Novikova (2000), in her study, tumor changes on the cervix were detected in 94.5% of cases. The cytological sampling is taken from three sites, from the vagina, at the site of the transition of the stratified squamous epithelium to the glandular one, from the cervical canal.

A disposable instrument is used to take the material, which includes a spatula, brush and glass slides. A fence is taken after the menstrual cycle, after careful processing and cleaning of cervical mucus, by lightly scraping with an Eyre spatula. The brush is also carefully inserted and a swab is taken from the canal in a clockwise circular motion.

The CIN-DIAG test, a modified express test for the detection of metaplastic epithelial cells of the cervical mucosa, was performed during a gynecological examination. The patient was located on the gynecological chair. The test kit (Anhui Deep blue Medical Technology Co., LTD., China) is a swab immersed in a special solution of folic acid, dye and glacial acetic acid. The method is based on changing the color of the indicator upon contact with active oxygen ions that accumulate in tumor cells. The number of active oxygen ions and, accordingly, the color intensity correlates with the severity of metaplasia.The color change is assessed after 30 seconds: if the tampon does not change color, this indicates the absence of pathologies on the epithelial tissues; light green or green color - inflammatory changes; dark green color - CIN1; blue-green, dark emerald colors - CIN2; blue color - CIN3; dark gray and black colors - CIN3 or carcinoma.

RESULTS AND DISCUSSION

During the study, all women with a positive HPV test and a positive cytology test underwent rapid CIN-DIAG testing to detect epithelial metaplasia. The test result implies 5 options: normal (no staining), inflammatory changes - ACSUS equivalent (light green or green), CIN-1 - LSIL equivalent (blue-green or emerald color), CIN-2 - HSIL equivalent (blue color).), CIN-3 –cancer (dark blue and black).

During the test, more than half of the women (54%) showed a normal functional state of epitheliocytes, 25% - inflammatory changes in

the epithelium (light green staining of the swab), the rest (21%) - manifestations of epithelial metaplasia (Fig. 1).

During the study, the distribution of the occurrence of various staining variants in the CIN-

DIAG test by age groups was analyzed (Fig. 2). A visual image shows that in women over 50 years of age, the frequency of normal test results decreases, which is probably due to the climacteric syndrome with corresponding dishormonal conditions.
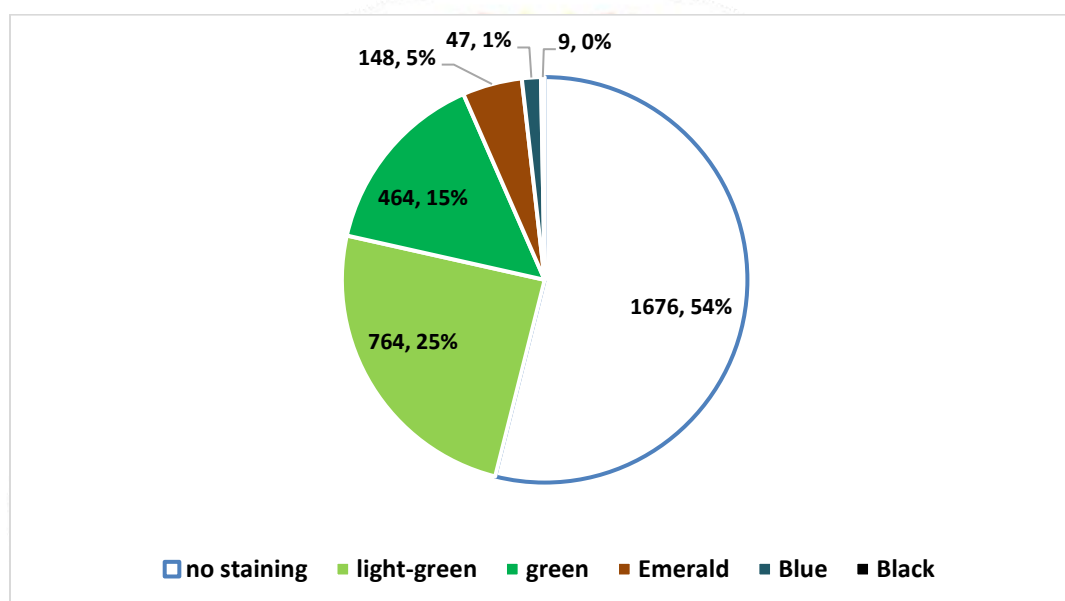

Fig. 1 Frequency of different staining patterns in the CIN-DIAG test in women with indications for colposcopy

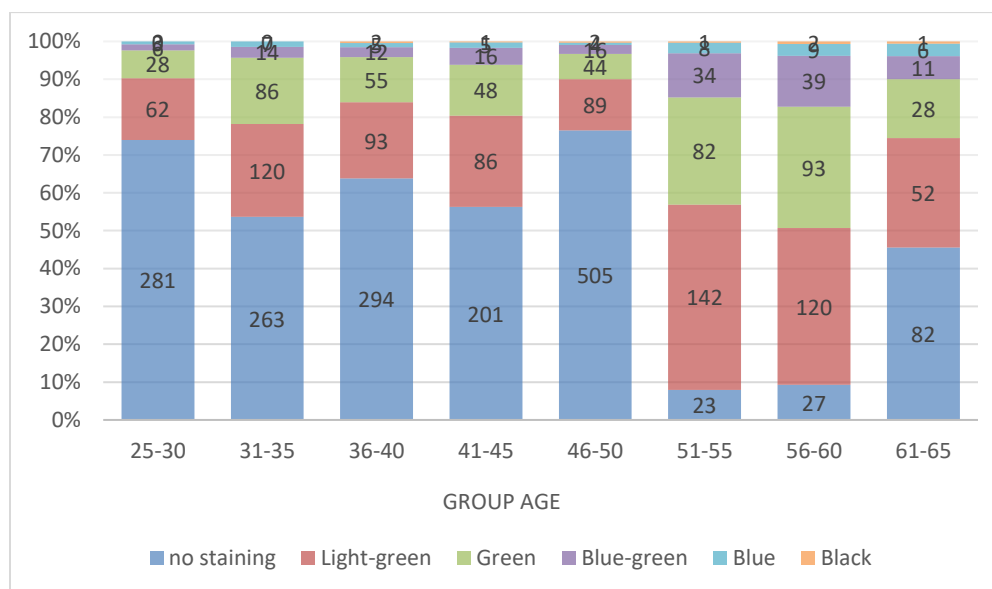Crossref doi Google Scholar WorldCat MENDELEY

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Fig. 2 Frequency of different CIN-DIAG swab staining patterns in women with indications for colposcopy by age

An assessment of the distribution of various results by age decades found that with increasing age of the examined women, the frequency of normal results decreases and the frequency of pathological - inflammatory changes and epithelial metaplasia increases ($\chi2=42.70$, $p<0.001$, Table 1).

Table 1

The frequency of detection of a normal result, inflammatory and metaplastic changes in the cervix according to the results of the CIN-DIAG test in women with indications for colposcopy by age decades.

Age Group	Regular	Inflammatory changes in the epithelium	Epithelia metaplasia
25-35	544	182	144
36-45	495	179	144
46-55	528	231	191
56-65	109	172	189
Total	1676	764	668

χ^2	42,70, p<0,001

The age distribution of various results of the CIN-DIAG test with signs of metaplasia found that with increasing age, the proportion of blue and black staining of the swab increases, indicating CIN-3 metaplasia and carcinoma (Table 2).

Table 2

The frequency of detection of various staining variants, indicating metaplastic changes in the cervix, according to the results of the CIN-DIAG test in women with indications for colposcopy by age decades.

Age Group	Green	Blue-green	Blue	Black
25-35	114	20	10	0
36-45	103	28	10	3
46-55	126	50	12	3
56-65	121	50	15	3
Total	464	148	47	9
$\chi^2=14{,}12$, p<0,01				

The study examined the diagnostic significance of the CIN-DIAG test in terms of detecting the pathology of the cervical epithelium in women with indications for colposcopy (Table 3).

Table 3

Sensitivity, specificity and diagnostic significance of the CIN-DIAG test in terms of detecting inflammatory and metaplastic conditions of the cervical epithelium in women with indications for colposcopy

Types of test response	critical +	critical -	Sensitivity	Specificity	Diagnostic significance
All pathological changes	1381 51	4 1672	99,71	97,04	98,23
Green, blue-green, blue, black	661 7	41 2399	94,16	99,71	98,46

Blue-green, blue	$\dfrac{201}{3}$	$\dfrac{3}{2901}$	98,53	99,90	99,81
Black color	$\dfrac{7}{2}$	$\dfrac{0}{2951}$	100,00	99,93	95,17

Note: (as a verification of the diagnosis, the results of colposcopy were used, the calculation method is given in Table 3.3, in the numerator - pathology +, in the denominator - pathology -)

It has been established that the rapid test is highly sensitive and specific, which allows it to be used to narrow indications for colposcopy. That is, to include in the screening scheme for women 25-65 years old with a positive HPV test and a cytological examination of the CIN-DIAG test to exclude women without pathological changes in the cervical epithelium and with inflammatory lesions of the epithelium. Thus, it is possible to limit the need for colposcopy in women with evidence of cervical epithelial metaplasia (all stages of metaplasia). Such a modification of the screening algorithm will reduce the financial, labor and time costs of colposcopy, as well as solve the problem of insufficient availability of the method.

The present study showed that the CIN-DIAG rapid test is a sensitive and specific method for detecting the pathology of the cervical epithelium, accessible, technically simple, and does not require special equipment and personnel. The test can be recommended for inclusion in the screening algorithm for women aged 25-65.

CONCLUSION

The CIN-DIAG rapid test has high sensitivity, specificity and diagnostic value in terms of detecting high-grade epithelial metaplasia and cervical cancer (98.53% and 100%, 99.90% and 99.93% and 99.81 and 95.17%, respectively). The use of the proposed algorithm for screening cervical cancer makes it possible to detect metaplasia of the epithelium of the cervical cancer at an early stage (precancer) and reduce the need for colposcopy by 4.65 times (up to 6.33% of the entire target population).

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