

MYOPERICARDITIS AND VACCINES: GAINING INSIGHTS INTO VACCINE ADVERSE EVENT REPORTING SYSTEM

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Aim Risk of myo-pericarditis by smallpox vaccination caused regulatory interventions in early 2000 (Nalca et al., 2010); conversely, only anecdotic cases of this event have been described for other vaccines. The aim of this study was to analyze and compare cases of myo-pericarditis recorded in the Vaccine Adverse Event Reporting System (VAERS) in order to identify whether recurrent patterns of reporting exist (potential risk categories and types of vaccine).

Methods We searched cases of myocarditis and/or pericarditis in VAERS (2011-2015). For each case, we assessed causality using an Italian adaptation of standardized WHO-AEFI (Adverse Event Following Immunization) algorithm (Tozzi et al., 2013). Disproportionality analysis was performed by calculating reporting odds ratio (ROR) with 95%CI for each type of vaccine, when at least three cases were reported. A relevant evidence-mapping was also carried out using a systematic search strategy in MEDLINE (as of February 2017).

Results Overall, 198 cases in VAERS registry were collected, 167 of them were referred to smallpox vaccine ACAM2000® (which can be viewed as positive control). The remaining 31 cases were divided in 'younger group' (YG; <18 years old, 15 cases) and 'older group' (OG; >18 years old, 35 cases). The main vaccines reported in YG were against HPV (Human Papilloma Virus; n=6), meningococcus (n=5), influenza (n=4), TDaP (Tetanus, Diphtheritis, Pertussis; n=5) and hepatitis A (n=4); the application of WHO-AEFI algorithm resulted in all cases "undeterminate". The main symptom was chest pain, and the mean time-to-onset was about 48 days. In OG, reported vaccines were against influenza (n=16); TDaP (n=7); meningococcus (n=1); pneumococcus (n=1); varicella (n=4); typhus (n=1); yellow fever (n=1). According to WHO-AEFI algorithm, we found 1 "correlated" case, 1 "correlated/undetermined", 30 "undetermined", 1 "not correlated" and 2 "unclassifiable". Again, the main symptom was chest pain and the mean time- to-onset was 26 days; no predisposing conditions (allergies, diseases, chronic treatment) were reported. Disproportionality analysis showed statistically-significant ROR in YG only for meningococcal vaccine either with MC (ROR=5.52; 95%CI=1.01-30.17) and MP (ROR=3.55; 95%CI=1.23-10.24). Weaker signals were emerged with influenza vaccine and MP and also with hepatitis A and MP. Conversely, in OG stronger signals were obtained: control group smallpox resulted very relevant in all three events (MC, ROR=73.53; 95%CI=41.87-129.14; PC, ROR=59.06; 95%CI=36.45-95.67; MP, ROR=71.88; 95%CI=49.25-104.89). Typhoid vaccine appeared likewise related to MC (ROR=11.11; 95%CI=7.01-17.62), PC (ROR=10.88; 95%CI=6.38-18.56) and MP (ROR=11.13; 95%CI=7.73-16.03). Evidence-mapping approach retained a total of 91 case reports; most of them regarded smallpox vaccine (n=26). Among others, 33 occurred with influenza vaccine, 2 with typhus and hepatitis B vaccines, and three cases with meningococcus vaccine.

Conclusions We found both in VAERS and literature an over-reporting of myo-pericarditis induced by smallpox vaccine (probably used following biological terroristic risk attack in early 2000). Cases reported for other vaccines are very scarce and confirm that the overall benefit largely outweighs this risk. However, VAERS together with the literature call for further investigation, especially for meningococcal vaccine in youngers and typhus vaccine in adults. By a clinical point of view, in younger patients recently immunized, the presence of chest pain as main presentation symptom may suggest a diagnosis of myo-pericarditis.

Nalca et al. (2013). *Drug Design, Development and Therapy*. 4, 71-79

Tozzi et al. (2013). *Vaccine*. 31 (44), 5041-5046