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RESEARCH

Analysis of adverse events following immunization caused by immunization errors

Análise da ocorrência de evento adverso pós-vacinação decorrente de erro de imunização

Análisis de la ocurrencia de eventos adversos posvacunales debido a errores de inmunización

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ABSTRACT

Objective: to analyze adverse events following immunization (AEFI) caused by immunization error in the state of Paraná, Brazil, from 2003 to 2013. **Method**: this is a descriptive, documental, retrospective, and quantitative research using secondary data from the Adverse Event Following Immunization Information System and the Immunization Program Evaluation System. We included cases confirmed and/or associated with different types of vaccines. For the analysis, we collected frequencies and incidence rates, and used simple linear regression models with Student's t-test. **Results**: it was observed an AEFI increase due to immunization errors, especially hot subcutaneous abscesses. BCG vaccine had the highest incidence of adverse events and children under one year old were the most affected individuals. **Conclusion**: the current scenario is worrisome because these are preventable AEFI – injuring patients due to bad vaccination practices – that may undermine the population's confidence, reducing immunization coverage, and the progress in the control of vaccine-preventable diseases.

Descriptors: Vaccination; Medication errors; Nursing; Public health nursing; Immunization.

RESUMO

Objetivo: analisar a ocorrência de Evento Adverso Pós-Vacinação (EAPV) decorrente de erro de imunização, no Paraná, de 2003 a 2013. **Método**: pesquisa descritiva documental, retrospectiva, quantitativa, utilizando dados secundários do Sistema de Informação de Evento Adverso Pós-Vacinação e do Sistema de Avaliação do Programa de Imunizações. Foram incluídos casos confirmados e/ou associados a outras vacinas. Para análise foram estimadas frequências, taxas de incidência e utilizados Modelos de Regressão Linear Simples com teste t-*Student*. **Resultados**: observou-se aumento da notificação de EAPV decorrente de erro de imunização, principalmente abscesso subcutâneo quente. BCG foi a vacina com maior incidência de eventos adversos, sendo que os menores de um ano, os mais atingidos. **Conclusão**: o cenário atual é preocupante, pois são EAPV evitáveis — que causam danos, ligados a prática da enfermagem, decorrentes de desvios da qualidade em vacinação — que podem interferir na confiança da população (reduzindo coberturas vacinais) e no controle de doenças imunopreveníveis.

Descritores: Vacinação; Erros de Medicação; Enfermagem; Enfermagem em Saúde Pública; Imunização.

RESUMEN

Objetivo: analizar la ocurrencia de Eventos Adversos Posvacunales (EAPV) debido a errores de inmunización, en Paraná, de 2003 a 2013. **Método**: investigación descriptiva documental, retrospectiva, cuantitativa, utilizando datos secundarios del Sistema de Información de Eventos Adversos Posvacunales y del Sistema de Evaluación del Programa de Inmunizaciones. Se incluyeron casos confirmados y/o asociados con otras vacunas. Para el análisis, se estimaron frecuencias, tasas de incidencia y se utilizaron Modelos de Regresión Lineal Simple con prueba t-*Student*. **Resultados**: se observó un aumento de la notificación de EAPV debido a errores de inmunización, principalmente abscesos subcutáneos calientes. BCG fue la vacuna con mayor incidencia de eventos adversos, siendo los menores de un año el grupo más afectado. **Conclusión**: la situación actual es preocupante, ya que son EAPV prevenibles — que causan daños, vinculados a la práctica de enfermería, resultantes de las desviaciones de la calidad en la vacunación — que pueden afectar la confianza de la población (reduciendo las coberturas de vacunación) y el control de enfermedades inmunoprevenibles.

Descriptores: Vacunación; Errores de Medicación; Enfermería; Enfermería en Salud Pública; Inmunización.

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INTRODUCTION

Vaccination is one of the most successful public health actions, contributing to reduce the incidence of vaccine-preventable diseases in Brazil through high rates of immunization coverage[1].

However, more types of immunobiological agents available in the public health network and more doses administered led to more adverse events following immunization (AEFI). AEFI is any untoward medical occurrence that follows immunization and does not necessarily have a causal relationship with the usage of the vaccine (immunobiologicals in general). It can be any untoward or not intentional event, an abnormal laboratory finding, a symptom, or a disease. This usage includes all processes after the production of a vaccine: storage, handling, prescription, and administration[2].

Over the years, to reduce risks to the client and maintain adherence to vaccination programs, many countries intensified surveillance on AEFI, rigorously monitoring the safety of immunobiological agents[3].

In 1992, following the recommendations of the World Health Organization (WHO), the National Immunization Programme/Ministry of Health (PNI/MS) began the National AEFI Surveillance System (SNVEAPV). One of its goals were to standardize detection and procedures for suspected cases of AEFI, create more knowledge on AEFIs, and detect flaws in transportation, storage, handling, or administration (immunization errors) that would result in adverse events[4].

Acknowledging the importance of surveillance on this kind of adverse event, the Ministry of Health Health Surveillance Secretariat (SVS) included it as notifiable disease under the 2005 decree No. 33/SVS/MS, revoked by 2014 decree No. 1.271/SVS/MS[4].

AEFI may have many causes related to immunobiological components, the vaccinated person, and the vaccine administration, considered an immunization error[4].

Immunization error is a medication error, classified as any preventable event that may cause or lead to inappropriate medication use (all immunobiologicals included) or cause harm to a patient while the product is handled by healthcare professionals, patients, or consumers. It may be related to professional practice, to the use of health products, procedures, and systems, which may happen if standards and techniques are not observed[4], causing or not an adverse event.

In this study, the AEFI caused by possible immunization error was defined as AEFI due to immunization error.

Concerns about immunization errors includes not only harms they may cause to the client, but also the negative impact on population's confidence on vaccination, which affects vaccination procedures and, consequently, reduces immunization coverage, compromising the control of vaccine-preventable diseases[5].

Vaccines are usually administered to healthy people, therefore, an adverse event, especially due to immunization error can result in low acceptance by the population, because it involves their security and is preventable[6].

A research in Iran investigated a cold abscess outbreak in 153 newborn children vaccinated in the hospital and found immunization error as its cause: the healthcare professional who gave the vaccines used the same syringe to administer the BCG vaccine and hepatitis B (HB) vaccine in the same child[7].

Nursing teams are the main responsible for immunization actions; however, their knowledge on AEFI is still limited, rendering difficult decision-making process when these events occur[8-9]. Alves and Domingos (2013)[9], in a study conducted in a Basic Health Unit (BHU), demonstrated that, for some nursing team members, actions that should be carried out in the case of an adverse event were restricted to observe and refer the patient to another professional or healthcare service.

The higher number of immunobiological agents available to the population and professionals involved in vaccination, as well as not following good immunization practices contribute to errors[10]. Therefore, monitoring their frequency will provide information that will provide knowledge to healthcare services to investigate causes and adopt measures to prevent and minimize them, especially in nursing actions, essential for a safe vaccination.

AEFI identification caused by immunization errors concerns public healthcare and may improve surveillance, services management, immunization performance of nurses, and professional training, also improving healthcare services quality and reducing the risk of injury.

OBJECTIVE

To analyze adverse events following immunization (AEFI) caused by immunization errors in the state of Paraná, Brazil, from 2003 to 2013.

METHODS

Ethical aspects

This research used secondary data only from post-vaccination adverse event caused by immunization errors, not requiring approval by the Research Ethics Committee.

Study design, location, and period

Descriptive research, documental, retrospective, quantitative approach, carried out in the state of Paraná from 2003 to 2013.

Sample; inclusion and exclusion criteria

We obtained empirical data from the AEFI Information System (SIEAPV) through AEFI records related to immunization errors notified in the state of Paraná, from 2003 to 2013. The sample consisted of all notifications of this adverse event. The inclusion criterion was AEFI case caused by immunization error, confirmed or associated with another vaccine, caused by an immunobiological agent administered in the state of Paraná. The exclusion criteria were cases with ignored information for one of the variables used in the study and/or having inconsistencies between the immunobiological agent and AEFI.

Study protocol

For data collection, we first searched in the surveillance of AEFI manual (VEAPV)[4] the types of adverse events description, identifying those that had among its causes immunization errors: cold subcutaneous abscess, hot subcutaneous abscess, granuloma, nonsuppurative lymphadenitis bigger than 3 cm, suppurative lymphadenitis, and ulcer bigger than 1 cm. Data

collection was carried out from April to June 2014, and we selected the following variables: event type, immunobiological agent, date of vaccine administration, gender, and closing (confirmed, associated to other vaccines, under investigation, and discarded). We stratified ages into age groups, as adopted by the National Immunization Programme (PNI).

Bearing in mind the possibility of duplicated records, inclusion of inaccurate data, and altering characters during database transfer from BDF to Excel®, it was necessary to check all selected records in SIEAPV individually to identify and correct possible mistakes. We found and excluded duplicated and inconsistent notifications, such as local event related to vaccine orally administered.

To calculate AEFI incidence rate (IR) due to immunization error for 100,000 doses of vaccine administered (d.a.) by year and event, we used as denominator the total doses of immunobiologicals administered on Paraná public healthcare network from 2003 to 2013, available in the Programme of Immunization Evaluation System (SIAPI) database. For IR by immunobiological type, the denominator was the number of vaccine doses administered from each product in the state of Paraná, registered on the SIAPI.

Analysis of results and statistics

We used tables and charts to present data distributed in absolute and relative frequency and IR using Microsoft Excel® 2010 and Epi Info (version 7.1.4), and examined data based on the scientific literature.

To analyze AEFI IR tendency caused by immunization error from 2003 to 2013, we used the software Statistical Package for the Social Sciences (SPSS) version 23.0. We generated a dispersion diagram adjusted to the simple linear regression model and conducted a goodness of fit test based on Snedecor's F distribution, adopting a significance level of $p < 0.05$. We used Student's t-test (significance level of $p < 0.05$) to test the linear regression model coefficients significance. Then, based on the growth rate we estimated point values for the two variables over the 2014-2018 period and the 95% confidence interval for the mean value over that period.

RESULTS

From 2003 to 2013, we found in SIEAPV 7,689 AEFI occurrences caused by immunization errors, confirmed and/or associated with another vaccine. After excluding 321 notifications with incorrect or duplicated data, we had to a total of 7,368 events. 604 events (8.2%) were records from the state of Paraná and served as the database for this study.

Cases distribution by sex was similar at a proportion of 51.8% of women and 48.2% of men.

Among the six types of AEFI caused by immunization error found in the period considered, the hot subcutaneous abscess had the highest percentage (40.7%) and incidence (0.32/100,000 d.a.). Analyzing adverse events per year, we found that until 2010 the highest IRs were cold subcutaneous abscess and regional suppurative lymphadenitis. Ulcers bigger than 1 cm maintained similar rates, except in 2007 (year without notification) and 2011 (registered a pronounced increase [0.11/100,000 d.] (Table 1).

Regarding vaccines related to AEFI caused by immunization error, BCG had the highest percentage recorded (57%), followed by diphtheria vaccine, tetanus vaccine, pertussis vaccine, and Haemophilus influenzae type b vaccine (DTP/Hib) (7.3%), and DTP/Hepatitis B (HB)/Haemophilus influenzae type b vaccine (DTP/HB/Hib) (6.6%).

We found that IR of AEFI caused by the administration of BCG vaccine recorded little variation until 2010, increasing in 2011 and 2013, having the highest incidence from 2003 to 2013 (19.14/100,000 d.a.). The same occurred to DTP/Hib and DTP/HB/Hib vaccines (in bold in tables and discussed as a whole, given that in 2012 the former was replaced by the latter). Human antitetanus immunoglobulin (HATIG) high IR in 2012 drew our attention (72.8/100,000 d. a.) (Table 2).

Table 1 – Percentage and incidence rate distribution of adverse events following immunization caused by immunization errors (100,000 doses administered), per year and type, state of Paraná, Brazil, 2003-2013

Year	Cold subcutaneous abscess		Hot subcutaneous abscess		Regional nonsuppurative lymphadenitis > 3 cm		Regional suppurative lymphadenitis		Ulcer > 1 cm		Total	
	n = 177		n = 246		n = 51		n = 95		n = 35		N = 604	
	%	IR	%	IR	%	IR	%	IR	%	IR	%	IR
2003	34.5	0.15	20.7	0.09	20.7	0.09	13.8	0.06	10.3	0.05	100	0.44
2004	42.1	0.20	18.4	0.09	5.2	0.02	26.3	0.12	7.9	0.04	100	0.46
2005	27.8	0.14	33.3	0.17	13.9	0.07	19.4	0.10	5.6	0.03	100	0.51
2006	39.3	0.17	21.4	0.09	3.6	0.02	28.6	0.13	7.1	0.03	100	0.44
2007	37.5	0.18	15.6	0.07	9.4	0.04	37.5	0.18	0	0	100	0.48
2008	31.4	0.10	17.1	0.05	11.4	0.04	34.3	0.11	5.7	0.02	100	0.31
2009	39.4	0.19	15.2	0.07	15.2	0.07	21.2	0.10	9.1	0.04	100	0.48
2010	19.4	0.08	22.6	0.09	12.9	0.05	29.0	0.12	16.1	0.06	100	0.40
2011	29.8	0.35	45.2	0.53	9.5	0.11	6.0	0.07	9.5	0.11	100	1.18
2012	30.4	0.42	53.2	0.76	5.1	0.07	6.3	0.09	5.1	0.07	100	1.38
2013	21.8	0.73	62.6	2.10	5.0	0.17	8.9	0.30	1.7	0.06	100	3.36
Total	29.3	0.23	40.7	0.32	8.4	0.07	15.7	0.12	5.8	0.05	100	0.78

Source: SIEAPV/PNI/MS-API/DVVPI/SESA/PR
Note: IR = incidence rate

Table 2 – Incidence rate distribution of adverse events following immunization caused by immunization error (100,000 doses administered), per immunobiological agent and year, state of Paraná, Brazil, 2003-2013

Immunobiological agent	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	Total
	n = 29	n = 38	n = 36	n = 28	n = 32	n = 35	n = 33	n = 31	n = 84	n = 79	n = 179	N = 604
	IR	IR	IR	IR	IR	IR	IR	IR	IR	IR	IR	IR
BCG	12.20	18.40	17.90	13.50	18.30	18.60	17.60	15.80	29.40	18.90	30.81	19.14
DTP/HB/Hib*	-	-	-	-	-	-	-	-	-	1.69	8.60	7.14
DTP/Hib*	0.82	0.42	0.21	0.87	0.22	0.69	0.67	0	3.23	3.33	-	0.98
HATIG	0	0	0	0	0	0	0	0	0	72.8	0	7.12
IPV	0	0	0	0	0	0	0	0	0	5.83	6.95	6.86
PPSV23	0	0	0	0	0	0	0	15.80	26.00	7.78	7.17	5.43
DTP	1.34	0.38	0.66	0.36	0	0	0	0.40	1.98	2.16	2.92	0.89
PCV10*	-	-	-	-	-	-	-	0	0	0.87	2.02	0.78
Td	0	0.25	0.11	0.14	0	0.10	0.29	0.27	0.81	0.44	5.73	0.46
IV	0	0	0	0	0	0	0	0	0	1.93	7.17	0.41
Men-C	0	0	0	0	0	0	0	0	0.20	0.23	0.23	0.20
HB	0.10	0	0.11	0	0.14	0	0	0.14	0.40	0.42	0.68	0.17
YF	0	0.21	0	0	0.29	0	0	0	0.33	0.24	0.99	0.15
RV	17.60	0	0	0	0	0	0	0	0	0	0	0.13
MMR	0	0	0	0	0	0.03	0	0	0.27	0.31	0.87	0.09

Source: SIEAPV/PNI/MS-API/DVVPI/SESA/PR

*Notes: * IR: Incidence rate; **IR estimated only with administered doses of Bacillus Calmette-Guérin (BCG) vaccine; DTP/HB/Hib: diphtheria, tetanus, pertussis vaccine (adsorbed) / hepatitis B vaccine (Recombinant) / Haemophilus influenzae type b conjugate vaccine; DTP/Hib: diphtheria, tetanus, pertussis vaccine (adsorbed) / Haemophilus influenzae type b conjugate vaccine; HATIG: human antitetanus immunoglobulin; IPV: polio vaccines 1, 2 and 3 (inactivated); PPSV23: 23-valent pneumococcal polysaccharide vaccine; DTP: diphtheria, tetanus, pertussis vaccine (adsorbed): PCV10: 10-valent pneumococcal conjugate vaccine; Td: diphtheria and tetanus vaccine adsorbed for adults; IV: influenza vaccine (fractional, inactivated); Men-C: Meningococcal C conjugate vaccine; HB: hepatitis B vaccine (Recombinant); YF: yellow fever vaccine (attenuated); RV: vero cell rabies vaccine; MMR: measles, mumps, and rubella vaccine (attenuated).*

When we related the type of AEFI caused by immunization error with the vaccines administered, we found that the highest incidence was hot subcutaneous abscess (IR = 0.46/100,000), caused mainly by HATIG (IR = 7.12/100,000), inactivated polio vaccine (IPV, IR = 6.86/100,000 d.a.), DTP/HB/Hib and DTP/Hib (IR = 6.27/100,000 d.a.), and 23-valent pneumococcal polysaccharide vaccine (PPSV23, IR = 5.43/100,000 d.a.).

We identified in supplementary analysis that of all cases of hot subcutaneous abscess after HB vaccination, one was a newborn, vaccinated at birth, probably in the hospital environment. Of the 37 notifications of ulcer bigger than 1 cm, three were BCG revaccination.

The BCG vaccine was responsible for 41.3% of all cases of cold subcutaneous abscess, lymphadenitis, and ulcer bigger than 1 cm. HATIG, IPV, PPSV23, Meningococcal C conjugate (Men-C), yellow fever (attenuated) (YF), and rabies (RV) vaccines did not have notifications of cold subcutaneous abscess (Table 3).

The distribution of types of AEFI caused by immunization error by age group showed that children under one year old were more affected in all events studied (70.5%) and regional nonsuppurative lymphadenitis > 3 cm was notified only in this population group (Table 4).

Children aged from 1 to 10 years comprised 18% of the records, distributed mostly in hot and cold subcutaneous abscess. We observed an increase in adverse events percentage in adults from 30 to 60 years old and older (8.9%), most of hot subcutaneous abscess (Table 4).

Additional data on AEFI cases caused by immunization error have revealed that, of the events notified per immunobiological agent and age group, the highest percentages were BCG vaccines administered in children under one year old (72.1%), aged one year (37.5%) and two years (57.1%). BCG vaccine administration also affected adults from 25 to 29 years old (50%) and from 50 to 59 years old (5.5%). Influenza vaccine (IV) caused 69.2% of adverse events in 3-year-old children, which also caused 44.4% of adverse events in 4-year-old children and 43.8% in children from 5 to 10 years old. DTP was responsible for 44.4% of AEFI in 4-year-old children, age when a booster dose is administered.

In the trend analysis of AEFI caused by immunization error the simple linear regression model showed that the immunization error growth rate over the years considered was 0.184, indicating also the average growth per year. Figure 1 presents values for the 2003-2013 period, as well as the estimated average for the 2014-2018 period, which ranged from 2.54 in 2014 to 3.27 in 2018. For 2014, the confidence interval was from 0.76 to 2.57 and for 2018 from 0.99 to 3.81, indicating an increasing tendency of occurrence of AEFI caused by immunization errors.

Table 3 – Incidence rate and frequency distribution per 100,000 doses administered of types of adverse events following vaccination caused by immunization error, per immunobiological agent, state of Paraná, Brazil, 2003-2013

Immunobiological agent	Cold subcutaneous abscess		Hot subcutaneous abscess		Regional nonsuppurative lymphadenitis > 3 cm		Regional suppurative lymphadenitis		Ulcer > 1cm		Total	
	%	IR	%	IR	%	IR	%	IR	%	IR	%	IR
BCG	41.3	7.90	6.1	1.17	14.8	2.84	27.6	5.29	10.2	1.95	100	19.14
DTP/HB/Hib*	22.5	1.61	77.5	5.53	0	0	0	0	0	0	100	7.14
DTP/Hib*	25.0	0.25	75.0	0.74	0	0	0	0	0	0	100	0.98
HATIG	0	0	100	7.12	0	0	0	0	0	0	100	7.12
IPV	0	0	100	6.86	0	0	0	0	0	0	100	6.86
PPSV23	0	0	100	5.43	0	0	0	0	0	0	100	5.43
DTP	7.7	0.07	92.3	0.83	0	0	0	0	0	0	100	0.89
PCV10*	17.6	0.14	82.4	0.64	0	0	0	0	0	0	100	0.78
Td	10.5	0.05	89.5	0.41	0	0	0	0	0	0	100	0.46
IV	8.1	0.03	91.9	0.38	0	0	0	0	0	0	100	0.41
Men-C	0	0	100	0.20	0	0	0	0	0	0	100	0.20
HB	14.3	0.02	85.7	0.14	0	0	0	0	0	0	100	0.17
YF	0	0	100	0.15	0	0	0	0	0	0	100	0.15
RV	0	0	100	0.13	0	0	0	0	0	0	100	0.13
MMR	14.3	0.01	85.7	0.08	0	0	0	0	0	0	100	0.09
Total	29.3	0.33	40.7	0.46	8.4	2.84**	15.7	5.29**	5.8	1.95**	100	1.12

Source: SIEAPV/PNI/MS-API/DVVPI/SESA/PR

*Notes: * vaccines not available in the PNI/MS vaccination calendar in those years; ** Estimated IR only with BCG doses administered.*
*IR : Incidence rate; **IR estimated only with administered doses of Bacillus Calmette-Guérin (BCG) vaccine; DTP/HB/Hib: diphtheria, tetanus, pertussis vaccine (adsorbed) / hepatitis B vaccine (Recombinant) / Haemophilus influenzae type b conjugate vaccine; DTP/Hib: diphtheria, tetanus, pertussis vaccine (adsorbed) / Haemophilus influenzae type b conjugate vaccine; HATIG: human antitetanus immunoglobulin; IPV: polio vaccines 1, 2, and 3 (inactivated); PPSV23: 23-valent pneumococcal polysaccharide vaccine; DTP: diphtheria, tetanus, pertussis vaccine (adsorbed): PCV10: 10-valent pneumococcal conjugate vaccine; Td: diphtheria and tetanus vaccine adsorbed for adults; IV: influenza vaccine (fractional, inactivated); Men-C: Meningococcal C conjugate vaccine; HB: hepatitis B vaccine (Recombinant); YF: yellow fever vaccine (attenuated); RV: vero cell rabies vaccine; MMR: measles, mumps, and rubella vaccine (attenuated).*

Table 4 – Percentage distribution of types of adverse events following vaccination caused by immunization error, per age group, state of Paraná, Brazil, 2003-2013

Age group (in years)	Cold subcutaneous abscess	Hot subcutaneous abscess	Regional nonsuppurative lymphadenitis > 3 cm	Regional suppurative lymphadenitis	Ulcer >1cm	Total
	n = 177	n = 246	n = 51	n = 95	n = 35	N = 604
	%	%	%	%	%	%
< 1	78.5	47.6	100	95.0	82.9	70.5
1	6.8	11.0	0	5.0	11.4	7.9
2	4.0	2.0	0	0	5.7	2.3
3	3.4	2.8	0	0	0	2.2
4	1.1	6.5	0	0	0	3.0
5 l-l 10	1.1	5.7	0	0	0	2.6
11 l-l 14	0.6	0.8	0	0	0	0.5
15 l-l 19	0	1.6	0	0	0	0.7
20 l-l 24	0	1.6	0	0	0	0.7
25 l-l 29	1.1	0.8	0	0	0	0.7
30 l-l 39	1.7	5.3	0	0	0	2.6
40 l-l 49	0	5.7	0	0	0	2.3
50 l-l 59	1.1	6.5	0	0	0	3.0
60 and older	0.6	2.0	0	0	0	1.0
Total	100	100	100	100	100	100

Source: SIEAPV/PNI/MS

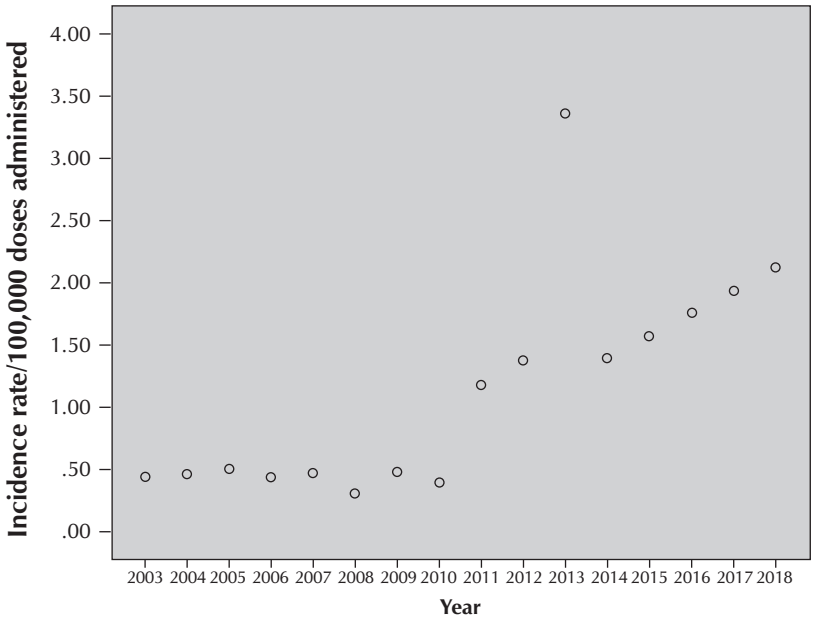

Figure 1 – Scatter plot of observed and estimated values for adverse event following immunization caused by immunization error over the 2003-2013 period and estimated for the 2014-2018 period, Paraná, Brazil, 2015

DISCUSSION

The notification of AEFI caused by immunization error increased from 2011 onwards, when new vaccines have been introduced and changes have been made in the National Vaccination Calendar. In 2011 HB vaccine was administered to older age groups and IV coverage expanded.

In 2012, DTP/HB/Hib and IPV vaccines were included, and HB vaccine was administered to older age groups. In 2013, varicella vaccine was incorporated into the national vaccination calendar[11].

The increased in adverse events is related to many factors, e.g., increased AEFI surveillance on the municipalities and lack of proper vaccine administration. Before the beginning of immunization campaigns and the introduction of a new vaccine, PNI sends to the states and the states to the cities a technical report with guidelines and targets to be achieved. This document emphasizes the importance and necessity of surveillance, citing adverse events caused by each type of vaccine, so that healthcare professionals stay informed and more alert to expected or unexpected situations[12].

The actions developed by the Paraná Immunization Program also contributed to the increase in adverse event notifications. In the second half of 2010, a workshop was held with discussions on immunization errors and had the participation of technicians from the Regional Health Administration (RS) and their host cities, so as to train and sensitize healthcare professionals who worked in the immunization program.

In the following years, healthcare professionals who work in the RS and in Brazilian cities participated in videoconferences on AEFI and, in 2013, 426 professionals participated in a training program on AEFI notification and investigation. In that same year, compared to 2012, notifications of adverse events in SIEAPV increased 20%, as well as the percentage of cities that notified adverse events (16%).

This indicates that, besides training healthcare technicians, it is important to discuss with health services managers strategies to improve epidemiological surveillance to monitor AEFI.

The analysis of AEFI incidence caused by immunization error showed that, although during the campaigns the demand of vaccination rooms increases, in the years in which they were held — 2004 (National Measles Immunization Campaign), 2008 (National Rubella Immunization Campaign), and 2010 (National Influenza A H1N1 Vaccination Campaign)[11] — IR did not increase.

The findings revealed that 40.7% of notifications concerned hot subcutaneous abscess associated to several vaccines administered via different routes, a percentage higher than the found by Piacentini and Contrera-Moreno (2011)[13] and by Moura et al. (2015)[14] for DTP/Hib. This type of abscess caused by BCG, however, had IR lower than the estimated in the VEAPV manual[4]. Infectious etiology modifies the treatment and an antimicrobial agent must be used[2,4]. Its cause is related to deviation from best immunization practices, especially poor hand hygiene.

Thuong et al. (2007)[17] investigated a serious AEFI outbreak, with one death after the administration of measles, mumps, and rubella vaccine (MMR): six cases (HB vaccine, two cases, and varicella vaccine, one case) in a healthcare center, involving nine children with abscess on the injection site. Methicillin-resistant Staphylococcus aureus was isolated, collected in the community (CA-MRSA) in samples of pus from the abscess, as well as nasal and throat colonization from the professional who administered the vaccine to eight children. During the investigation, they have identified inadequate infection control practices in the vaccination room, e.g., the use of the same pair of gloves to prepare the immunobiological agents and administer the vaccine to three to six people, without hand washing. They concluded that the infection was transmitted by the healthcare professional, possibly contaminating the vaccine or the needle during the dose preparation, or even, the skin surface on the injection site. They also emphasized that poor hand hygiene contribute to AEFIs.

Tan et al. (2010)[16] identified other MRSA infections following immunization in their retrospective study. The authors identified seven cases of infectious abscess on DTPa/Hib/IPV vaccine injection site, four of them vaccinated in the same healthcare center. After investigating, they concluded that the adverse events were caused by immunization error, by contamination during the vaccine administration.

For the biosecurity of healthcare professionals and vaccinated persons, PNI establishes that the professional must wash

his or her hands before and after handling materials and immunobiologicals, administer every vaccine and perform activities within the vaccination room[15]. Research conducted in Brazil, however, confirm Thuong et al. (2007)[17] findings regarding negligence of many professionals in washing their hands, because 68.3% of them in a BHU did not wash their hands in accordance with the National Sanitary Surveillance Agency (Anvisa)[18] rules. The authors also observed this in professionals from other units, who did not wash their hands properly before and after procedures[19].

These findings strengthen the theory of contamination caused during vaccine administration, probably related to the high incidence of hot subcutaneous abscess after HATIG in 2012, showing the risk of exposure to AEFI caused by immunization error, also with immunobiological agents administered in emergency units and hospitals. In these environments, quality deviation may occur during vaccine administration due to the lack of qualified professionals. The reduced number of doses administered do not provide opportunity for training and skill development.

In Brazil, the BCG vaccine is administered via intradermal route[4], which requires knowledge, technique, and skill. BCG vaccine administration is safe if administered correctly[18], but deep injection into subcutaneous tissue, contamination during administration, and overdoses may cause abscess, ulcers bigger than 1 cm, lymphadenitis, etc., which require follow up and/or drug treatment[4,18,20].

Although among AEFIs there is a significant incidence of hot subcutaneous abscess and suppurative or nonsuppurative lymphadenitis (after BCG), results obtained in this study indicated frequencies lower than those estimated by the PNI[4], even if another research found much lower values than our research[20]. It is worth mentioning that these data may have been influenced by underreported cases using passive surveillance, which is adopted by the SNVEAPV[3].

Nonsuppurative lymphadenitis bigger than 3 cm, after BCG, may be caused by vaccination errors, while nonsuppurative lymphadenitis up to 3 cm is expected in 10% of vaccinated persons, with a benign, self-limited course[4]. The correct diagnosis of this adverse event in clinical trials requires skills from the assistant and the lack of experience can difficult the explanation of its causes, leading to an underreported AEFI.

Another important measure to avoid notifying AEFI caused by immunization error by mistake is to investigate BCG revaccination, for this vaccine may cause a faster and exacerbated development of ulcer on the injection site[4,21-22], not configuring thus AEFI caused by immunization error.

Cold subcutaneous abscess (sterile) following immunization occur generally by incorrect administration and is observed in BCG and vaccines containing aluminum hydroxide adjuvant in their composition[4,23]. As found in this study, out of nine vaccines that caused this adverse event, six contained aluminum. This may be a sign of incorrect subcutaneous administration, when it should be administered intramuscularly. It happens more frequently in DTP/Hib and DTP/HB/Hib.

Therefore, whereas MMR vaccine and some types of IV vaccines do not contain adjuvant and cold subcutaneous abscess is not an expected AEFI[4], data recorded were probably bad diagnosis. These vaccines cause local, mild, and with low frequency inflammatory reactions[4]. These reactions may have been taken for cold subcutaneous abscess by a low experienced professional who lacked proper knowledge on the subject.

Children have been more affected by AEFI caused by immunization error. This is due to anxiety during vaccination; some professionals lack of skills; and mostly the types of immunobiologicals and the amount of doses administered in children under 5 years in public healthcare system. Until this age, 13 vaccines are administered, eight with two or more doses and/or booster dose, increasing chances of AEFI, as demonstrated by the high percentage in this age group (85.9%). These data confirm findings from another research, in which 73% of notified events were also in children under 5 years old[24].

The high percentage of adverse events notified in 4-year-old children coincides with the period when must be administered the second booster dose of this vaccine.

AEFI caused by immunization error numbers are increasing, especially in the past few years, with upward tendency until 2018, as the linear regression model shows. This may be a consequence of improved surveillance, but may also indicate poor nursing practices in the vaccination room.

Alves e Domingos (2013)[9] identified deficiency in vaccination and AEFI management by nursing professionals, indicating the need for vaccination room training, including immunobiologicals and PNI standards. It is also important to address basic procedures for safe vaccination, e.g., child's inadequate positioning, which may facilitate their movements during vaccine administration, with risk of damage.

One must consider also other factors that contribute to immunization error occurrences, associated to organizational structure, environment, and other factors that should be addressed by the investigation of its causes, to ensure a safe vaccination.

Study limitations and contributions to nursing and healthcare

This study presented some limitations for using SIEAPV and SIAPI database, subject to problems in the quality of the records and underreported cases, which may affect some results. It contributed, however, to nursing and healthcare, because the knowledge on types of AEFI caused by immunization error occurrences allows investigating its causes, plan, and develop actions that have an impact on determinants and conditions of errors, contributing to the safe vaccination practices and keeping the population confidence high in the immunization program.

CONCLUSION

This study made it possible to identify and characterize the types of AEFI caused by immunization error notified in the state of Paraná, and analyze occurrences, collaborating with deeper knowledge on this subject that arose interest in many segments of society.

The results revealed important data for immunization safety, showing the risk population is subjected to AEFI caused by immunization error. We highlight the hot subcutaneous abscess event, with the highest IR (0.32/100,000 d.a.), increasing in the period studied; BCG vaccine, responsible for the higher incidence of adverse events studied (19.14/100,000 d.a.); and under-one-year children, those who most suffered AEFI caused by immunization error (70.5%).

The IR's increasing tendency for the next years of these adverse events is preoccupying, mostly because of the damages they cause and which may be prevented, intimately related to nursing immunization practices. This scenario may the affect population acceptance of immunobiologicals and reduce vaccine coverage, putting at risk the control of some vaccine-preventable diseases.

Although the available literature has shown that ulcers and some lymphadenitis are caused by factors related to vaccination, there is little evidence of these events occurring solely by immunization error. To elucidate and confirm the causes, it is important to develop prospective studies to investigate all the whole vaccination process and identify the factors involved in the occurrence of AEFI caused by immunization error.

The current scenario requires changes to reduce the incidence of AEFI caused by immunization error. Therefore, it is important to identify the causes of the errors and the influence of multiple factors, not just those related to the individual. The actions developed must be effective, especially together with the nursing staff, considering organizational, environmental, psychological, and other factors so as to contribute to immunization security and quality.

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