Current Topic

HUMAN PAPILLOMAVIRUS VACCINE: A NEW APPORTUNITY FOR THE TREATMENT OF HUMAN PAPILLOMAVIRUS INFECTIONS

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INTRODUCTION

Genital human papillomavirus (HPV) is associated with number of vulvar epithelial disorders including genital warts, vulvar intraepithelial neoplasia (VIN) and some vulvar carcinomas.However, the majority of individuals infected with HPV have a subclinical transient infection that is limited by viral type, local environment factors, and the host immune response[1].More than 120 HPV subtype have been identified out of which more than 30 are specific for anogenital tract, 15% of which are high risk or oncogenic.HPV infects the basal and parabasal cell epithelium; transmission is enhanced by irritation, abrasion and micro trauma.It also capable of inducing a local immune deficiency thus allowing prolonged viral manifestation[2].Clinically two distinct types of vulvar carcinoma begin to emerge.One type is having typical keratinizing vulvar squamous carcinoma, in older women with HPV infection ranges from 2% -23% while another arise in young women, HPV-related basaloid and warty carcinoma, harbor 75%-100% HPV[3].

HPV related VIN tends to be asymptomatic and diagnosed on evaluation of Pap smear having, lesion which may involve vulva, periurethral and perianal areas.Vulvoscopy or biopsy can be helpful in the diagnosis[2,4]. The signs and symptoms of early invasive vulvar carcinoma are same as of symptomatic VIN. Most of the females complain of persistent itching and presence of a growth, pain, burning, bleeding and dysuria[3].Thus VIN types 2/3must be treated due to an increased risk of malignant trransformation[3].A large majority of genital warts are caused by HPV 6 or 11, while HPV 16 and HPV 18 are responsible for 70% of high grade cervical dysplasia and invasive cervical cancers.[5]

HPV VACCINE

Most HPV infections do not cause disease and genital tract infections are transient.Only few HPV (HPV-16) infected women develop an abnormal pap, indicating of high risk of developing premalignant cervical disease[5].Other recognized cofactors which increase the risk of invasive cervical cancer include cigarette smoking, younger age at first intercourse, high parity, long term use of oral contraceptive pills, and other sexually transmitted infections.Low risk HPV (type 6 and 11) causes benign hyper proliferative lesions[5,6].

At present, two prophylactic HPV vaccines have been licensed, which utilize recombinant DNA technology, where HPV late protein gene (encoded for outer viral capsid) is expressed in a vector.These capsid self assembled and form viral- like particles (VLP), which mimic a natural HPV viral infection but not infectious.In terms of antigen, bivalent HPV vaccines (VLPs of 16 and 18 HPV) and quadrivalent (contain HPV 16 and 18 and VLP of 6 and 11 in addition) are available which are given by intramuscular injection in three individual doses over 6 months duration.Phase I and phase II studies show high vaccine safety, tolerability and immunogenicity[6,7]. Large phase III clinical trial show efficacy for HPV-16 and 18 related high grade dysplasia for both vaccines (approaching 100% protection). Effectiveness is less among women with current prevalent infection or disease[6].

The immunogenicity studies of quadrivalent vaccine in girls and women after three intramuscular injections at months 0, 2 and 6 is suggest, that it is safe, tolerable and effective with specific anti HPV antibodies response.At the month 7, one month after the third dose of vaccine, seroconversion rates were 99-100% in girls and women aged 15-26 years and then declined and reaching a plateau by month 24 and remain stable at this level through to at least month 60.

Seroconversion rates of quadrivalent HPV vaccines arealmost 99.6% in girls aged 9-15 years and 97-99% inolder females suggestive of high efficacy in younger group. Co-administration of other vaccines e.g. hepatitis B, diphtheria/tetanus pertusis/poliovirus (DPT/P) vaccine and meningococcal polysaccharide conjugate vaccine did not significantly interfere with the immune response of the either vaccine[8].

Immunogenicity of bivalent HPV vaccine (16, 18 types) were found higher than quadrivalent vaccine at the month 7[9].In addition to protecting against the four vaccine HPV types, quadrivalent HPV vaccine also provide cross protection against persistent infection and lesions caused by non-vaccine high risk HPV types (31, 33, 45, 52 and 58).

The monovalent HPV 16 vaccine (which is the same as the HPV16VLP) show efficacy for up to 9.5years without any break through disease[10].

SAFETY TOLERABILITY AND DOSE

Quadrivalent HPV vaccines are generally well tolerated with few adverse effects e.g. erythemaat injection site, fever, pain.Hypersensitivity (arthritis, urticaria, bronchospasm), reaction was observed in <1% of recipient.The recommended dosage regimen is 0.5ml intramuscular injection given at 0, 2, 6 months (three doses) [8].Quadrivalent HPV vaccine should be avoided during pregnancy, but may me given to breast feeding women[8, 11].

To conclude, persistent infection of the cervix with high risk HPV types can result in the development of low grade (cervical intraepithelial neoplasia CIN or-VIN) or high grade pre cancerous lesion, which can progress to invasive cervical cancer.HPV types 16 and 18 are responsible for causing a high proportion of cancer e.g. cervical, vulvular, vaginal, anal mouth or oropharyngeal cancer.Monovalant (16 type), bivalent (16 and 18) and quadrivalent (6, 11, 16, 18 types) vaccine can be used prophylactically.Quadrivalent HPV vaccine was found safe, well tolerated, both during clinical trial and during post marketing surveillance as three doses and offers high level protection against HPV.

REFERENCE

1. Gunter J.Genital and perianal warts:New treatment opportunities for human papillomavirus infection.Am J Obstet Gynecol 2003; 18:S3-S11.
2. Kennedy CM and Boardman LA.New approaches to external genital warts and vulvular intraepithelial neoplasia.Cli Obstet. Gynecol 2008;51(3): 518-526.
3. Centre for Disease control and Prevention. Sexually Transmitted Disease Treatment Guidelines MMWR 2006;55(NO RR 11): 1-94.
4. Maw R.Critical appraisal of commonly used treatment for genital warts.Int J STD AIDS 2004; 15:357-364.
5. Ault KA.Human Papillomavirus Vaccines: An update for gynecologists.Cli Obstet Gynecol 2008;51(3):527-532.
6. Garland SM and Smith JS.Human papillomavirus vaccines: Current Status and future prospects Drug 2010; 70(9):1079-1098.
7. Villa LL, Costa RL, Petta CA, et al.High sustained efficacy of a prophylactic quadrivalent human papillomavirus types 6/11/16/18 L1 virus like particle vaccine through 5-years of follow-up.Br. J Cancer 2006 Dec 4;95(11): 1459-1466.
8. Mc Cormack PL and Joura EA.Quadrivalent human papillomavirus (Types 6,11,16,18) recombinant vaccine: A review of its use in the prevention of pre malignant genital lesions, genital cancer and genital warts in women.Drug 2010; 70(18): 2449-2474.
9. Einstein MH, Baron M; Levin MJ et al.Comparison of the immunogenicity and safety of Cervarix™ and Gardasil™ human papillomavirus (HPV) cervical vaccine in healthy women aged 18-45 years.Hum Vaccin2009 Oct;5(10): 705-719.
10. Rowhani-Rahbar A, Mao C, Hughes JP et al.Long-term efficacy of a prophylactic monovalent human papillomavirus type 16 vaccine.Vaccine 2009 Sept 18;27(41): 5612-5619.
11. European Medicines Agency: Gardasil (Human papillomavirus vaccine [type 6, 11, 16, 18] recombinant absorbed): Summary of product characteristics (online).Available from URL:(http://www.ema.europa.Eu/humandocs/Humans /EPAR/gardasil/gardasil.htm).