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Opinion Article

Should Age Still Be a Limiting Factor in Adapting Universal HPV Vaccination?

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Abstract

Prevention of HPV linked cervical carcinogenesis by means of vaccination should not be limited by age, instead it should be universal vaccination, like for other vaccine preventable cancers.

Keywords: HPV Vaccine; Older Age; Efficacy; Immunogenicity; Seroconversion; Cervical Cancer

Introduction

Human Papilloma Virus (HPV) vaccine was first approved in 2006. Nearly two decades on, our understanding of HPV related carcinogenesis has grown manifold, as also data pertaining to vaccine safety, efficacy & immunogenicity. Few indisputable facts emerged from the early trials on HPV vaccination. Firstly, the earlier the age of vaccination, higher the antibody titers. Secondly, sero-conversion after vaccination is greater and longer lasting than natural infection. Thirdly, HPV vaccination is most efficacious before the onset of sexual activity (in HPV naïve population). Based on safety & efficacy data and modelling studies, the recommended age for vaccination became 9-14 years, with catch up vaccination up to the age of 26 years [1]. As per these guidelines, vaccination between the ages of 26 and 45, although not routinely recommended, should be discussed on a shared decision basis. In a recent update to this, a practice advisory was released, to consider HPV vaccination for immunocompetent women undergoing treatment for CIN2+ [2]. However, for those over the age of 45 years, cervical cancer screening is more cost effective.

Although the burden of HPV induced carcinogenesis in becoming better defined, there are still gaps in our understanding of how long the immunity lasts after vaccination, whether booster dose is needed, what is the cut off antibody titer for waning immunity and revaccination. This is unlike that for Hepatitis B causing hepatocellular carcinoma, where vaccination dosing schedules are independent of age, and antibody cut-offs are well-defined. With HPV, there are other variables at play - cervical cancer occurs after many years of persistent infection, persistence of infection cannot be predicted with certainty, although risk factors for persistence have been defined. The onset of sexual activity varies among populations and it is uncommon for a person to be infected by more than one high risk HPV type. In addition, access to vaccination is a barrier in resource limited settings where the burden of cervical cancer is actually higher.

With these realities in mind, one needs to consider whether limiting vaccination to those up to the age of 26 years is prudent and whether we should change tracks to promote universal vaccination as and when possible.

The evidence-based argument for this is supported by studies showing non-inferiority of immune response [3], long-term efficacy [4] and safety HPV vaccination in women over 25 years of age. When recommending vaccination under programmatic settings, however cost is also a deciding factor. The economics of it are not as encouraging, as per a Health Economic Analysis, model assumptions for adult vaccination, the number needed to vaccinate

(NNV) to prevent one case of anogenital warts, >CIN2 or cancer would be 9, 22 & 202. For women up to 45 years NNV would be 120, 800 & 6500 [5]. This implies that the additional health benefits may be small compared to the cost incurred to extend vaccination up to 45 years [6]. This can be offset by insurance coverage and individual paying capacity.

The fact that adolescents are the target age group for vaccination should not deter older women from seeking and receiving vaccination. There are several caveats to the age based advocation of HPV vaccination. As longevity increases, so do the number of sexually transmitted infections including HPV. The duration of protection from HPV vaccination is uncertain, so it's open to debate whether vaccination in early teens would still provide protection decades after, or when sexual activity peaks. Safety & immunogenicity in older women is well proven, while efficacy may be lower if they are not HPV naïve. Even so, it will not be nil. Vaccination will still protect against the unexposed strains, and it is unlikely for someone to be exposed with more than 2-3 strains, even with high-risk behaviour. Real world data indicates a high burden of HPV infection in older women, with nearly 43 % of the causal infections causing CIN2+ occurring in women older than 27 years [7]. The risk of persistent high-risk HPV infection is significantly higher in older women, up to three times more than in young women. HPV prevalence starts to rise within 5-10 years of first sexual activity, and peaks in women 25-30 years, and in those over 55 years according to several studies conducted in developing countries [8]. Thus, HPV vaccine in previously unimmunized older women could reduce risk of this second peak of HPV infection later in life. Seroconversion after natural infection is lower than with vaccination. The latter offers protection from several strains, and herd immunity.

HPV vaccination is already being explored in preventing recurrent disease in women undergoing cervical conization and radical surgery for cervical cancer.

Thus, from an individual perspective, considering vaccination at all ages may be beneficial. We could be looking at HPV vaccination with the same perspective as Hepatitis B vaccination in the future, and age may no longer be a factor precluding vaccination.

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