Opinion: Cervical cancer – a vaccine preventable disease

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Cervical cancer will develop in one out of every 35 South African women and it is the leading cause of cancer deaths amongst South African women. Approximately nine South African women die every day from cervical cancer (1). What makes this picture worse is the fact that we are dealing with a preventable disease.

Challenges of a population based screening programme

Secondary prevention of this disease by means of cervical cytology has been available for more than five decades, and despite the absence of randomised controlled trials to show its efficacy, it has reduced the prevalence of the disease by up to 75% in countries where formal population based screening has been implemented (2). Formal population based screening is associated with many challenges making it quite difficult to implement in developing countries.

A substantial amount of resources and effort are required to have a successful well functioning population based screening programme for cervical cancer in any given country. Infrastructure requirements include: clinics, hospitals and laboratories that are equipped and staffed to perform and interpret the screening tests. Properly staffed treatment facilities to manage abnormal test results are also required. Besides a screening policy, knowledge amongst women in the general population of the disease and the screening test to prevent it is an important prerequisite, because if all the facilities are in place but the population is not knowledgeable about the disease and the test, the uptake would be low. Adequate communication channels to inform women about abnormal test results and timing of follow-up screening tests are also crucial to ensure proper functioning of a formal population based screening programme.

It is clear from the discussion above that formal population based screening is problematic to implement in the setting of a developing country. Many women are minimally literate and poorly informed about cervical cancer and its screening tests. Besides infrastructure related challenges, the majority of women are not easily contactable or reached by postal services to receive adequate correspondence with reference to their screening arrangements and test results. Additionally in many developing countries there are insufficient colposcopy services to offer treatment should all women theoretically be screened. This is mainly why cervical cancer has remained a rampant disease in most resource poor settings including South Africa.

The reality in South Africa is that screening is mainly opportunistic. Some women in the public sector might be fortunate enough to be offered a screening test when visiting a clinic for other health related problems. After the screening test has been performed it will remain the screened woman's responsibility to arrange a follow-up visit for discussion of the results and referral for further investigation and treatment. In the private healthcare setting most women will undergo opportunistic screening, sometimes too frequently. Although opportunistic screening should be encouraged, it is mostly done in women who probably have the lowest risk of contracting the disease, while the highest risk population are subsequently seldom or inadequately screened.

Vaccination against HPV prevents cervical cancer

Risk factors for the development of cervical cancer have been described and are well-known (3). These include early onset of sexual intercourse, multiple sexual partners, immune status and cigarette smoking. It has now also been well established that persistent infection with certain high risk types of human papilloma virus (HPV) is the underlying cause of cervical cancer (4). There are more than 40 mucosal HPV types that can infect the lower genital tract in human beings. Approximately 15 of these types are associated with carcinogenesis and are the so called high risk HPV types. HPV 16 and 18 are the two high risk viruses that are responsible for approximately 70% of all cervical cancers worldwide. HPV types 6 and 11 are not carcinogenic but they are responsible for approximately 90% of genital warts worldwide.

HPVs are small DNA viruses that initially infect the basal layer of epithelial cells through microscopic defects in the superficial layers. Transmission is mainly sexual and most infections, including the high risk ones will be transient and resolve within six to 24 months. In a small percentage of women their immune system will not be able to neutralize the infection and if these women develop persistent disease with high risk HPV types, there is a serious risk of developing cervical cancer (5).

HPV infection does not result in a systemic inflammatory response that activates the humoral immune system. Women who develop persistent HPV seem to have some sort of defective cellular immunity that fails to clear the virus from the cervix. This is especially prevalent in HIV infected women.

In recent years it has become possible to vaccinate women against certain HPV strains. Two different preparations are available. The bivalent vaccine (Cervarix®) targets HPV 16 and 18 which, as already mentioned, are the two strains involved in 70 % of cervical cancer cases worldwide. The quadrivalent vaccine (Gardasil®) targets HPV 16 and 18 as well as HPV 6 and 11, which are involved in 90% of cases with genital warts. In addition to cervical cancer protection the quadrivalent vaccine also protects against genital warts and its associated morbidity which can be quite substantial especially in HIV infected women.

Several studies have been performed measuring the efficacy of both the bivalent and quadrivalent vaccines. It is not possible in these trials to use cervical cancer prevalence or prevention as the endpoint as the natural pathophysiology for the development of cervical cancer from the incident HPV infection is much too long. Therefore it is necessary to use surrogate markers such as incident HPV infection, persistent HPV infection (>6 months, >12 months), abnormal cytology and abnormal histology. Histologically confirmed cervical intra-epithelial neoplasia (CIN II and CIN III) is regarded as the best surrogate marker as abnormal cytology can be caused by many HPV types and most HPV infections will resolve spontaneously (6).

Results from these studies have consistently shown high seroconversion rates with high antibody levels that have remained up to nine times higher than levels following natural infection over time after an initial small decrease (7-10). Vaccination has been shown to protect up to 98% of women from developing CIN II or III compared to women receiving placebo. The vaccine was shown to be very efficacious even in those women who had not

received all three doses. The vaccine is well tolerated with tenderness at the vaccine site being the most commonly reported adverse event.

The important issues to address include who to vaccinate and when to vaccinate the identified group. HPV vaccines are most effective if administered to individuals who have not been previously exposed to HPV. As HPV is sexually transmitted the target population should focus on females who have not initiated sexual activity. Most guidelines recommend vaccination in girls from age 9 and older, with “catch up” vaccination to include young women up to 26 years of age at the initiation of an immunisation programme (11,12). Vaccinated women will still need to undergo cervical cancer screening as the vaccine does not offer 100% protection against the disease.

Both vaccine preparations are currently registered in South Africa and are available in the private sector. Both vaccines need to be administered intra muscularly in three doses over a six month period. South Africa has a good track record as far as vaccination is concerned with up to between 80% and 90% of vaccine coverage for DPT, polio, measles and Hepatitis B vaccination (13). It is much easier to vaccinate the identified target population of girls between the ages of 10 to12 years. The girls in this age group are still at primary school. The logistics behind vaccinating school girls are far less complicated than implementing a screening programme involving the adult female population requiring several screening episodes in their lifetime.

For five decades we have missed the opportunity to significantly reduce the prevalence of cervical cancer in South Africa because we have - for many reasons - not been able to introduce a well-functioning system of cervical cytology screening. In the process many thousands of women have died prematurely and unnecessary from a disease that is preventable and treatable in its early stages.

We now have the unique situation of a vaccine that is able to substantially reduce the number of women that will suffer from cervical cancer. Primary prevention of the cause of 70% of cervical cancer is now possible. It has been shown to be safe, efficacious and cost-effective.

The question that remains to be asked is if we will have the will and the means to produce and deliver a well worked out primary cervical cancer prevention programme. Or should we rather ask why have we not yet produced and delivered a well worked out primary prevention programme for cervical cancer? It has been possible for a few years now.

For many decades we have been allowing at least nine women to die of cervical cancer every day in this country. Only time will tell how long it will take to finally reduce the burden of cervical cancer which is caused by a disease that is now vaccine preventable.

Note that the views expressed in this article are those of the author(s) and do not necessarily represent the views of PHASA.

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