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Original Research

Surveillance of adverse events following vaccination in the French armed forces, 2011–2012

A. Mayet [a,*], S. Duron [a], J.-B. Meynard [a,b], J.-L. Koeck [c], X. Deparis [a,b], R. Migliani [a,b]

[a] French Army Centre for Epidemiology and Public Health, Marseille, France
[b] École du Val-de-Grâce, Paris, France
[c] Department of Biology, Robert Picqué Military Teaching Hospital, Bordeaux, France

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ABSTRACT

Objectives: French military personnel are subject to a compulsory vaccination schedule. The aim of this study was to present the results of surveillance of vaccine adverse events (VAEs) reported from 2011 to 2012 in the French armed forces.

Study design: VAEs were surveyed among all French armed forces from 2011 to 2012 by the epidemiological departments of the military health service. For each case, a notification form providing patient and clinical information was provided.

Methods: Case definitions were derived from the French drug safety guidelines. Three types of VAE were considered: non-serious, serious and unexpected. Incidence rates were calculated by relating VAEs to the number of vaccine doses delivered.

Results: In total, 161 VAE cases were reported. The overall VAE reporting rate was 24.6 VAEs per 100,000 doses, and the serious VAE rate was 1.3 per 100,000 doses (nine cases). The serious VAEs included two cases of Guillain-Barré syndrome, one case of optic neuritis, one case of a meningeal-like syndrome, one case of rheumatoid purpura, one case of acute asthma and three cases of fainting. The highest rates of VAE were observed with the Bacille Calmette–Guérin vaccine (BCG) (482.3 per 100,000 doses), inactivated diphtheria–tetanus–poliovirus with acellular pertussis vaccine (dTap-IPV) (106.1 per 100,000 doses) and meningococcal quadrivalent glycoconjugate vaccine (MenACWY-CRM) (39.3 per 100,000 doses).

Conclusions: The global rates of VAE observed in 2011 and 2012 confirm the increase that has been observed since 2009 in the French armed forces, which could reflect improved practitioner awareness about VAEs and the use of certain vaccines added to the vaccination schedule recently (dTap-IPV in 2008 and MenACWY-CRM in 2010). VAEs appear to be relatively rare, particularly serious VAEs, which indicates acceptable tolerance of vaccines.

* *Corresponding author*. Centre d'épidémiologie et de santé publique des armées, GSBdD Marseille Aubagne, 111 avenue de la Corse, BP 40026, 13568 Marseille, Cedex 02, France. Tel.: +33 4 91 63 79 89; fax: +33 4 91 63 78 22.
E-mail address: aurelie_marie@hotmail.fr (A. Mayet).
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Introduction

According to a vaccination strategy that aims to provide individual and collective protection, French military personnel are subject to a compulsory vaccination schedule on enlistment and throughout their service period.[1] This schedule includes several vaccines that are often injected concurrently: Bacille Calmette–Guérin vaccine (BCG), inactivated diphtheria–tetanus (toxoids)–poliovirus vaccine (dT-IPV), acellular pertussis vaccine (dTap-IPV), inactivated influenza vaccine, tetravalent meningococcal vaccine, subunit hepatitis B vaccine, whole-virus-inactivated hepatitis A vaccine, typhoid vaccine, live yellow fever vaccine and measles–mumps–rubella vaccine (MMR). In this context, the monitoring of vaccine adverse events (VAEs) remains topical because it assures military personnel that the safety of required vaccines is taken seriously. The results from the surveillance of VAEs in the French armed forces from 2002 to 2010 estimated a global VAE reporting rate of 14.0 per 100,000 doses.[1] The rate of serious VAEs was 1.1 per 100,000 doses, which was comparable to rates observed among civilians and US military personnel.[2,3] An increase in VAEs among military personnel was observed from 2009, which was partly explained by increased practitioner awareness about VAEs following the influenza A(H1N1)pdm09 pandemic.[1]

The military vaccination schedule is reviewed each year by a committee of experts and, if necessary, adapted to the epidemiological context, in accordance with the recommendations of the French health authorities. Thus, a mass vaccination campaign for measles was implemented from 2010 to 2012 in response to the outbreak spreading in Europe: MMR booster vaccination was performed for subjects who had close contact with measles cases during their contagious period, new recruits, personnel deployed overseas, healthcare personnel and women of childbearing age.[4,5] This booster vaccination aimed to achieve two-dose status among adults born since 1980, and one-dose status among subjects born between 1965 and 1979. Another recent modification of the military vaccination schedule is the use, since 2011, of the novel semi-synthetic meningococcal quadrivalent glycoconjugate vaccine (MenACWY-CRM) (Menveo) as a replacement for the polysaccharide vaccine (Mencevax).

This article aims to present the results of VAE surveillance in the French armed forces from 2011 to 2012 in order to confirm the increase in VAEs observed since 2009, and to estimate the extent to which the above-mentioned modifications of the vaccination schedule could affect VAE rates.

Methods

French military VAE epidemiological surveillance, conducted by the Centre for Epidemiology and Public Health [Centre d'épidémiologie et de santé publique des armées (CESPA)], is mandatory and covers all active military personnel. The detailed methodology of this passive surveillance system has been published previously.[1] Reporting criteria for VAE cases are as follows.[6]

- Non-serious adverse events: VAEs following vaccination, which can be:
  - local events (pain, lump at the injection site, redness >5 cm, etc.) that persist for at least two days;
  - regional events (ulcer, lymph node tenderness and/or enlargement, adenitis, abscess at the injection site, etc.); or
  - systemic events (fever ≥38 °C or any event thought to be related to vaccination, with sick leave for more than two days).
- Serious adverse events: VAEs with hospitalization, persistent or significant disability, life-threatening illness or death. This category of events has to be reported immediately to the CESPA and requires a review of the subject's medical records.

Whether serious or non-serious, VAEs that are not listed in the French Summary of Product Characteristics are considered as unexpected VAEs.

In the case of simultaneous administration of several vaccines, the following vaccine suspicion algorithm is used. For local or regional VAEs, the vaccine suspected is the vaccine administered at the site of VAE occurrence. For systemic or serious VAEs, all administered vaccines are suspected. The use of this algorithm explains how the number of suspected vaccines exceeds the number of VAEs. Moreover, one vaccine could be responsible for several simultaneous VAEs in the same subject (e.g. fever associated with a lump at the injection site). For this reason, the number of VAEs presented exceeds the number of cases initially reported. This study investigated VAEs following all vaccines administered from 1 January 2011 to 31 December 2012. Vaccine-specific VAE reporting rates (rates per 100,000 doses) were calculated by dividing the number of VAEs (according to the vaccine suspicion algorithm) for each vaccine by the number of doses distributed according to the French military drug supply department. Poisson 95% confidence intervals (95% CI) were computed for VAE rates. A binomial law was used for 95% CIs of proportions. Data analysis was performed using Stata Version 9 (StataCorp, College Station, TX, USA).

Results

From 2011 to 2012, 1,005,044 vaccine doses were administered in the French armed forces (Table 1) and 193 VAE cases were reported, of which 27 (14.0%) were excluded because they did not meet reporting criteria (systemic events that did not lead to sick leave for more than two days or local events that persisted for less than two days). Analyses were thus performed on 166 VAE cases. After applying the vaccine suspicion algorithm, 258 vaccine injections were suspected in the occurrence of VAEs. The overall VAE reporting rate (all vaccines) for the 2011–2012 period was therefore 25.7 (95% CI 22.6–29.0) VAEs per 100,000 doses [19.0 (95% CI 15.4–23.1) per 100,000 doses in 2011 and 33.1 (95% CI 28.2–38.7) per 100,000 doses in 2012]. The serious VAE rate was 1.3 (95% CI 0.7–2.2) per 100,000 doses. As shown in Table 2, the highest VAE rates were observed for BCG [482.3 (95% CI 99.5–1409.5) per 100,000 doses], dTap-IPV [106.1 (95% CI 82.4–134.5) per 100,000 doses] and MenACWY-CRM [39.3 (95% CI 28.9–52.2) per 100,000 doses]. The VAE rate following