Vaccine safety evaluation: Practical aspects in assessing benefit and risks

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Abstract

Introduction: Vaccines are different from most medicines in that they are administered to large and mostly healthy populations including infants and children, so there is a low tolerance for potential risks or sideeffects. In addition, the long-term benefits of immunisation in reducing or eliminating infectious diseases may induce complacency due to the absence of cases. However, as demonstrated in recent measles outbreaks in Europe and United States, reappearance of the disease occurs as soon as vaccine coverage falls. Unfounded vaccine scares such as those associating the combined measles-mumps-rubella vaccine with autism, and whole-cell pertussis vaccines with encephalopathy, can also have massive impacts, resulting in reduced vaccine uptake and disease resurgence. The safety assessment of vaccines is exhaustive and continuous; beginning with non-clinical evaluation of their individual components in terms of purity, stability and sterility, continuing throughout the clinical development phase and entire duration of use of the vaccine; including post-approval. The breadth and depth of safety assessments conducted at multiple levels by a range of independent organizations increases confidence in the rigour with which any potential risks or side-effects are investigated and managed. Industry, regulatory agencies, academia, the medical community and the general public all play a role in monitoring vaccine safety. Within these stakeholder groups, the healthcare professional and vaccine provider have key roles in the prevention, identification, investigation and management of adverse events following immunisation (AEFI). Guidelines and algorithms aid in determining whether AEFI may have been caused by the vaccine, or whether it is coincidental to it. Healthcare providers are encouraged to rigorously investigate AEFIs and to report them via local reporting processes. The ultimate objective for all parties is to ensure vaccines have a favourable benefit-risk profile.

Background: Before a vaccine is administered to humans, vaccine manufacturers undertake extensive safety evaluation of individual vaccine components and of the final formulation to be administered. Raw materials must be of the highest possible purity and quality (or 'clinical grade'), their origin must be properly traced and their ongoing supply must be guaranteed. The vaccine components and the final product are tested in the laboratory for purity, sterility, potency, consistency, activity and stability. Many of these tests are conducted in the laboratory, and many, such as tests for efficacy, toxicity, safety and effects on reproductive health, are conducted in animal models.

Method:- The perception of a relationship between a vaccine and serious AE can have profound effects on vaccine confidence, leading to widespread rejection of some vaccines, with devastating consequences. Changing these perceptions is highly challenging and requires the communication of up-to-date and detailed information to providers and their patients, for maintaining trust in vaccines. For example, a gastroenterologist claimed a causal association between MMR immunisation and autism when he investigated a series of patients with autism of whom 8 out of 12 had onset of symptoms within 2 weeks of immunisation. This assertion was made in 1998 and since then, dozens of studies and several data reviews by independent organizations have all concluded that there is no evidence to support a causal association between MMR immunisation and autism. However, 17 years later there are still fears within the public that MMR immunisation will cause autism.

Results: The benefit-risk profile of each vaccine is assessed constantly during the entire duration of its use. Increased knowledge of the safety surveillance processes that are in place to collect, analyse and communicate around AEFI can increase confidence of healthcare providers and the public in immunisation. Healthcare providers have a central role in enhancing knowledge of vaccine safety by ensuring AEFI are identified quickly, that high-quality data is collected to allow thorough assessment of the AE, and to Change to Undesirable Effects Thrombocytopenia is a well-recognised complicaon of many viral infecons including measles and rubella. Post-licensure studies confirmed an increased risk of thrombocytopenia aer MMR vaccinaon, although the risk was lower and disease clinically milder than aer natural infecon. Thrombocytopenia was added as a very rare undesirable effect in the Prescribing Informaon Change to Warnings and Precauons Syncope may occur aer administraon of any vaccine to adolescents and adults. Syncope has been reported following vaccinaon of adolescent and young women with human papillomavirus (HPV) vaccines, and has a plausible relaonship given the populaon and the se_ngs where vaccinaon is given (e.g., schools). Although not unique to HPV vaccines, syncope was added to the Prescribing Informaon to alert prescribers to take preventave measures and to closely observe subjects for 15 minutes aer vaccinaon Change to the Schedule Post-

licensure studies have established that oral rotavirus vaccine is associated with a small increase in the background risk of intussuscepon. Intussuscepon is most common in children aged 6-12 months. Risk minimisaon is achieved by compleng the vaccinaon course before 6 months of age PMS can lead to changes in the Prescribing Informaon Fig. 2. Recent examples where post-marketing surveillance (PMS) has led to updates of the Prescribing Information. 6678 A. Di Pasquale et al. / Vaccine 34 (2016) 6672–6680 determine the likelihood that immunisation may have been (or not) the cause of the event. Ultimately these events should be reported via national pathways. The ability to detect and communicate AEFI is not adequate in all countries, but could be improved with a global approach to vaccine safety monitoring.

This work is partly presented at 40th Global Summit and Expo on Vaccines & Immunology May 18-19, 2020