Available online at www.sciencedirect.com

Public Health

journal homepage: www.elsevier.com/puhe

Original Research

Surveillance for adverse events following immunization (AEFI) for 7 years using a computerised vaccination system

A.M. Alguacil-Ramos [a,b,c,*], J. Muelas-Tirado [d], T.M. Garrigues-Pelufo [e], A. Portero-Alonso [a], J. Diez-Domingo [b,c], E. Pastor-Villalba [a], J.A. Lluch-Rodrigo [a]

[a] Dirección General de Salud Pública, Conselleria de Sanidad Universal y Salud Pública, Valencia, Spain
[b] Fundación para el Fomento de la Investigación Sanitaria y Biomédica (FISABIO), Valencia, Spain
[c] Universidad Católica de Valencia 'San Vicente Mártir', Valencia, Spain
[d] Dirección General de Farmacia y Productos Sanitarios, Conselleria de Sanidad Universal y Salud Pública, Valencia, Spain
[e] Facultad de Farmacia, Universitat de Valencia, Valencia, Spain

ARTICLE INFO

Article history:
Received 6 May 2015
Received in revised form
12 November 2015
Accepted 12 November 2015
Available online 12 March 2016

Keywords:
AEFI (adverse event following immunization)
Passive surveillance
Vaccine safety
Immunization registry

ABSTRACT

Objectives: The surveillance of vaccine safety is an essential requirement in vaccination programmes. Computerized immunization registries such as the Vaccination Information System (SIV) of Valencian Community (Spain) offer the opportunity to estimate the incidence of adverse events according to individual information. The aim of the study was to analyze adverse events following immunization reported through SIV from 2005 to 2011 by age, sex, type of vaccine and dose, and adverse event, and highlight the advantages of this type of reporting.

Study design: A retrospective cohort study of subjects vaccinated in the Valencian Community using population health databases was carried out.

Methods: Analysis of vaccinations and reported AEFI via SIV in Valencian Community was carried out.

Results: More than 13 million vaccines doses were administered during 2005 through 2011, the reporting rate of adverse events was 12.4/100,000 doses administered with the highest value in 2009 (27.4), with differences by age and sex. DTaP vaccine had the highest reporting in children (96.6/100,000) while influenza A(H1N1)pdm09 in adults (87.7/100,000). An increased reporting of adverse events was seen with DTaP in children 5–6 years of age, detected in real time, drove to swap this vaccine to a low dose Tdap which was followed by a decrease in administration site events.

Conclusions: SIV demonstrates advantages for passive surveillance. Reporting rates by individual characteristics are calculated accurately and it also allows detecting shifts in

* *Corresponding author*. Dirección General de Salud Pública, Conselleria de Sanidad Universal y Salud Pública, Av. Cataluña 21, 46020, Valencia, Spain.
E-mail address: alguacil_ana@gva.es (A.M. Alguacil-Ramos).
http://dx.doi.org/10.1016/j.puhe.2015.11.010

reporting rate on real time for specific vaccines. The study shows that vaccines included in the routine vaccination schedule for children and adult vaccination programs are safe.

Introduction

Recommendations for vaccination represent a dynamic balance between benefits and risks.[1] Before immunization, vaccine-preventable diseases were highly prevalent and the benefit for vaccination was easy to estimate and perceive. As the incidence of disease decreased, concerns about vaccine safety increased. This scenario highlights the importance of obtaining data about actual events occurring after vaccine administration in a high number of people in order to maintain the risk-benefit ratio and the reliability on vaccination programmes.[2,3]

Electronic vaccine registries are important tools to monitor national immunization programmes.[4] The availability of unique personal identifiers such as that provided by the Population Information System (SIP) of the Valencian Community,[5] represents an opportunity to link vaccine registers to disease data and to identify specific health outcomes, and also to investigate vaccine safety signals of existing and new vaccine programmes.[6]

The objectives of passive surveillance systems of Adverse Events Following Immunization (AEFI) include: to detect new, unusual or rare vaccine adverse events; to assess the safety of newly licensed vaccines and to determine patient risk factors for particular types of adverse events.[7,8] The advantage of Vaccination Information System (SIV) is that it provides individual information of the vaccinated person, so data related with age, sex and risk group is complete and reliable.

The Valencian Community has a population of five million inhabitants, representing slightly over 10% of the Spanish population. The immunization registry of the Valencian Community was set up in 2002 and since then, over 30 million vaccinations have been registered. The registry of vaccine adverse events through the SIV began in 2005.[5]

The main objective of the study was to calculate the reporting rates of reported AEFI through SIV of the Valencian Community between January 2005 and December 2011 by age, sex, type of vaccine and dose, and to highlight the advantages of computerized immunization registers.

Methods

Description of SIV

Immunizations carried out in the Valencian Community are recorded through SIV. Over 1800 health care workers have access to this immunization registration platform. SIV is a population-based individual register, linked to other health databases through a unique personal identification number (SIP). SIV includes patient data such as date of birth, sex and residence.

This system allows the individual registration of administered vaccines: type of vaccine, manufacturer, expiry date and batch number and if required subjects' special health conditions, i.e. type of risk group.

Health care workers from public and private clinics could register administered vaccines and AEFI. An AEFI form is used to collect the data. Health care workers report adverse events considered as possibly related to vaccination in accordance with biological plausibility and coherence or other criteria.

Over 98% of AEFIs notified in the Valencian Community are reported through SIV linking the events with one or more administered vaccines. All this information is submitted online to the Pharmacovigilance Center (PhV Center) of the Valencian Community where each single report is analyzed according to causality assessment criteria.[6] The PhV center belongs to the *Conselleria de Sanitat Universal I Salut Pública* and it is responsible for the communication of adverse events related to medicines to the Ministry of Health of Spain. PhV Center can receive reports from SIV or from an AEFI form sent by health care workers directly to it (postal or webpage).

Data collection

All vaccines recorded in SIV were collected including the AEFIs reported during the study period.

Global AEFI data received by the PhV Center were linked to the information from SIV for the study time period.

Study time period

The period of analysis was from 1st January 2005 to 31st December 2011.

Study variables

Age, sex, date of vaccination, adverse event [recorded as MedDRA[9] classification and System Organ Class (SOC)], type of vaccine declared as responsible of the AEFI and number of vaccine dose (for vaccines with a more than one dose schedule).

Data analysis

A retrospective cohort study of subjects vaccinated in the Valencian Community using population health databases was carried out.

The vaccine-specific reporting rate and 95% confidence intervals was calculated for each vaccine type, age group (0–15; 16–64 and $\geq$ 65 years) and sex as the number of reports per 100,000 doses administered. A comparison test of proportions adjusted for multiple comparisons (*Bonferroni* adjustment) was applied to ensure that the significance level