·Gynecologic Oncology·

Perspective of cervical cancer prevention and control in developing countries and areas

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[Abstract] Cervical cancer ranks the second common cancer in women, affecting women severely in developing countries. It is a critical issue to develop simple, rapid, accurate, safe, acceptable, and inexpensive screening tests which can be used in cervical cancer prevention programs in developing countries. Due to the shortage of funding and qualified cytological professionals in most developing countries, WHO has been actively promoting visual inspection with acetic acid/iodine solution (VIA/VILI) as the alternative approach to screening cervical cancer. After the discovery of a link between human papillomavirus (HPV) and cervical cancer, the HPV prophylactic vaccine and CareHPV test have been successfully developed. The cervical cancer will be the first cancer eliminated by the combination of vaccination, screening, early diagnosis and treatment.

Key words: Cervical cancer, human papillomavirus, cancer prevention, developing country

Cervical cancer is the second most common malignancy in women, which affects women's health severely. According to WHO database, there are about 500 000 cases of newly diagnosed cervical cancer and 274 000 cases of cervical cancer-related death in every year, 83% of the cases are from developing countries, accounting for 15% of women's malignancies; while in developed countries, cervical cancer only accounts for 3.6% of women's malignancies.[1] The risk factors, newly diagnosed cases, morbidity and mortality of cervical cancer in developing counties are all on the rise, which brings great anguish to the patients and their families. Cancer-caused reduction of labor force will negatively impact the social development. If prompt strategies are not initiated, the mortality of cervical cancer patients will increase by 25% in the following ten years.[2] How to prevent and control cancers has become a global health issue.

Breakthroughs in research on the causes and screening tests of cervical cancer

The 2008 Nobel prize of physiology and medicine is shared by a German scientist Harald zur Hausen and two French scientists Françoise Barré -Sinoussi and Luc Montagnier. The achievement of Dr. Hausen was the discovery that human papillomavirus (HPV) was the cause of cervical cancer. Cervical cancer has become one of a few cancers whose etiology has been defined. This discovery elucidated the pathogenesis of cervical cancer and natural history of HPV infection, provided theoretical basis of the causal relationship between HPV infection and cervical cancer, thereby, paved the way for the quick diagnosis of cervical cancer and its precancerous lesions by HPV DNA detection and the development of the first cancer vaccine — cervical cancer prophylactic vaccine in human history. Hence, cervical cancer will be the first malignant tumor to be prevented or even eradicated through comprehensive strategies of vaccination, screening, early diagnosis and treatment.[3]

Up to now, more than 200 strains of HPV have been identified, of which, 15 strains can cause cervical intraepithelial neoplasia (CIN) and cancer. CIN usually occurs several years early prior to cervical cancer, which lends rationale that early screening and effective intervention can avoid the occurrence of cervical cancer. Pap smear has been widely used as a cervical cancer screening test for over half a century, and it has made great contribution to the prevention of cervical cancer. With the progress of cytological techniques, liquid-based cytology (LBC) and computer-assisted diagnosis with an automatic slides process system have been approved for the use of cervical cancer screening in the mid 1990s. The technique has not only improved the quality of slides and accelerated slides interpreting, but also promoted the sensitivity and specificity of pathologic identification to 87% and 94%, respectively, reduced the false negative rate greatly. The following HPV DNA detection

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techniques, represented by the second generation hybrid capture (hc2), have improved the sensitivity and specificity of cervical cancer and precancerous lesion detection to 95% and 85% , respectively. This is a breakthrough in the field of cervical cancer screening, greatly improving the quality of cervical cancer screening.[4] In 2005, WHO announced that there were sufficient evidence showing that HPV DNA detection can be used for cervical cancer screening and can decrease the mortality and morbidity of cervical cancer.[5] An Indian prospective study lasted for eight years showed that, as compared with controls, HPV DNA (hc2) screening was able to significantly reduce the mortality and morbidity of advanced cervical cancer (by 50%).[6] Recently, a HPV rapid screening technique (CareHPV) that was sponsored by Bill & Melinda Gates Foundation has been tested in China, which provides a convenient, simple and economical method for the early detection and intervention of cervical cancers in developing regions.[7] The ever progressing techniques for cervical cancer screening, especially the development of HPV rapid screening techniques, open a new era of the cervical cancer prevention and control.

Cervical cancer screening techniques applicable to developing countries

The etiology of cervical cancer is clear, the techniques for early detection and prevention are mature, and multiple diagnosis and treatment methods are available in regions of various economical levels. Thus, the prospect of cervical cancer control is promising. WHO recommended screening, early diagnosis and intervention of cervical cancer in worldwide, and considered that cervical cancer prevention is less dependent on the abundance of resources, but on the government's attitude and effectiveness of health organizations.[2] Currently, the medical insurances of most countries cover cervical cancer screening, which greatly reduces the mortality and morbidity of cervical cancer.

Epidemiological data of developed countries and some developing countries with screening programs show that organized cervical cancer screening program (primarily based on cytology and HPV detection) can significantly reduce the mortality and morbidity, which has been reached a consensus.[2] Internationally, advanced cervical cancer and associated death are regarded as ineffectiveness indices of medical resource availability and health care equality.[2] Therefore, the implementation of health care measures to prevent cervical cancer reflects the priority of women (especially middle aged women) in a society, as well as the civilization and progress of a country. However, this measure has not been employed by developing countries, and the goal to screen cervical cancer for middle aged women has not been realized. This is probably attributed to the imbalance of health care resources in developing countries, limited medical resources are used in a small population.

Secondly, the lack of quality control system of cytological screening and qualified cytotechnologist and cytologists are common problems in developing countries and regions. Pap smear is unfavorable due to its low sensitivity (high false negative rate), and because the screening result is not immediately available, many women who underwent screening are lost to follow-up, therefore, this technique cannot be widely employed in developing countries.[8] Using Pap smear to extensively and repeatedly (every two to three years) screen cervical cancer faces numerous difficulties and challenges. Due to these shortcomings of Pap smear, it is urgent to establish a cervical cancer screening technique which is simple, rapid, effective and economical and is suitable to be used in developing countries.

In recent years, WHO/IARC conducted a population-based, randomized, controlled, large-sample trial in India, and proved that with the prerequisites of short-term training and effective quality control, visual inspection with acetic acid/iodine solution (VIA/VILI) can be used as an effective cervical cancer screening method in developing countries.[9] It does not require laboratory platform, is technically undemanding, easy to master and cheap, which can be performed by experienced physicians or other medical workers (such as nurses and midwives). It is the primary cervical cancer screening method recommended by WHO to be used in developing countries. HPV rapid screening test (careHPV) which is suitable for developing countries has recently been developed and is now under registration trial. It is expected to be put into market in 2010 and will be promoted by WHO.

Prospect of comprehensive cervical cancer prevention

Using safe and effective HPV vaccine is an important measure to block HPV transmission and prevent cervical cancer. The development of cervical cancer vaccine is no doubt the milestone in the history of combating cancer, and is a big step forward in the research of human cancers. Since 2007, in all cancer control meetings organized by WHO, member states have being discussing the prospect of cervical cancer control with the utilization of HPV vaccine. All members agreed that, in an effort to reduce cervical cancer burden, every county should enhance the cervical cancer screening program, improve strategies of treatment and monitoring, and introduce HPV vaccine in appropriate regions. In November 2008, the results of all regional meetings and a comprehensive introduction of HPV vaccine background were hand over to Strategic Advisory Group of Experts (SAGE) on Immunization, proposing the global HPV vaccine immunization policy to share this state-of-the-art achievement of cervical cancer vaccine with developing countries.[10]

The undergoing medical reform in China makes a great opportunity for this intervention. Experts have been discussing the specific steps to carry out cervical cancer screening program. The Ministry of Health and Cancer Foundation of China established the demonstration base of cervical cancer early detection and treatment in 2005, the Ministry of Finance funded the cancer early detection and treatment programs in 2006, and ten-million rural woman cervical cancer screening program is initiated in 2009. The cervical cancer prevention has drawn tremendous attention from the government and public in China. Although the choice of specific method for cervical cancer

screening is debated, we are glad to see many administrations that concerning cancer, reproductive health, adolescent health, immunization and gender equity are eager to take part in the cervical cancer prevention cooperatively. In making specific steps of cervical cancer prevention program, we have to face the challenges of local financial ability, feasibility of service ability and culture acceptability, which require the cooperation of administrations responsible for vaccine immunization, cancer prevention and reproductive health. There will be numerous unpredictable difficulties other than the price and techniques before the conduction of the program. Some difficulties are originated from attitude and awareness, thus, we have to eradicate the prejudice towards the simple screening technique that can be mastered by local medical workers. Currently, the most important thing is to promote the awareness of health requirements, cost-effectiveness and the prospects of upcoming novel technique, thereby the leaders and administrators can be prepared to face the coming opportunities and challenges.

Cancer prevention program should be integrated into a comprehensive health care service system and managed as a whole. We should spare no effort to extend the cervical cancer prevention strategies of cervical cancer vaccine inoculation, precancerous lesion screening and treatment to Chinese women. As a result, the measures fitting for women of appropriate ages and aiming to prevent cervical cancer radically will be issued by the government in the near future to eradicate the threats imposed by cervical cancer.

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