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Molecular Methods Associated to Cervical Intraepithelial Neoplasia Diagnosis for Viral DNA

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ABSTRACT *This study emphasizes the importance of early cervical cancer diagnosis through the main molecular techniques used in HPV-DNA molecular detection.*

KEYWORDS : cervical cancer, molecular techniques, HPV.

iNTRODUCTION

Cervical cancer is a malignant neoplasia in the cell layer of uterine cervix. It occurs in a process that involves early neoplastic lesions classified in cervical intraepithelial neoplasia for carcinoma invader.

It´s noticed that advanced molecular biology techniques have allowed knowledge about biomolecular basis involved in the lesions source. Therefore, today it´s known that high risk-HPV- especially common types 16 and 18 - is the main risk factor for cervical intraepithelial neoplasia and its progression to cancer.

High risk-HPV types are presented in 99,7% cervical cancer cases. Population tracking is performed every year based on cervical intraepithelial neoplasias through usual Pap test. This method hasn´t presented ideal sensibility index for lesions detection, with a 50% and 60% variation.

Even without morphological changes induced by virus, molecular tests are capable to detect HPV-DNA, to classify viral types in high and low risk, and predict lesions development risk, as well as its progression to invader cancer. In this context, lots of studies indicate that the detection of high-risk types of HPV-DNA predict early lesion in patients presenting negative or unreliable cytology results.

In this way, it can be supposed that molecular techniques, Polymerase Chain Reaction (PCR) and Hybrid Capture 2 (HC2), are fundamental methods for tracking cervical cancer with a Pap Test.

LITERATURE REVIEW

This paper was developed after approval by *Centro Universitário Hermínio Ometto – UNIARARAS´* Ethical committee in Research and Scientific Merit, under 187/2010 protocol number.

A literature review in books and scientific articles was performed for this study. The bibliographic review of scientific articles was performed by key-words as method, in addition to data banks research, health online library, *Scielo* and in Scholar *Google*.

RESULTS AND DISCUSSION

After review, it was detected that molecular biology advance, in the last decades, was essential in understanding the relation among HPV, intraepithelial neoplasia and its progression to high-risk lesions, CIN II and III.

Through biology molecular techniques it´s possible to verify HPV subdivision in types: oncogenic low-risk and high-risk HPV, establishing them as necessaries co-factors, but not enough, to the development of CIN. In this case, other factors as virus´ oncogenity, persistent infection, high viral cargo and host immune response are necessary for progression.

It´s known that cervical carcinoma is mostly associated to HPV infection. The more high-risk virus, the bigger the progression risk of early lesions, especially when the infection is persistent and highly viral.

The high-risk HPV-DNA identification in 92,9% and 99,7% cervical cancer cases denotes the importance of early diagnosis of the risk to neoplastic lesion development and its progression to invasive carcinoma. Therefore, PCR and hybrid capture II are the main molecular techniques used in HPV-DNA detection and they have been recognized for many authors as tools for decreasing incidence and mortality by cancer.

PCR is the technique based on DNA-HPV *in vitro* enzyme amplification. In this manner, it´s possible to identify specific viral types, diagnose or predict coexistence of cellular changes and HPV infection.

Hybrid capture II is the molecular hybridization procedure of nucleic acids capable to detect presence or absence of oncogenic low and high-risk viral types´ DNA, providing quantitative and qualitative measures of viral types. In addition to high-risk HPV typing, it´s possible to measure viral cargo and to predict the risk level for lesions development and progression.

During review, articles have indicated that women with normal cytology and high viral cargo for high-risk HPV were 116 more probable to develop CIN II and III than those ones who were negative for virus. In this manner, associated use of these tests to cytology contributes significantly to false-negative results women´s treatment, with a low level or cytology inaccurate diagnosis, with persistent infection and high viral cargo for high-risk HPV. So, women with cervical HPV infection present cervical cancer risk.

Molecular tests importance regards to diagnostic sensitivity and specificity increase for this neoplasia, helping in the patient clinical leading. So, these tests are fundamental as support to cytology in investigation and follow-up of positive HPV women with or without changes in cytological result, promoting high-index decreasing of false-negatives and positives of cytology tests.

FINAL CONSIDERATIONS

Although preventive early measures are the basis to cervical cancer cases decreasing, it´s considered that early or predictive diagnosis by molecular techniques is viable and necessary in tracking programs.

It´s also considered that, associated to cytology, it increases diagnostic sensitivity and effectiveness. In view of the five hundred thousand people incidence a year in the whole world, which 80% occur in developing countries where diagnosis is taken in advanced or in metastasis stage, in addition to the fact that in Brazil it is the second cause of death in women with cancer, the expectation is these techniques are established in a tracking population program with the cytology in order to decrease significantly the disease in population.

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