EDITORIAL
Obstetrics & Gynecology

JKMS

http://dx.doi.org/10.3346/jkms.2014.29.6.749 • J Korean Med Sci 2014; 29: 749-750

# HPV Vaccine, Is It Really Harmful?

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Cervical cancer is considered a preventable disease because it has causative agent called Human Papilloma Virus (HPV). HPV infection was detected in up to 99% of women with squamous cell carcinoma of uterine cervix. Two HPV vaccines are approved by the U.S. Food and Drug Administration (FDA) and protect against subtypes 16 and 18. The first, GARDASIL®, was licensed in 2006 and is now recommended as a routine vaccination for girls and women between the ages of 9-26 in the US. The second HPV vaccine, CERVARIX®, was licensed in 2009. The World Health Organization (WHO) recommends the introduction of HPV vaccination into national immunization programs (NIP) where prevention of cervical cancer is a public health priority and the introduction is programmatically feasible.

However, until now, there are some doubts about the safety of HPV vaccine. For example, the claim that "HPV vaccines have an impressive safety profile is only supported by highly flawed design of safety trials and is contrary to accumulating evidence from vaccine safety surveillance databases and case reports which continue to link HPV vaccination to serious adverse outcomes (including death and permanent disabilities)". In June 2013, there were a few reports described as complex regional pain syndrome (CRPS) and other chronic pain following HPV vaccination in Japan. After this issue, the safety of HPV vaccine rises to the surface again in Korea.

Since the introduction of HPV vaccines in the US, adverse events related to the vaccination have been reported to US Adverse Experience reporting system (VAERS). The most common events reported were: Syncope (or fainting)–common after injections. Of the 12,424 reports of adverse events, 772 (6% of all reports) described serious adverse events, including 32 reports of deaths, the remaining 11,652 (93.8%) were classified as non-serious. The 32 death reports were reviewed and there was no common pattern to the deaths that would suggest they were caused by the vaccine. In cases where there was an autopsy, death certificate, or medical records, the cause of death could be explained by factors other than the vaccine. Some causes of death determined to date include diabetes, viral illness, illicit drug use, and heart failure (1). US Vaccine Safety Datalink (VSD) active surveillance confirmed no significant risk for any of the pre-specified adverse events after vaccination like Guillain-Barre Syndrome (GBS), seizures, syncope, appendicitis, stroke, venous thromboembolism (VTE) and other allergic reactions. A total of 600,558 HPV vaccine doses were administered during the study period. Also, there was no increase in rate of anaphylaxis following HPV vaccine as compared to previous VSD studies. In the Kaiser Permanente (US managed care organization) post-licensure safety study in females showed no association between vaccination with GARDASIL® and congenital anomalies, miscarriages/16 pre-specified autoimmune conditions/VTE/Death/any other general safety events. This study showed an increase in syncope on day of vaccination associated with GARDASIL® (RR [95% CI]: 6.00 [3.91-9.21]), but external Safety Review Committee (SRC) determined syncope associated with vaccination due to temporal association and clinical plausibility. Also, this study showed that local skin infection (cellulitis/abscess) can be possibly associated with GARDASIL® (RR [95% CI]: 1.64 [1.17-2.3]), but the SRC concluded the cases are more likely to be caused by injection site reactions.

In a Weekly Epidemiological Record published in February, the WHO's Global Advisory Committee on Vaccine Safety (GACVS) stated that multiple epidemiological studies have demonstrated no evidence to support any causal link between HPV vaccination and the onset of multiple sclerosis (MS) and other autoimmune diseases. The committee reviewed the safety of HPV vaccines based on data collected in the US, Australia and Japan and data submitted HPV vaccine manufacturer and others and concluded there was no confirmation of clinical symptoms related to GBS, seizure, stroke, VTE, anaphylaxis and allergic reaction, which were suspected as adverse outcomes following HPV vaccination and there were no reports of adverse pregnancy outcomes in women after HPV vaccination. In addition, the committee continues to affirm that available scientific evidence does not support any causal link between aluminum containing vaccines and any increased risk of disease, as it said in 1999, 2002, 2004, and 2012. This is also stated in < Statement on the continued safety of HPV vaccination > published in March 2014 (2).

In HPV vaccine safety study in general population from France

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pISSN 1011-8934
eISSN 1598-6357

with 113 autoimmune disorders (AD) cases, none of the cases of GBS was exposed to HPV vaccine. In the main analysis, the adjusted OR for quadrivalent HPV (qHPV) vaccination in these AD cases and their matched controls was 0.9 (95% CI, 0.5-1.5). Therefore, no evidence of an increase in the risk of the studied AD was observable following vaccination with GARDASIL within the time periods studied. Also, there was insufficient statistical power to allow conclusions to be drawn regarding individual AD (3). In a safety study in general population from Denmark and Sweden with vaccinated 997,585 girls aged 10-17, the rate ratios for 20 of 23 autoimmune events were not significantly increased (4). The rate ratios for five neurological events were not significantly increased and there were inverse associations with epilepsy and paralysis. There was no association between exposure to qHPV vaccine and VTE. This study found no evidence supporting associations between exposure to qHPV vaccine and autoimmune, neurological, and venous thromboembolic adverse events (4).

In summary, according to careful examination of the available evidence, HPV vaccines benefit-risk profile remains favorable. While safety concerns about HPV vaccines have been raised, these have systematically been investigated: to date, the WHO's GACVS has not found any safety issue that would alter any of the current recommendations for the use of the vaccine. Based on benefit-risk profile, the Korea Food & Drug Administration (KFDA), Korean Society of Obstetrics and Gynecology (KSOG), and Korean Society of Gynecologic Oncology (KSGO) recommend HPV vaccination to prevent cervical cancer.

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 http://dx.doi.org/10.3346/jkms.2014.29.6.749