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Post-immunization adverse human papilomavirus events in teenagers

Ventos adversos post-vaccinarios del papiloma humano en adolescentes

Eventos adversos pós-vacinais papilomavírus humano em adolescentes

ABSTRACT
To assess the occurrence of post-vaccine adverse events in adolescents related to the human papillomavirus quadrivalent vaccine 6, 11, 16 and 18 (recombinant) through the National Immunization Program Information System Post-Vaccination Adverse Events of the Program Area Health Coordination 5.1 from the Basic Health Units. The sample consisted of adolescents between 9 and 17 years old. Retrospective, exploratory, descriptive, and quantitative study from November 1, 2016 to June 1, 2019. The study analyzed 22 reporting forms, 19 of adverse events following vaccination and 3 Immunization Errors (IS). Adverse events in adolescents are related to anxiety and fear of vaccination occurring in the administration of the first dose of the predominant male HPV vaccine occurring within the first 30 minutes after immunobiological administration. In this research, the most frequent adverse events were classified as non-serious, with evolution to cure without sequelae, related to manifestations such as pallor, hypotension, fainting and syncope.
DESCRIPTORS: Human Papillomavirus (HPV); Adolescent Health; Immunization; Adverse effects.

RESUMEN
Evaluar la aparición de eventos adversos posteriores a la vacuna en adolescentes relacionados con la vacuna cuadrivalente al virus del papiloma humano 6, 11, 16 y 18 (recombinante) a través del Sistema Nacional de Inmunización del Sistema de Información de Eventos Adversos Post-Vacunación del Área del Programa Coordinación de Salud 5.1 de las Unidades Básicas de Salud. La muestra estuvo conformada por adolescentes entre 9 y 17 años. Estudio retrospectivo, exploratorio, descriptivo y cuantitativo del 1 de noviembre de 2016 al 1 de junio de 2019. El estudio analizó 22 formularios de informe, 19 de eventos adversos después de la vacunación y 3 errores de inmunización (IS). Los eventos adversos en los adolescentes están relacionados con la ansiedad y el miedo a que ocurra la vacunación en la administración de la primera dosis de la vacuna contra el VPH masculina predominante dentro de los primeros 30 minutos después de la administración inmunobiológica. En esta investigación, los eventos adversos más frecuentes se clasificaron como no graves, con evolución para curar sin secuelas, relacionados con manifestaciones como palidez, hipotensión, desmayos y síncope.
DESCRIPTORES: Virus del Papiloma Humano (VPH); Salud del Adolescente; Inmunización; Efectos adversos.

RESUMO
Avaliar a ocorrência dos eventos adversos pós-vacinais em adolescentes relacionados à vacina quadrivalente Papilomavírus Humano 6, 11, 16 e 18 (recombinante) através do Sistema de Informações do Programa Nacional de Imunizações Eventos Adversos Pós-Vacinação da Coordenadoria de Saúde da Área Programática 5.1 procedentes das Unidades Básicas de Saúde. A amostra foi composta por adolescentes entre 9 a 17 anos de idade. Estudo retrospectivo, de caráter exploratório, descritivo e quantitativo no período de 01 de novembro de 2016 até 01 de junho de 2019. Analisadas no estudo 22 fichas de notificações, sendo 19 de eventos adversos pós-vacinais e 3 Erros de Imunização (EI). Os eventos adversos nos adolescentes estão relacionados a ansiedade e medo frente a vacinação, ocorridos na administração da primeira dose da vacina HPV, predominante no sexo masculino, ocorrendo nos primeiros 30 minutos após administração do imunobiológico. Nesta pesquisa, os eventos adversos com maiores frequências, foram classificados como não graves, com evolução para cura sem sequelas, relacionados à manifestações como a palidez, hipotensão, desmaio e síncope.
DESCRITORES: Papilomavírus Humano (HPV); Saúde do Adolescente; Imunização; Efeitos Adversos.

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INTRODUCTION

The Human Papilloma Virus is a sexually transmitted infection, there are more than 200 variations of this type of virus that attack, especially, the oral, genital or anal mucosa, both male and female, however, in the majority, it is associated with benign lesions, such as warts, that can be clinically removed[1].

Condoms (male and female) prevent most Sexually Transmitted Infections (STIs), in the case of HPV, they do not completely prevent infection by the virus. Transmission can occur even without vaginal or anal penetration, and lesions may be present in areas not protected by condoms, such as: vulva, pubic, perineal and perianal regions or testicular pouch[2].

According to the Ministry of Health(1) in Brazil, there is a predominance in the circulation of four subtypes that affect both men and women and, according to scientific literature, 12 HPV subtypes are associated with cancers of the cervix, penis, oropharynx and even rectal cancer.

According to INCA publication[3] Cervical cancer is the fourth most common cancer of death among women, with the exception of non-melanoma skin cases, with approximately 530 thousand new cases per year worldwide and responsible for 265 thousand annual deaths. It is associated with persistent infection by oncogenic subtypes of the HPV (Human Papillomavirus) virus, especially HPV-16 and HPV-18, which account for about 70% of cervical cancers.

Vaccines are biological products with excellent safety and the occurrence of adverse events related to immunobiological should be immediately reported[4]. Created in 1973, the National Immunization Program (PNI) is responsible for organizing the national vaccination policy for the Brazilian population. Vaccination contributes to the reduction of morbidity and mortality from communicable diseases in Brazil[5].

The National Immunization Program (PNI) has been offering, in an orderly manner, in the immunization rooms of the Health Units, vaccines against communicable diseases through campaigns, favoring the control and eradication of diseases. In cases of hypersensitivity to routine vaccines or in some situations of immunodepression, in these particular situations, vaccines are carried out at the Special Immunobiological Reference Centers - CRIE[6].

It is considered an adverse event after vaccination (AEFI), according to the Ministry of Health[4], any unwanted medical occurrence after immunization and which, without fail, has a causal association with the use of a vaccine or other immunobiological (immunoglobulins and heterologous sera). Most occurrences of adverse events are mild local and systemic manifestations. Their intensity can vary from mild and expected effects, such as local manifestations, to moderate, severe or rare cases. classified as unexpected[7].

The components of the immunobiological, the vaccinated and the vaccination process are factors that can be related to an AEFI, however, when professional practice, standards and techniques are not met, resulting, or not, in an adverse event, this, is characterized with an Immunization Error (IE). Any preventable event that can cause or lead to inappropriate use or harm to a patient[8].

According to the Ministry of Health(1), in 2014, the introduction of the recombinant quadrivalent HPV vaccine began in the National Immunization Program (PNI), contemplating girls between 11 and 13 years old with the main objective of immunizing women against cervical cancer. Studies show malignancy associated with Human Papillomavirus in women and non-malignant in men[9].

The Ministry of Health of Brazil and other countries reevaluated their cost-effectiveness analyzes of the inclusion of boys in immunization campaigns and, in 2017, the age range for vaccination among boys from 11 years old up to 15 years old incomplete and girls from 9 to 15 incomplete. The vaccine should be taken in two doses, with a minimum interval of six months and

a maximum of one year between them. Individuals aged 9 to 26 years of both sexes living with HIV/AIDS, cancer patients undergoing chemotherapy and / or radiation therapy; transplanted from solid organs or bone marrow are also contemplated with the immunobiological[1].

The Brazilian Society of Pediatrics (SBP), as well as the Brazilian Society of Immunizations (SBIm) and the Brazilian Federation of Gynecology and Obstetrics Associations (FEBRASGO), recommend the vaccination of girls and women from 9 to 45 years of age and boys and young people from 9 to 26 years old. Men and women at ages outside the licensing range can also benefit from vaccination, according to medical criteria[9].

As it is a vaccine recently incorporated into the adolescent's vaccination schedule by the Ministry of Health in Brazil and with reports of adverse events, which disqualify this form of prevention, this fact motivated the present study. The research is justified by the need to evaluate the cases of adverse events after vaccination, whether they are associated with the vaccine substance or are cases of isolated events related to the individual himself. The study of the safety profile for the group in which the vaccine is available is relevant, since it is a population with little adherence to immunization programs and its use as a prophylactic means prevents infectious diseases and reduces the incidence of cervical cancer[4].

Vaccination against HPV is an important advantageous and favorable benefit for society, as a collective protection. In the academic space, the study provides data and guidance for future research associated with adverse events after vaccination of Human Papillomavirus. Thus enriching the training of new professionals, whether at the technical, undergraduate or graduate levels[4].

And the general objective is to evaluate the occurrence of post-vaccine adverse events in adolescents related to the quadrivalent Human Papillomavirus 6, 11, 16 and 18 (recombinant) vaccine through the Information System of the National Immunization Program Adverse Events Post-Vaccination of the Coordination of Programmatic Health 5.1.

METHODOLOGY

This research is a retrospective, exploratory, descriptive, and quantitative study. Second study[10], the exploratory approach is developed in order to provide an overview of the topic studied, it consists of deepening the topic, providing more information and contributing to the clarification of issues addressed in the subject.

The main objective of descriptive research is to describe characteristics of a given population or phenomenon, establishing relationships between the variables, taking care to observe the facts, registering, analyzing, classifying and interpreting without interference by the researcher in the results obtained[11].

Exploratory research is usually the first step for those who do not know enough about the field that they want to allude to and being carried out in an area in which there is little accumulated and systematized knowledge[12], and in the retrospective study cases and controls are studied, the effect is known and the cause is sought[13].

In quantitative research, determining the composition and size of the sample is a process in which statistics has become the primary medium. The answers to some problems can be deduced for the whole, so the sample must be very well defined; otherwise, problems may arise when using the solution for the whole[14].

Prepared from a survey of data from the Information System of the National Immunization Program module Information System Adverse Events Post-Vaccination (SI-PNI/SI-EAPV), coming from the Basic Health Units (UBS) being these, referring to the Programmatic Area Health Coordination (CAP) 5.1, located in Jardim Sulacap, in the municipality of Rio de Janeiro. Records of notifications of adverse post-vaccination adverse events of the quadrivalent Human Papillomavirus 6, 11, 16 and 18 recombinant vaccine in adolescents were included.

The choice of the Information System of the National Immunization Program module Information System Adverse Events Post-Vaccination (SI-PNI/SI-EAPV) for the study was relevant because of the comprehensibility of monitoring adverse events, with dizzying identification of cases, classifications and conduct occurring in Program Area 5.1.

The notification forms with the age group between 9 to 17 years of age, both sexes, with complaints of AEFI, referring to the quadrivalent immunobiological of the Human Papillomavirus, were sources, from November 1, 2016 to June 1, 2019, conducting a survey of all post-vaccine adverse events.

The variables of the adolescents' age, sex, color, vaccine dose, type of adverse events, such as local manifestations, systemic clinics (skin/mucous membranes, cardiovascular, respiratory, neurological, and gastrointestinal) and other manifestations were analyzed in the study. In addition to the start interval, vaccines administered simultaneously, opinion from the Immunization Program Coordination (CPI) and whether there is a direct relationship between these events and the vaccine, based on the notifications made by the Basic Health Units of the Health Coordination of Programmatic Area 5.1.

The data were reported from the results of the variables, submitted to statistical analysis in a simple way, presented through tables in Microsoft Excel that facilitated the interpretation of the information. As it involves data collection involving human beings, the research was submitted to the Research Ethics Committee (CEP) according to Resolution No. 466/12 and Resolution No. 510/16, with approval by the Research Committee. Ethics of the Municipal Health Secretariat of Rio de Janeiro (SMS/RJ) opinion No. 3,593,283.

RESULTS AND DISCUSSION

Twenty-two notification forms were analyzed in the study, 19 of which were post-vaccine adverse events and 3 Immunization Errors (IS), preserving

the identity of individuals, referring to the immunobiological of quadrivalent Human Papillomavirus 6, 11, 16 and 18 (recombinant).

Between 2016 and 2019 in the 22 cases notified as EAPV on the SIPNI / SIEAPV platform, the highest frequency of notifications occurred in 2016 and 2017, with 10 each year, and 2 in 2018. In the year 2019 there is no record of notifications in the System.

When performing the insertion of the notification in the Information System of the National Immunization Program module Information System Adverse Events Post-Vaccination, in the field of manifestations, the registered patient who presents any sign and symptom that is not described, this must be specified and classified as other manifestations.

The sample consisted of adolescents, boys, and girls between 9 to 18 years of age, 14 males and 8 females. Among the 22 cases, 03 were reported as Immunization Error (IS), aged 9, 10, 17 and 18 years, 02 males and 01 females.

A search was made in the Health Information System of the SUS computer department (TABNET-DATASUS) to analyze the predominance of adverse events in male adolescents. DATASUS provides information that can be useful for objective analysis of the health situation, design of health action programs and evidence-based decision making. The results demonstrate the increase in the number of male adolescents vaccinated in the analyzed age group.

Analyzing the results using the TABNET-DATASUS source, in relation to the greater number of adverse reactions in male adolescents, the primary objective of HPV vaccination in 2014 was to protect women against cervical cancer and, from 2017, it extended to men. Due to the inclusion of boys in the Immunization Program to offer the HPV vaccine, the number of male adolescents vaccinated increased, the probability of adverse events became more evident.

Regarding the vaccine dose, all adverse events that occurred were related to the first dose of the quadrivalent Human Papillomavirus vaccine schedule. The notifications inserted in the platform as EI present a 9-year-old girl who was given D1 on 11/8/2016 and D2 on 3/29/2017, that is, administration of the vaccine with an interval of approximately 3 months and 15 days between doses, with the recommended 6 months from D1 to D2. Another case, the 10-year-old male teenager was outside the age groups recommended by the National Immunization Program (PNI), at the time girls 09 to 14 years old and boys from 12 to 13 years old. Two errors occurred in 01 adolescent, the first with 17 years and the second dose with 18 years, which were also administered outside the age range recommended at the time for boys.

Regarding the color of the adolescents, in 12 cases the color was not informed, however, in the informed the predominance is the brown color. There are no reports in the literature associating adverse events with the individual's skin color, however, the Continuous National Household Sample Survey (Continuous Pnad)

Table 1. Description of the variables age, sex, color, dose of the vaccine and time of onset of cases related to post-vaccine adverse events related to the quadrivalent Human Papillomavirus 6, 11, 16 and 18 (recombinant) vaccine. Rio de Janeiro, RJ, Brazil, 2016-2019.

Variáveis	Quantidade	Erro de Imunização
Idade		
9	4	1
10	1	1
11	4	
12	4	
13	4	
14	**2**	
17 e 18		1
Sexo		
Feminino	**08**	**1**
Masculino	14	2
Dose da vacina		
1ª dose	**21**	**2**
2ª dose	01	1
Cor		
Amarela	2	
Branca	5	
Parda	7	1
Não informada	5	2
Tempo de início do efeito adverso		
30 minutos	**4**	
3 horas	1	
4 horas	1	
6 horas	1	
Não informado	12	

2016, released by the Brazilian Institute of Geography and Statistics (IBGE), reveals that, the majority of the resident Brazilian population is brown, 95.9 million people, representing 46.7% of the total.

Regarding the time of onset, between the application of the immunobiological and the beginning of signs and symptoms, for 04 adolescents it occurred about 30 minutes after the vaccine administration, 01 adolescent after 3 hours, 01 after 4 hours, 6 hours after application of the 01 adolescent vaccine and for 12 notified the interval time was not informed.

Regarding the time of onset, the Early Systemic Reaction Syndrome (SRSP) usually appears within three hours after the vaccine is administered and has one or more of the following signs and symptoms: tremors, chills, fever, severe headache, vomiting, drowsiness, prostration, perioral or finger cyanosis[4].

About the post-vaccine events evaluated, according to the classification, 01 was classified as a Severe Adverse Event (AGE) According to a study[4], which requires hospitalization of at least 24 hours or prolongation, or which have a cause of significant dysfunction or persistent disability, death or death risk (ex: anaphylaxis), among other severities. This case was subsequently reclassified and closed as a non-serious, maintained scheme, as the AEFI was related to anxiety about vaccination.

Classified as type of Adverse Non-Serious Event (EANG), 18 cases were found. According to the results of a study [4], which presented systemic or local events, moderate or intense, requiring or not an outpatient medical treatment, complementary exams and which do not fit the criteria of Serious Adverse Event.

In this research, the most frequent adverse events were related to skin/mucosa manifestations, such as pallor, cardiovascular manifestation, hypotension and neurological fainting and syncope. Such manifestations occurred in 07 adolescents.

It was observed that 05 adolescents manifested gastrointestinal reactions related to diarrhea and vomiting, 03 presented local events such as pain, heat, erythema or flushing and local itching. Other manifestations related to headache and fever (axillary) of 38.8ºC and> = 39ºC were presented by 03 adolescents, vertigo, and dizziness in 02 adolescents.

The manifestations of lower frequencies analyzed in this research were: altered level of consciousness, paraesthesia, malaise, lethargy, nausea, decreased auditory acuity, dyspnea, fatigue, fever of 38.8ºC (axial), myalgia, sweating, indisposition, drowsiness, dizziness, exhaustion, pain in the lower limbs and tremors in the body.

Findings from this study show that adverse events, such as pain at the application site, fever of 38ºC or> = 39ºC (axial), headache and syncope, are related to the

Table 2. Description by Programmatic Area 5.1, classification, discarded, closed and Immunization Error of cases related to notified post-vaccine adverse events of the quadrivalent Human Papillomavirus vaccine 6, 11, 16 and 18 (recombinant). Rio de Janeiro,

AP	Não grave	Grave	Mudança de classificação	Total	Descartados	Encerramento	Erro de Imunização
5.1	18	1	1	19	0	22	3

Table 3. Description of adverse events presented by adolescents related to the quadrivalent Human Papillomavirus 6, 11, 16 and 18 (recombinant) vaccine. Rio de Janeiro, RJ, Brazil, 2016-2019.

Evento adverso	Adolescentes
Dor, calor, eritema ou rubor e prurido local	3
Alteração do nível de consciência e parestesia	1
Palidez, hipotensão, desmaio e síncope	7
Diarreia e vômitos	5
Vertigem e tontura	2
Mal-estar	1
Letargia	1
Náuseas	1
Diminuição da acuidade auditiva	1
Dispneia	1
Cefaleia	3
Fadiga	1
Febre de >= 39°C (axial)	3
Febre de 38,8°C (axial)	1
Mialgia	1
Sudorese	1
Indisposição	1
Sonolência	1
Tontura	1
Esgotamento	1
Dor em membros inferiores	1
Tremores no corpo	1

vaccine. In relation to fever, it is associated with the body's immune response, it is often benign and self-limiting. Fever produces inflammatory cytokines that act in the hypothalamus, with release of prostaglandins and elevation of temperature, being a physiological response to the administration of antigens[4].

According to a study[4], loss of consciousness is also brief, lasting less than 1 minute, averaging 20 to 30 seconds. The patient returns to normal in 5 or 10 minutes. Immediately, after losing consciousness, small muscle spasms may occur in the arms, neck and/or legs, lasting less than 15 seconds.

The change in the level of consciousness is occasionally immediate and is preceded by symptoms of hypotension, cold sweating, pallor, visual turbidity, paresthesia (tingling in the upper and/or lower limbs) and, if no measures are taken, the individual usually to faint[4].

Regarding the opinion of the Immunization Program Coordination, of the 22 cases studied, 01 presents a neurological diagnosis to be clarified, unclassifiable, with evolution to cure without sequelae and closure with pending matters. The case was closed as pending by the CPI, la-

Table 4. Description of cases closed by the Coordination of the Immunization Program of adverse events presented by adolescents Post-vaccinated with quadrivalent Papillomavirus 6, 11, 16 and 18 (recombinant). Rio de Janeiro, RJ, Brazil, 2016-2019.

Diagnóstico	Idade	Sexo	Dose	Evolução	Encerramento pela CPI
Evento neurológico à esclarecer	9	Feminino	1ª	Cura sem sequelas	Caso com encerramento, no entanto, apresentando pendências
Síncope	12	Feminino	1ª	Cura sem sequelas	Caso encerrado reclassificado como não grave. Esquema mantido, pois EAPV relacionado à ansiedade frente à vacinação
Erros de prescrição ou indicações (fora da idade recomendada)	10	Masculino	1ª	Dose considerada válida	Solicitado ratificar as indicações da vacina HPV conforme faixas etárias recomendadas pelo Programa Nacional de Imunização (PNI), meninas 09 a 14 anos e meninos de 12/13 anos. Caso este menino retorne pleiteando a D2 (06 meses depois) atender, pois esquema aberto deve ser encerrado, apesar do erro cometido.
Vômitos, diarreia e febre	13	Masculino	1ª	Cura sem sequelas	Realizado o acompanhamento até a regressão dos sintomas. Caso encerrado sem a necessidade de adoção de precauções ou substituição do esquema. Manter calendário para idade conforme a indicação clínica e preconização do Ministério da Saúde.
Desmaio após forte emoção	12	Masculino	1ª	Cura sem sequelas	Realizado o acompanhamento com visita medica domiciliar, orientada sobre os cuidados e referenciada para acompanhamento neurológico devido episódios anteriores. Caso encerrado sem a necessidade de adoção de precauções ou substituição do esquema. Manter calendário para idade conforme a indicação clínica e preconização do Ministério da Saúde.
Vômitos e vertigem	13	Feminino	1ª	Cura sem sequelas	Realizado o acompanhamento por 4 semanas, mas houve melhoras logo após o único episódio de vômito. Caso encerrado sem a necessidade de adoção de precauções ou substituição do esquema. Manter calendário para idade conforme a indicação clínica e preconização do Ministério da Saúde.
Tontura, vertigem, sonolência, mal estar geral e indisposição	13	Masculino	1ª	Cura sem sequelas	Realizado o acompanhamento por 4 semanas. Caso encerrado sem a necessidade de adoção de precauções ou substituição do esquema. Manter calendário para idade conforme a indicação clínica e preconização do MS.
Erros de prescrição ou indicações (fora da idade recomendada)	17 e 18	Masculino	1ª e 2ª	Doses consideradas válidas	Reforçamos sobre a necessidade de avaliar a caderneta vacinal e conferindo idade correta, para decidir sobre a vacina a ser aplicada, ler atentamente os frascos dos imunobiológicos antes da inoculação, sem esse procedimento estaremos fragilizados, sob risco de cometer novos erros de imunização. Houve dois erros na 1ª e 2ª doses fora da faixa etária preconizada. Validar as doses aplicada, oportunizar imunização segura com o calendário preconizado para idade.

Erros de prescrição ou indicações (fora da idade recomendada)	9	Feminino	2ª	Dose considerada válida	Realizado D1 em 08/11/16 e D2 em 29/03/17, ou seja, administração da vacina com intervalo de aproximadamente 3 meses e 15 dias entre as doses, sendo o preconizado 6 meses. Reforçamos sobre a necessidade de avaliar a idade do paciente, e doses já aplicadas com seus respectivos intervalos e conferindo dados fundamentais para uma imunização segura. Sem esse procedimento estaremos fragilizados, sob risco de cometer novos erros de imunização. Validar as doses aplicadas. Caso encerrado com necessidade de completar esquema HPV e as demais vacinas do calendário vacinal para idade.
Dor no local da injeção e sonolência	12	Masculino	1ª	Cura sem sequelas	Realizado acompanhamento até regressão dos sintomas, com uso de compressas frias e uso de antitérmico profilático, prescrito pelo profissional médico. Caso encerrado cura sem sequela, com adoções de precaução.
Vômitos	13	Masculino	1ª	Cura sem sequelas	Caso encerrado sem a necessidade de determinação de conduta específica ou orientação. EAPV já descrito em literatura (Manual de Vigilância de EAPV - MS) para os imunobiológicos em questão.
Lipotímia	11	Masculino	1ª	Cura sem sequelas	Mantido esquema, considerando precaução em Atenção Primária como realizar acolhimento, fornecendo ambiente privativo e confortável para reduzir algum "stress" antes da vacinação. Vacinação do adolescente sentado, realizar monitoramento do mesmo por 1 hora após a vacinação e liberar para domicílio com orientações, após certificar que está clinicamente bem.
Cefaléia, palidez, fadiga intensa e esgotamento	12	Masculino	1ª	Cura sem sequelas	Caso encerrado após remissão completa das manifestações clínicas. Esquema de HPV mantido, vacina da Febre Amarela e Meningocócica C encerrados.
Síncope	14	Masculino	1ª	Cura sem sequelas	Caso encerrado com síncope, relacionada à ansiedade pela vacinação. Esquema HPV mantido.
Dor muscular, dor no local da Injeção, cefaleia e febre	10	Feminino	1ª	Cura sem sequelas	Orientamos vacinar com precauções no CRIE. Agendar. Aguardamos
Síncope	9	Feminino	1ª	Cura sem sequelas	Caso encerrado com cura sem sequelas. Recomenda-se dar continuidade ao esquema vacinal de rotina de acordo com o calendário vigente e intervalos preconizados pelo Programa Nacional de Imunizações e de acordo com a faixa etária da usuária. Conforme recomendação técnica, vacinar a adolescente sentada e orientar que a mesma aguarde cerca de 15 a 30 minutos após a vacinação. Tendo como objetivo avaliar a possível ocorrência de Eventos Adversos imediatos. Orientar o usuário/responsável quanto à importância do retorno à Unidade em caso de ocorrência de reações pós-vacinais visando a notificação e o acompanhamento clínico até a melhora do quadro.
Cefaléia e náuseas	11	Masculino	1ª	Cura sem sequelas	Caso encerrado com cura sem sequelas. Recomenda-se se manter o esquema sequencial conforme calendário vacinal vigente do Programa Nacional de Imunizações. Reforçar a orientação ao responsável pela adolescente quanto à importância do retorno à Unidade em caso de ocorrência de EAPV, após a completude do esquema com a 2° dose de HPV.
Prurido, eritema, dor no local da injeção e calor no local da injeção	9	Feminino	1ª	Cura sem sequelas	Após a remissão completa das manifestações clínicas e sem relato de agravamento do quadro, o caso pode ser encerrado com o esquema vacinal mantido. Enfatizamos a importância da orientação sobre a aplicação de compressas frias intermitentes nos casos de reação local.

Cefaléia, síncope vago-vagal e reação febril	11	Masculino	1ª	Cura sem sequelas	Caso encerrado com cura sem sequelas. Recomenda-se a continuidade do esquema sequencial de HPV e Febre Amarela conforme calendário vigente e os intervalos entre as doses preconizados pelo Programa Nacional de Imunizações, considerando a faixa etária do usuário. Sendo este um adolescente com condições específicas de saúde e com predisposição a apresentar reações de ansiedade, reforçamos a orientação de vaciná-lo sempre sentado, orientar a equipe técnica para que realize a observação clínica deste usuário durante no mínimo 40-60 min dentro da Unidade de Atenção Primária após a aplicação de vacinas, tendo como objetivo avaliar precocemente a possível ocorrência de Eventos Adversos. Orientar o responsável quanto à importância do retorno à Unidade em caso de ocorrência de reações pós-vacinais visando a notificação e o acompanhamento clínico até a melhora do quadro.
Sudorese excessiva ou hiperidrose, vômitos e palidez	11	Masculino	1ª	Cura sem sequelas	Caso encerrado com cura sem sequelas. Reações compatíveis com quadro de ansiedade relacionado à vacinação. Recomenda-se a continuidade do esquema sequencial conforme calendário vacinal vigente, considerando a faixa etária do adolescente e os intervalos entre as doses recomendados pelo Programa Nacional de Imunizações. Este adolescente deverá receber vacinas de rotina na posição sentado e deverá ser observado clinicamente dentro da Unidade por no mínimo 20 minutos após a administração de imunobiológicos tendo como objetivo a identificação precoce de possível EAPV. Em caso de novo EAPV, o tratamento deverá ser sintomático.
Cefaleia e dispneia	14	Masculino	1ª	Cura sem sequelas	Com encerramento, no entanto no sistema não há justificativas / recomendações.
Febre	9	Feminino	1ª	Cura sem sequelas	Caso encerrado com cura sem sequelas. Recomenda-se manter esquema de HPV quadrivalente, conforme calendário vacinal vigente do Programa Nacional de Imunizações e considerando a faixa etária do usuário. Em caso de febre no período pós-vacinal, utilizar antitérmico de acordo com a conduta médica. Reforçar a orientação junto ao responsável quanto à importância do retorno à Unidade em caso de novas reações.

cking details, requiring a report or opinion from the neurologist. Adolescent with a diagnosis of epilepsy in childhood, with no changes in the neurological condition and the mother did not wish to continue the Human Papillomavirus vaccine scheme.

The 3 Immunization Errors (IE) showed prescription errors or indications outside the recommended age. Professionals received guidance from the Coordination of the need to evaluate the vaccine booklet, checking the correct age, to decide on the vaccine to be applied. Evaluate the doses already applied with their respective intervals and checking fundamental data for a safe immunization. Ratify the indications for the HPV vaccine according to the age groups recommended by the National Immunization Program (girls from 9 to 14 years old and boys from 12 to 13 years old). Without these procedures, the evaluation becomes fragile, at risk of making new immunization errors.

The diagnoses of vomiting, diarrhea, fever, feverish reaction, dizziness, drowsiness, general malaise, headache, nausea, pallor, intense fatigue, exhaustion, indisposition with evolution to cure without sequelae, follow-ups were carried out until the symptoms regressed, cases closed with the opinion of the Coordination without the need to adopt precautions or replace the scheme. The age calendar was maintained according to the clinical indication and recommended by the Ministry of Health, AEFIs already described in the literature (AEFI Surveillance Manual - MS) for the immunobiological in question. In case of fever in the post-vaccination period, use antipyretic according to the medical conduct and reinforce the guidance with the person in charge regarding the importance of returning to the unit in case of new reactions.

Related to local manifestations, diagnoses, such as pain and heat at the injection site, pruritus and erythema, after regression of signs and symptoms, without reports of worsening of the

condition and follow-up for 30 days, with closure of cure without sequelae, the justifications and Coordination recommendations were for the use of prophylactic antipyretic, prescribed by the medical professional. Emphasized the importance of guidance on the application of intermittent cold compresses in cases of local reaction. The diagnosis of muscle pain, pain at the injection site, headache and fever occurred in 1 case, this, with the opinion of the Coordination with guidance on vaccinating with precautions at CRIE. Registration of 01 case with diagnosis of headache and dyspnea with cure without sequelae, with closure, however, in the system there are no justifications and recommendations.

The cases diagnosed with syncope and fainting after strong emotion ended with cure without sequelae. Reactions compatible with vaccination-related anxiety. The Immunization Program Coordination recommends the continuation of the sequential scheme according to the current vaccination schedule, considering the adolescent's age range and the intervals between doses recommended by the PNI. These adolescents should receive routine vaccinations in a sitting position and should be observed clinically within the unit for at least 20 minutes after the administration of immunobiological, aiming at the early identification of possible AEFI. In the case of a new AEFI, treatment should be symptomatic and guide the user/guardian about the importance of returning to the unit in case of occurrence of post-vaccine reactions aimed at notification and clinical follow-up until the condition improves.

According to a study[4], events related to vasovagal syncope can occur after any vaccination, it is very common in adolescents and young adults, being common in people with affective instability. Some factors increase the likelihood of syncope, such as: fasting, hot and overcrowded rooms, standing for a long time and fatigue. It is recommended to vaccinate the adolescent while seated and after the vaccine administration, wait at least 15 minutes for any reaction to be observed.

The cases diagnosed with syncope and fainting after strong emotion ended with cure without sequelae. Reactions compatible with vaccination-related anxiety. The Immunization Program Coordination recommends the continuation of the sequential scheme according to the current vaccination schedule, considering the adolescent's age range and the intervals between doses recommended by the PNI.

To be related to a vaccination procedure, the pain must occur at the time of administration or shortly thereafter. It is a personal experience whose measurement depends on the subjective response of the person experiencing it and the expectation of pain or a sudden emotional shock. Of all local reactions, pain is the biggest challenge and difficult to describe, quantify and standardize[4].

According to the research, the systemic neurological clinical manifestations were mostly presented as vasovagal syncope, more frequent in adolescents and young adults after some triggering stimulus such as intense pain, expectation of pain or a sudden emotional shock. Local events, gastrointestinal, skin/mucosa, cardiovascular and other manifestations, are related to the vaccine.

In this study, 13 cases of adverse events are related to HPV vaccination performed simultaneously with other immunobiological. Concomitantly with the Human Papillomavirus vaccine, Meningococcal Conjugate C, Yellow Fever, and Influenza were administered. The main adverse events associated with vaccines administered simultaneously with HPV, in relation to the local manifestation of pain, in HPV and Yellow Fever vaccines are expected[1].

General manifestations, such as fever and headache, according to the Ministry of Health(1), are described in the literature for HPV immunobiological, Yellow Fever and Meningococcal C. Classified as anaphylaxis, Adverse Events such as hypotension and paresthesia have been related to HPV, Yellow Fever and Meningococcal C vaccines.

CONCLUSION

The research allowed a wide knowledge about the theme. Based on the stu-

dies carried out, it was demonstrated that the most frequent adverse events evolved to cure without sequelae, related to skin/mucosa manifestations such as pallor, cardiovascular manifestation to hypotension and neurological fainting and syncope.

The survey states that the majority of post-vaccine adverse events in adolescents are related to anxiety and fear regarding vaccination, with the absence of adverse events that are considered serious, so much so that of the 22 notification forms analyzed, 19 of which adverse post-vaccination and 03 Immunization Errors (IE), only 01 was classified as serious and this was subsequently reclassified and closed as non-serious.

It is suggested an improvement in the qualification of the records of adverse events analyzed in this research. Most of them were fragile without much detailed information on the signs and symptoms and monitoring of the adolescents' clinical condition. In addition, it is also worth emphasizing the need to sensitize professionals who work in vaccination rooms, the importance of timely notification, good practices in immunizations, ensuring safe, effective immunization and avoiding negative and inappropriate vaccination noises. In order that the population has reliability in the quality and safety of the HPV vaccine.

After the analysis, the small number of notifications inserted in the System is pointed out in a period of 2 years and 7 months. However, it is not possible to affirm the underreporting of adverse events by collecting data used to develop the work in question.

Given the above, it is concluded that, even in the face of the occurrence of such adverse events, it is relevant and advantageous as a strategy to prevent this viral infection and cervical cancer, the completion of the complete vaccination schedule. And that the quadrivalent vaccine Papillomavirus 6, 11, 16 and 18 (Recombinant) has good tolerability and is safe.

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