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CERVICAL CANCER ELIMINATION PROGRAM

Cervical cancer is one of the most common types of malignant neoplasms in women. According to Globocan, in 2018, 570000 new cases of cervical cancer and 311 thousand deaths from this pathology were registered. More than 85 % of cases of cervical cancer are registered in developing countries, where a third of all women are detected in the advanced stage of the disease.

The association of cervical cancer with the chronic persistence of the human papillomavirus is unquestionable. To date, more than 200 types of HPV (human papillomavirus) are known, 12 of which are dangerous to humans and can cause the development of cervical cancer

The discovery of the link between HPV infection and breast cancer has changed the approach to cervical cancer screening in many ways. The fact that cervical cancer is primarily associated with an infectious agent has led to the development of new, more sensitive HPV-based screening tests for secondary prevention of cervical cancer and three HPV vaccines that are used for primary prevention.

The only method that prevents the development of cervical cancer is HPV vaccination and cervical cancer screening. To date, there are 3 recombinant HPV vaccines: a bivalent HPV vaccine of type 16 and 18, a quadrivalent HPV vaccine of types 16, 18, 6 and 11, and a nine-valent vaccine of types 6,11,16,18,21,33. 45,52 and 58 . HPV vaccination has entered the immunization calendar in more than 100 countries where the experience of using the vaccine is more than 10 years.

Large international randomized clinical trials have shown that HPV vaccines are safe and highly effective against persistent infection and precancerous lesions of the cervix in women (vaccine efficacy $\geq 93\%$). These vaccines target high-risk HPV types, which are responsible for the development of about 90% of cervical cancer. Countries that achieved high vaccination coverage saw a 73-85% decrease in HPV prevalence and a 41-57% decrease in high-grade lesions among young women less than 10 years after the introduction of HPV vaccination

Organized, well-designed primary and secondary prevention strategies can have a positive impact on the incidence and mortality rates caused by cervical cancer.

Key words: cervical cancer, HPV, vaccination, screening.

Introduction

Cervical cancer is one of the most common types of malignant neoplasms in women. According to Globocan, in 2018 were registered 570,000 new cases of cervical cancer and 311,000 deaths from this pathology. In more than 85% of cases, cervical cancer is registered in developing countries, where one third of all women are diagnosed in an advanced stage of the disease.

With the invention of the Pap test in the 1940s by George N. Papanicolaou and H.F. Trout, cervical smear cytology has become a reliable and uncomplicated method for screening for cervical cancer [1]. This process entails the detachment of cervical cells, which are then fixed, viewed under a microscope and subsequently morphologically interpreted. The pap test allows assessing changes in nuclear chromatin, necrosis, determining the degree of cellular degeneration and distinguishing the maturity of squamous epithelial cells [2].

Screening for cervical cancer using a cytological smear is widely accepted as a public health policy in many countries. The International Agency for Research on Cancer (IARC) has determined that the incidence of cervical cancer can be reduced by at least 80% by introducing Pap-based cervical cancer screening programs every three to five years for women aged 35-64 [3,4,5]. Nevertheless, there are disadvantages of cytological examination. The main disadvantages of the PAP test are that the results depend on the quality of the sample collected during the study, the identification of morphological changes in the cells and the need to retest if the results are unsatisfactory or questionable, which has serious medical, economic and legal consequences. [6]. Despite constant efforts to improve the results of cytological examination of the cervix, its sensitivity is not optimal, and the method still gives a large number of borderline results.

The association of cervical cancer with chronic persistence of human papillomavirus is undeniable. To date, more than 200 types of HPV (human papillomavirus) are known, 12 of which are dangerous to humans and can cause the development of cervical cancer [7,8].

It has been proven that (HPV (16/18/31/35/39/45/51/52/56/58/66/68) are responsible for the development of more than 97% of cases of cervical cancer, while low-risk types (HPV6) / 11/40/42/43/44/54/61/72) are associated with anogenital and laryngeal papillomas. The aforementioned HPV16 and HPV18 are the most common types of HPV and are responsible for 70% of cervical cancers worldwide (~ 50% HPV16, ~ 20% HPV18) [9,10].

It is estimated that approximately 80% of sexually active women will contact the infection during their lifetime, and in most cases (> 90%) it will be a temporary asymptomatic infection that is cleared by the immune system within the first year of infection [11,12]. Only chronic persistence of HPV infection can lead to the development of low or high grade cervical intraepithelial neoplasia, which can ultimately progress to cervical cancer [12,13].

Conclusion

The discovery of the link between HPV infection and cervical cancer has changed the approach to cervical cancer screening in many ways. The fact that cervical cancer is primarily associated with an

infectious agent has led to the development of new, more sensitive HPV-based screening tests for the secondary prevention of cervical cancer and three HPV vaccines that are used for primary prevention. Unlike screening methods based on cytology, HPV testing does not rely on morphological interpretation and is based on the detection of HPV DNA and RNA, or other viral markers. Over the past two decades, HPV testing has been recognized as an effective screening tool in developed countries [13]. The results of the ATHENA multicenter study of 47,000 women showed that 10% of women positive for HPV types 16 and 18 had severe cervical lesions (HSIL) and were not detected during cytological examination. Data on false negative Papsmears indicate that the failure rate of the PAP test in developed countries is about 28-41%. The low sensitivity of the PAP test, as well as errors in the analysis and interpretation, necessitate re-screening and increases the interest in the development of more accurate and reliable screening tests. Given the problems of cytological screening, researchers began to look for solutions through the introduction of liquid cytology and HPV testing.

A study in Mexico comparing two screening methods found that a combination of a PAP test and an HPV test was more cost effective than using a single PAP test [13]. In 2007, IARC recommended HPV testing as the primary screening.

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