World Academy of Science, Engineering and Technology
International Journal of Biomedical and Biological Engineering
Vol:12, No:07, 2018

Safety Profile of Human Papillomavirus Vaccines: A Post-Licensure Analysis of the Vaccine Adverse Events Reporting System, 2007-2017

Authors : Giulia Bonaldo, Alberto Vaccheri, Ottavio D'Annibali, Domenico Motola

Abstract : The Human Papilloma Virus (HPV) was shown to be the cause of different types of carcinomas, first of all of the cervical intraepithelial neoplasia. Since the early 80s to today, thanks first to the preventive screening campaigns (pap-test) and following to the introduction of HPV vaccines on the market; the number of new cases of cervical cancer has decreased significantly. The HPV vaccines currently approved are three: Cervarix® (HPV2 - virus type: 16 and 18), Gardasil® (HPV4 - 6, 11, 16, 18) and Gardasil 9® (HPV9 - 6, 11, 16, 18, 31, 33, 45, 52, 58), which all protect against the two high-risk HPVs (6, 11) that are mainly involved in cervical cancers. Despite the remarkable effectiveness of these vaccines has been demonstrated, in the recent years, there have been many complaints about their risk-benefit profile due to Adverse Events Following Immunization (AEFI). The purpose of this study is to provide a support about the ongoing discussion on the safety profile of HPV vaccines based on real life data deriving from spontaneous reports of suspected AEFIs collected in the Vaccine Adverse Events Reporting System (VAERS). VAERS is a freely-available national vaccine safety surveillance database of AEFI, co-administered by the Centers for Disease Control and Prevention (CDC) and Food and Drug Administration (FDA). We collected all the reports between January 2007 to December 2017 related to the HPV vaccines with a brand name (HPV2, HPV4, HPV9) or without (HPVX). A disproportionality analysis using Reporting Odds Ratio (ROR) with 95% confidence interval and p value ≤ 0.05 was performed. Over the 10-year period, 54889 reports of AEFI related to HPV vaccines reported in VAERS, corresponding to 224863 vaccine-event pairs, were retrieved. The highest number of reports was related to Gardasil (n = 42244), followed by Gardasil 9 (7212) and Cervarix (3904). The brand name of the HPV vaccine was not reported in 1529 cases. The two events more frequently reported and statistically significant for each vaccine were: dizziness (n = 5053) ROR = 1.28 (CI95% 1.24 – 1.31) and syncope (4808) ROR = 1.21 (1.17 – 1.25) for Gardasil. For Gardasil 9, injection site pain (305) ROR = 1.40 (1.25 – 1.57) and injection site erythema (297) ROR = 1.88 (1.67 – 2.10) and for Cervarix, headache (672) ROR = 1.14 (1.06 – 1.23) and loss of consciousness (528) ROR = 1.71 (1.57 – 1.87). In total, we collected 406 reports of death and 2461 cases of permanent disability in the ten-year period. The events consisting of incorrect vaccine storage or incorrect administration were not considered. The AEFI analysis showed that the most frequently reported events are non-serious and listed in the corresponding SmPCs. In addition to these, potential safety signals arose regarding less frequent and severe AEFIs that would deserve further investigation. This already happened with the referral of the European Medicines Agency (EMA) for the adverse events POTS (Postural Orthostatic Tachycardia Syndrome) and CRPS (Complex Regional Pain Syndrome) associated with anti-papillomavirus vaccines.

Keywords : adverse drug reactions, pharmacovigilance, safety, vaccines
Conference Title : ICPCT 2018 : International Conference on Pharmacovigilance and Clinical Trials
Conference Location : Paris, France
Conference Dates : July 19-20, 2018