

Adverse Post-Vaccination Events to BCG in Cacoal City, Rondonia, Brazil - 2016-2018 Period

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Abstract— The Calmette-Guérin Bacillus (BCG) vaccine is used against severe forms of tuberculosis. Although BCG post vaccination adverse events (EAPV) are uncommon, when identified they should be reported. The objective was to characterize the EAPV to BCG in the Municipality of Cacoal / RO from 2016-2018. This is a documentary, cross-sectional and descriptive study of quantitative approach, conducted with secondary data obtained from the reporting / investigation forms of AEFI to BCG, in the period 2016-2018 of individuals residing in Cacoal / RO. The population consisted of 13 notification forms, and they were part of sample 11, since 02 met the exclusion criteria. Data were collected through a collection instrument prepared by the researchers and the project was executed after authorization by the Municipal Secretary of Health and CEP under CAAE No. 2556919.0.0000.5298. During the study period, 4,677 individuals were vaccinated with BCG, data collected through the SI-PNI. Of the 11 AEFIs reported, 7 were male and 4 female. The AEFIs identified with the respective proportion of cases in the study population were: cold subcutaneous abscess (2.67: 2.500), non-suppurative regional lymphadenopathy (1.6: 2.500), warm subcutaneous abscess (1.07: 2.500) and lymphadenopathy. regional suppuration (0.5: 2,500). Among the 11 cases studied, 04 did not follow the AEFI management protocol. It was concluded that VAPA to BCG predominated in males, in children younger than 1 year old and that cold subcutaneous abscess, non-suppurative regional lymphadenopathy and warm subcutaneous abscess are above the standard recommended by NIBP.

Keywords— Calmette-Guérin Bacillus Vaccine. Adverse event. Notification of grievance.

Eventos Adversos Pós-Vacinação à BCG No Município De Cacoal, Rondônia, Brasil -Período De 2016-2018

Resumo— A vacina Bacilo de Calmette-Guérin (BCG) é utilizada contra formas graves da tuberculose. Embora os eventos adversos pós vacinação (EAPV) à BCG não sejam frequentes, quando identificados devem ser notificados. Objetivou-se caracterizar os EAPV à BCG no Município de Cacoal/RO no período de 2016-2018. Trata-se de um estudo documental, transversal e descritivo de abordagem quantitativa, realizado com dados

secundários obtidos através das fichas de notificação/investigação de EAPV à BCG, no período 2016-2018 de indivíduos que residem em Cacoal/RO. A população foi composta por 13 fichas de notificação, e fizeram parte da amostra 11, pois 02 se enquadraram nos critérios de exclusão. Os dados foram coletados através de um instrumento de coleta elaborado pelos pesquisadores e o projeto foi executado após autorização pelo Secretário Municipal de Saúde e CEP sob CAAE nº 2556919.0.0000.5298. No período do estudo foram vacinados com BCG 4.677 indivíduos, dados levantados por meio do SI-PNI. Dos 11 EAPV notificados, 07 eram do sexo masculino e 04 do sexo feminino. Os EAPV identificados com a respectiva proporção de casos na população do estudo foram: abscesso subcutâneo frio (2,67:2.500), linfadenopatia regional não supurada (1,6:2.500), abscesso subcutâneo quente (1,07:2.500) e linfadenopatia regional supurada (0,5:2.500). Dentre os 11 casos estudados, 04 não seguiram o protocolo de manejo dos EAPV. Conclui-se que os EAPV à BCG predominaram no sexo masculino, em crianças menores de 01 ano e que os EAPV do tipo abscesso subcutâneo frio, linfadenopatia regional não supurada e abscesso subcutâneo quente estão acima do padrão preconizado pelo PNI.

Palavras-chave— Vacina Bacilo de Calmette-Guérin. Evento adverso. Notificação de agravo.

Eventos Adversos Después De La Vacunación A BCG En Cacoal City, Rondonia, Brasil - Período 2016-2018

Resumen— La vacuna Calmette-Guérin Bacillus (BCG) se usa contra formas graves de tuberculosis. Aunque los eventos adversos posteriores a la vacunación con BCG (EAPV) son poco frecuentes, cuando se identifican, deben informarse. El objetivo fue caracterizar el EAPV a BCG en el Municipio de Cacoal / RO desde 2016-2018. Este es un estudio documental, transversal y descriptivo de enfoque cuantitativo, realizado con datos secundarios obtenidos de los formularios de informe / investigación de AEFI a BCG, en el período 2016-2018 de individuos que residen en Cacoal / RO. La población constaba de 13 formularios de notificación, y formaban parte de la muestra 11, ya que 02 cumplía los criterios de exclusión. Los datos fueron recolectados a través de un instrumento de recolección preparado por los investigadores y el proyecto fue ejecutado después de la autorización del Secretario Municipal de Salud y CEP bajo el CAAE No. 2556919.0.0000.5298. Durante el período de estudio, 4.677 personas fueron vacunadas con BCG, datos recopilados a través del SI-PNI. De los 11 AEFI reportados, 7 eran hombres y 4 mujeres. Los AEFI identificados con la proporción respectiva de casos en la población de estudio fueron: absceso subcutáneo frío (2.67: 2.500), linfadenopatía regional no supurativa (1.6: 2.500), absceso subcutáneo cálido (1.07: 2.500) y linfadenopatía supuración regional (0.5: 2,500). Entre los 11 casos estudiados, 04 no siguieron el protocolo de gestión AEFI. Se concluyó que VAPA a BCG predominaba en varones, en niños menores de 1 año y que el absceso subcutáneo frío, la linfadenopatía regional no supurativa y el absceso subcutáneo cálido están por encima del estándar recomendado por NIBP.

Palabras clave— Vacuna Calmette-Guérin Bacillus. Evento adverso. Notificación de quejas.

I. INTRODUCTION

Tuberculosis (TB) is a classic disease related to poverty, being one of several neglected diseases. The predominance of TB affects the most vulnerable, being poor and marginalized, who for years make up the majority of those affected by the disease (MACIEL, 2016).

Worldwide, the TB mortality rate declined by 40% between 1990 and 2010, with a 70.7% drop in the Americas. Brazil currently ranks 16th among the 22 countries with the most tuberculosis cases worldwide (BRASIL, 2014a).

In the state of Rondônia, the incidence rate of TB

in the year of 1990 was 68.6 / 100 thousand inhabitants, a significant decrease is observed when compared to the year of 2015, which the incidence rate was 29.1 / 100 thousand inhabitants (BRASIL, 2017). It is also observed in the Café Region, in which the municipality of Cacoal belongs, that during 2015, 16 new cases of TB were registered, with a 81.3% cure rate. This percentage, when compared to the other regions of the state, occupies the 3rd position, just behind the Region of Zona da Mata and the Central Region, with regard to the rate of cure of the disease (SINAN; AGEVISA, 2016).

One of the most effective ways of preventing severe forms of TB is the Bacillus Calmette-Guérin (BCG) vaccine, which in Brazil is recommended at birth and in leprosy contacts. Adverse reactions resulting from BCG are not frequent in the literature, but the risks of local events vary between 0.01 to 6.0 per 1,000 live births. Adverse events characterized as disseminated infections occur between 6 (six) to 12 (twelve) months after vaccination and are more rare events (BARRETO; PEREIRA; FERREIRA, 2006).

The usual time for BCG to evolve is 6 to 12 weeks, and may rarely extend until the 24th week. During the normal course of the vaccine lesion, axillary and supra or infraclavicular ganglionic infarction may occur, single or multiple, without suppuration. The lymph node appears three to six weeks after vaccination, it is homolateral to the application site, firm, mobile, clinically very noticeable, cold, painless, measuring up to 3 cm in diameter and not accompanied by general symptoms. It can evolve for a variable time, usually around four weeks and remains stationary for one to three months (BRASIL, 2014a).

Although adverse events to BCG are not frequent, every vaccinated individual may develop an adverse event after vaccination (AEFI), which are undesirable clinical situations, which can occur in people who have received some type of immunobiological. Regarding immunobiologicals, the vast majority can develop AEFV, which are considered mild, such as fever and local reaction, they can also develop as moderate and severe, leading to the individual's hospitalization and disability, and even death (SILVA et al., 2016).

Among the expected events, we can have relatively trivial events, such as: fever, pain and local edema; or more serious events, such as: febrile seizures, among others. Unexpected events are those arising from problems related to product quality, such as contamination of lots; causing local abscesses, or undue endotoxin content in certain vaccines, leading to feverish reactions and sepsis-like symptoms (BRASIL, 2014a).

Three basic points are used for the investigation of an adverse event, namely: factors related to the vaccine, factors related to vaccines and factors related to administration (BRASIL, 2014a).

Serious adverse events after vaccination are part of the national list of Compulsory Notification diseases / diseases, that is, it is mandatory to be notified, and any health professional who identifies the adverse event is responsible for this notification (BRASIL, 2016).

Given the above, this research is relevant, as the data collected in this study regarding the characterization of adverse events to BCG, as well as the proportion of these

events, will serve as a basis to identify whether these adverse events are within the parameters expected by the Ministry of Health (MS), as well as serving as a subsidy for the development of actions to improve the quality of care provided, together with the National Immunization Program (PNI), with regard to the BCG vaccine.

This work aims to characterize the adverse events after BCG vaccination in the municipality of Cacoal / RO in the period 2016-2018, according to gender and age, to identify the proportion of these events for correlation with the normal parameters of the PNI, to classify the types adverse events according to the signs and symptoms presented and verify the evolution and conclusion of the reported adverse events.

II. MATERIALS AND METHODS

This is a documentary, cross-sectional and descriptive study with a quantitative approach, carried out with secondary data obtained through the notification / investigation forms of adverse events after vaccination of patients who presented some type of adverse event after BCG vaccination, in the period from January 2016 to December 2018, of residents in the municipality of Cacoal / RO.

The study population consisted of 13 patients who had an adverse event to the BCG vaccine in the period proposed by the study and were notified by means of the notification / investigation form of adverse events after vaccination, with the sample consisting of 11 patient notifications, as 02 were excluded from the study, as they met the exclusion criteria, as they were not vaccinated in Cacoal and do not reside in the municipality.

As inclusion criteria, they were determined by means of notification / investigation forms of adverse events after vaccination and medical records of patients residing in the municipality of Cacoal / RO and who presented some type of adverse event after vaccination to BCG, in the period from January 2016 to December 2018. As exclusion criteria, medical records with illegible handwriting, adverse event notification forms to BCG with illegible handwriting and adverse event notification forms to other vaccines, which were not BCG, were determined.

The data collection questionnaire was developed by the researchers, containing 07 closed questions and 06 open questions, with information about the gender and age of the study population and variables related to the notified AEFI, namely: proportion of reported adverse events that will be correlated with the expected events standardized by the Ministry of Health through the PNI, classification of the AEFIs reported according to the signs and symptoms presented, classification of the evolution of the case and

conclusion of the notified case.

The data collected through the adverse event notification form were collected according to the availability of the time of the technician in charge, who works in the municipality's Health Department and in the Specialized Outpatient Clinic, on 07/05/2019 and 07/31 / 2019, in the morning period. At this moment, the number of vaccinees with the BCG vaccine in the municipality of Cacoal / RO was made available by the digitizer of the National Immunization Program Information System (SI-PNI), and the number of individuals vaccinated in 2016 was 1,435 , in 2017 the total was 1,675 and in 2018, 1,567 individuals, totaling 4,677 vaccinated individuals between January 2016 and December 2018.

Access to patients' medical records was made impossible due to the lack of computerization in basic health units, which made it impossible to locate them.

After data collection, they were arranged in tables, using Microsoft Office® programs (Word 2013 and Excel 2013). Descriptive statistics were used, using mean, relative frequency, absolute frequency and proportion calculation.

To carry out the research in accordance with Resolution 466/12 of the National Health Council, it was necessary to approve the Ethics and Research Committee (CEP) of the Faculty of Biomedical Sciences of Cacoal-RO FACIMED, under protocol No. 3,347,996 and CAAE No. 12556919.0.0000.5298, and authorization from the Municipal Health Secretariat of Cacoal (SEMUSA).

III. RESULTS AND DISCUSSIONS

The present study was carried out by analyzing 11 (100%) of notification / investigation forms of adverse events after BCG vaccination performed in the municipality of Cacoal. Since the number of cases notified in 2016 was 05 (45.5%) cases, 05 (45.5%) in 2017 and 01 (9%) in 2018.

According to the study, among the 11 reported cases (100%), 04 (36.4%) were female, and 07 (63.6%) were male. The average age of vaccinated individuals who experienced an adverse event in this period was 01 month and 16 days, the minimum age was 03 days and the maximum age 04 months and 27 days.

A study carried out in Recife / PE in 2017, showed the incidence of adverse events after vaccination in children,

among which 373 AEFIs were identified, with 83.90% adverse events temporarily related to the vaccine (EATV) and 16.10% to errors immunization (IS). The most frequent occurred in male children and under one year old (BRAGA, 2017).

Although the BCG vaccine is also indicated for contacts of patients with leprosy, in which it can be administered to individuals older than 1 year according to the MS protocol (BRASIL, 2016), there were no cases of adverse events to BCG in the age group of adult individuals. This may be related to the fact that the adult individual is more resistant to going to the vaccination room to refer to an adverse event or to other factors, because according to Brasil (2014c), the adverse events may be related to the individual's immune system. Another factor may be related to the ease of administration of BCG in an adult individual, when compared to administration to a newborn, who has thinner and more sensitive skin for administration of the immunobiological agent intradermally.

The collected data resulted in 04 types of adverse events to the BCG vaccine, being cold subcutaneous abscesses, hot subcutaneous abscesses, non-suppurated regional lymphadenopathy and suppurated regional lymphadenopathy. Of the 11 (100%) cases of AEFI to BCG reported during the study period 05 (45.5%) were of the type cold subcutaneous abscesses, 03 (27.3%) unsuppurated regional lymphadenopathy, 02 (18.2%) hot subcutaneous abscesses and suppurated regional lymphadenopathy, 01 (9%). The main symptoms presented in the notification forms were nodule, abscess and pain related to the four types of adverse events. Other symptoms were observed, such as fever, erythema, flushing and regional adenopathy, among others. Among the 04 types of adverse events, 03 presented the use of Isoniazid as conducts, as shown in table 01.

Table 01 also presents data on the final classifications of AEFIs to BCG, in which they presented four types of manifestations, namely, local, systemic skin / mucosa clinics, systemic / respiratory clinics and systemic / neurological clinics. Among the manifestations presented, the most prevalent was the local manifestation, followed by the systemic clinical manifestation / skin and mucosa.

Table.1: Distribution of results regarding the types of adverse events, signs and symptoms, conduct and classification of AEFIs of patients vaccinated with BCG notified in the period from 2016 to 2018. Cacoal / RO, 2019.

ADVERSE EVENT TYPE	n (%)	SIGNALS AND SYMPTOMS	CONDUCT	CLASSIFICATION EAPV
		Nodule and pain.	Isoniazid use, notification and follow-up.	Local demonstrations.
		Cold abscess, pain, erythema,	Isoniazid use for 10 days,	Local demonstrations.

		flushing and lump.	notification and follow up	
Cold subcutaneous abscesses	05 (45,5%)	Cold abscess.	60-day use of isoniazid, notification and follow-up	Local demonstrations.
		Cold abscess.	Oral antipyretic, notification and follow-up.	Local demonstrations.
		Cold abscess and lump.	Isoniazid use, notification and follow-up.	Local demonstrations.
		Nodule		Local demonstrations;
		Reaction adenopathy		Systemic clinical manifestations / skin and mucosa;
		Sneezing;	Isoniazid use for 15 days, notification and follow-up.	Systemic clinical manifestations / skin and mucosa
		Agitatio		Systemic / neurological clinical manifestations
Hot Subcutaneous Abscesses	02 (18,2%)	Fever		Other manifestations
		Hot abscess, heat, pain, edema, erythema or flushing.	Isoniazid use, notification and follow-up.	Local demonstrations
		Regional lymphadenopathy		Systemic clinical manifestations / skin and mucosa
		Sneezing and dry cough	Notification and Tracking	Systemic / respiratory clinical
Unsuppressed regional lymphadenopathy	03 (27,3%)	Agitation		manifestations; Systemic / neurological clinical manifestations
		Axillary regional lymphadenopathy, less than 3 cm	Notification and Tracking.	Systemic clinical manifestations / skin and mucosa
		Right axillary lymph node measuring 3 cm.	Isoniazid use, notification and follow-up.	Systemic clinical manifestations / skin and mucosa.
			60-day use of isoniazid, notification and follow-up.	Systemic clinical manifestations / skin and mucosa.
Suppurative regional lymphadenopathy	01 (9%)	Lymphadenopathy	Notification and Tracking.	Systemic clinical manifestations / skin and mucosa.
Source: Sales; Mendonça; Faria, Romanholo, Romanholo (2020).				
Caption: EAPV - Adverse Event After Vaccination.				

It is noted that health professionals are aware of the attendance, notification and follow-up of BCG-related adverse events, as all reported events presented in table 1

are part of the compulsory notification adverse events according to the conduct to be adopted in the Manual. of adverse events to immunobiologicals (BRAZIL, 2014b).

Regarding the behaviors adopted by health professionals regarding what is advocated by the MS through the PNI, it is noted that health professionals need to have greater knowledge of the protocols established by the program, given that some behaviors adopted in relation to AEFIs do not according to Brazil, according to Brazil (2014b), the cases of AEPS of non-suppurative regional lymphadenopathy and hot subcutaneous abscess is not indicated for use of isoniazid, but it is noted as a conduct, the prescription and use of medication, and in one of the cases of cold subcutaneous abscess that indicated the use of isoniazid according to the protocol, it was not prescribed.

According to the 2014 AEFI epidemiological surveillance manual, BCG is naturally resistant to pyrazinamide. The Moreau Rio de Janeiro strain is isoniazid sensitive, so administration of isoniazid is used as the gold standard for treatment (BRASIL, 2014a).

Regarding the classification of AEFIs to BCG, local clinical manifestations, and systemic clinical manifestations / skin and mucous membranes were the most predominant. Local manifestations are the most common in cases of AAPV to BCG and are considered at or near the site of administration and may occur after application of any vaccine. These reactions are consequences of the introduction of the needle and the vaccine content into muscle tissue, hyperesthesia, reactive vasodilation, pruritus and urticarial papules and ganglionic infarction. This may cause an abscess at the site of administration, cellulitis, near hardening or at the site of administration, near edema or at the site of administration, lump and pain (BRASIL, 2014a).

Systemic manifestations can be defined as an acute hypersensitivity reaction, with involvement of multiple systems being considered of greater severity (BRASIL, 2014a).

Table 2 shows the proportion of reported AEFIs in the municipality of Cacoal during the study period compared to the proportion of AEFIs recommended by the MS through the NIP, and the cold subcutaneous abscess type AEFIs presented 2.67 cases for every 2,500 vaccinated, followed by unsuspected regional lymphadenopathy, the number of cases was 1.6 for every 2,500 vaccinated. Hot subcutaneous abscess adverse events presented 1.07 cases for every 2,500 vaccinated patients, while the proportion of suppurative regional lymphadenopathy adverse events was 0.5 cases for every 2,500 vaccinated.

The MS through the PNI, recommends that for every 2,500 vaccinated, 01 individual will present adverse event to BCG (BRAZIL, 2014a). Among the results obtained, three types of adverse events were above the recommended standard, only the suppurative regional lymphadenopathy adverse event was below the EAPV

expected by the PNI.

Table.2: Comparative analysis of the presented ratio of AEFI to BCG, with the standard recommended by the PNI. Cacoal / RO, 2019.

ADVERSE EVENT TYPE	EAPV PROPORTION NOTIFIED	PREFER RED NIBP
Cold subcutaneous abscesses	2,67:2.500	1:2.500
Hot Subcutaneous Abscesses	1,07:2.500	1:2.500
Regional lymphadenopathy not suppurative	1,6:2.500	1:2.500
Suppurative regional lymphadenopathy	0,5:2.500	1:2.500

Source: Sales; Mendonça; Faria, Romanholo, Romanholo (2020).

Caption: EAPV - Post-Vaccination Adverse Event, PNI - National Immunization Program.

According to Brazil (2014a), BCG vaccine has been used for decades and is the main form of prevention of severe forms of TB, but may cause local, regional or systemic adverse events, and local and regional adverse events such as abscess, lymphadenopathy. regional suppuration greater than 3 cm, regional suppurative lymphadenopathy may be directly linked to incorrect vaccine administration technique.

Note the importance of nurses working directly in the vaccine room, because they are responsible for their nursing staff, being important their training and constant updating, as well as promoting continuing education for their team.

IV. FINAL CONSIDERATIONS

Taking into account the above data, it was observed that males were the most affected by adverse events to BCG and the prevailing age was in children under 01 (one) year. It was found that VAPE of cold subcutaneous abscess, hot subcutaneous abscess and non-suppurative regional lymphadenopathy are above the standard recommended by the NIBP, and only the adverse event of suppurative regional lymphadenopathy is within the recommended.

It is suggested a proposal for the study presented, where professionals who attend the AEFI are constantly trained and updated to attend and follow up these cases, and that professionals who work directly with immunization are regularly trained regarding errors of immunization,

application, proper handling and storage conditions of immunobiologicals. It is also suggested new scientific studies that seek to analyze the quality of care provided to the population, with regard to immunization.

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