ASSOCIATION BETWEEN THE USE OF MEDICINES AND ADVERSE REACTIONS RELATED TO VACCINATION AGAINST COVID-19 IN RIO BRANCO, ACRE

ASSOCIAÇÃO ENTRE O USO DE MEDICAMENTOS ÀS REAÇÕES ADVERSAS RELACIONADAS À VACINAÇÃO CONTRA A COVID-19 EM RIO BRANCO, ACRE

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Abstract

COVID-19, originated by the new coronavirus SARS-CoV-2, has become a global pandemic. Despite the rapid development of vaccines against it, adverse reactions can occur and understanding individual responses and post-vaccination therapeutic decisions is essential. This study sought to evaluate the relationship between medications and reactions after vaccination in Rio Branco, Acre. The research involved 150 participants who received the 3rd or 4th dose of the COVID-19 vaccine. After vaccination, these participants were monitored by telephone for 30 days to check for any adverse reactions. Demographic data, information on adverse reactions after vaccination and use of medications associated with possible reactions to the vaccine were collected. Statistical analysis was represented by descriptive analysis and the association between variables and their influence according to the logistic regression model. The most common symptoms were local pain (42.9%), headache (22%), tiredness (8.8%) and fever (8.8%). Regarding gender, 42.9% of women and 44.1% of men reported pain at the application site. Furthermore, 8.7% chose anti-inflammatories and 6.5% used antibiotics after vaccination. Participants who experienced adverse reactions were almost 8 times more likely to resort to medication to relieve symptoms compared to those who did not experience such reactions (OR = 7.9895, p < 0.05). The significant association between adverse reactions and medication use highlights the importance of personalized and inclusive approaches to immunization against COVID-19, recognizing that different reactions can impact post-vaccination therapeutic choices.

Key-words: SARS-CoV-2; Vaccines; Adverse reactions; self-medication.

Resumo

A COVID-19, originada pelo novo coronavírus SARS-CoV-2, tornou-se uma pandemia global. Apesar do rápido desenvolvimento de vacinas contra ela, reações adversas podem ocorrer e compreender as respostas individuais e as decisões terapêuticas pós-vacinação torna-se essencial. Este estudo buscou avaliar a relação entre medicamentos e reações após vacinação em Rio Branco, Acre. A pesquisa envolveu 150 participantes que receberam a 3ª ou 4ª dose da vacina contra a COVID-19. Após a vacinação, esses participantes foram acompanhados por telefone ao longo de 30 dias para a verificação de eventuais reações adversas. Coletou-se os dados demográficos, informações sobre reações adversas após a vacinação e uso de medicamentos associados a possíveis reações à vacina. A análise estatística foi representada por análise descritiva e a associação entre as variáveis e sua influência conforme modelo de regressão logística. Os sintomas mais comuns foram dor local (42,9%), cefaleia (22%), cansaço (8,8%) e febre (8,8%). Em relação ao sexo, 42,9% das mulheres e 44,1% dos homens relataram dor no local de aplicação. Além disso, 8,7% escolheram anti-inflamatórios e 6,5% usaram antibióticos após a vacinação. Participantes que apresentaram reações adversas tiveram quase 8 vezes mais chances de recorrer a medicamentos para alívio de sintomas em comparação com aqueles que não apresentaram tais reações (OR = 7,9895, p < 0,05). A associação significativa entre reações adversas e uso de medicamentos destaca a importância de abordagens personalizadas e inclusivas na imunização contra COVID-19, reconhecendo que as diferentes reações podem impactar nas escolhas terapêuticas pós-vacinação.

Palavras-chave: SARS-CoV-2; Vacinas; Reações adversas; Automedicação.

Introduction

COVID-19, caused by the new coronavirus SARS-CoV-2, is a serious respiratory disease that has become a global pandemic since it was declared by the World Health Organization - WHO in March 2020 [1].

Due to the high transmissibility of the virus through respiratory secretions, COVID-19 spread rapidly around the world, resulting in millions of cases, hospitalizations, and deaths [2]. To contain the spread of the virus, prevention and control measures were adopted, such as hand hygiene, use of personal protective equipment, and social distancing [3].

However, these measures were not enough to control the pandemic, making it necessary to search for effective and safe vaccines against SARS-CoV-2. Vaccines are biological products that stimulate the immune system to produce specific antibodies against a specific infectious agent, providing protection to the vaccinated individual and reducing the risk of transmission and complications of the disease [4]. Vaccines are subjected to a rigorous development and evaluation process, which involves stages of exploratory research, pre-clinical trials (in vitro and in vivo) and clinical trials in humans (phases I, II and III), to verify their effectiveness and security [5].

Faced with the health emergency caused by COVID-19, there was an effort by the scientific community and regulatory authorities to accelerate the development and approval of vaccines against SARS-CoV-2 [4].

In Brazil, four vaccines received authorization for emergency use by the National Health Surveillance Agency - ANVISA: the CoronaVac vaccine (Butantan/Sinovac), which uses the inactivated virus; the Comirnaty vaccine (Pfizer/BioNTech), which uses synthetic messenger RNA; the Covishield vaccine (AstraZeneca/Oxford) and the Janssen vaccine (Johnson & Johnson), which use the recombinant adenovirus vector. Vaccination against COVID-19 in Brazil began in January 2021 by the National Immunization Program - PNI, with the aim of immunizing the entire eligible Brazilian population [5].

Despite the benefits of COVID-19 vaccines, some people may experience adverse reactions after vaccination, which are unwanted or harmful events that occur after receiving a vaccine. Adverse reactions can be classified as local (at the site of application) or systemic (in other parts of the body), and can vary in intensity, frequency and severity [6]. The most common adverse reactions are pain, redness and swelling at the injection site, fever, headache, muscle pain and fatigue. These reactions are usually mild and transient, disappearing within a few days. More serious or rare adverse reactions, such as severe allergic

reactions (anaphylaxis), thrombosis or myocarditis, may occur in isolated cases and require immediate medical attention [7,8].

Post-vaccination adverse reactions may be related to several factors, such as the characteristics of the vaccine (composition, dose, route of administration, etc.), the characteristics of the vaccinated individual (age, sex, health conditions, use of medications, etc.), the characteristics of the environment (temperature, humidity, etc.) and the characteristics of the surveillance system (notification, investigation, analysis, etc.) [8,9].

One way to avoid adverse reactions to the COVID-19 vaccine is to inform healthcare professionals about the medications being used before vaccination. Furthermore, caution must be taken with medications taken without medical advice after vaccination.

There are individuals who use analgesics and antipyretics to alleviate the symptoms of post-vaccination adverse reactions [7,10]. However, the use of medications can interfere with the immunological response to vaccination [11], which may increase or decrease the risk of adverse reactions.

However, there are still few studies on the association between the use of medications and adverse reactions following vaccination against COVID-19. In this context, the present study aims to evaluate the relationship between reports of adverse reactions after vaccination against COVID-19 and the use of medications in Rio Branco – Acre.

Material and Methods

This is a sectional analytical observational study carried out in the city of Rio Branco, Acre, in patients with an ongoing vaccination schedule.

The state of Acre (Figure 1), located in the southwestern portion of the Northern Region of Brazil, establishes territorial limits with two federative units: to the north, it borders Amazonas, and to the east, with Rondônia. Furthermore, it has international borders with two countries: to the southeast, it shares a border with Bolivia, while to the south and west, it shares a border with Peru. Within state borders, Acre is home to a total of 22 municipalities. Standing out in this context is Rio Branco, the state capital, which holds the title of most populous municipality. According to the first results of data from the last census carried out in 2020, the city of Rio Branco reached a population of 364,756 inhabitants [12], solidifying its position as the demographic epicenter of the state.

This research was approved by the Human Research Ethics Committee – CEP of the Northern Educational Union – UNINORTE under number CAE 60578222.80000.8028.

Figure 1. Geographical location of Rio Branco, state of Acre, Brazil
Source: Amaral et al., (2021) [13], adapted by Authors (2023)

The study voluntarily recruited individuals who received the COVID-19 vaccine in vaccination campaigns carried out in October and November 2022. Participants did not have COVID-19 at the time of vaccination, were healthy, and aged 18 or over. They signed the free and informed consent form before joining the study.

Before starting the research, participants received clear and objective information about the purpose, methods and advantages of the study. They were also instructed about their rights to consent or not to participate, or to revoke consent at any stage, without suffering any harm. Furthermore, compliance with the ethical principles of protecting their privacy and the confidentiality of their data was ensured, as well as the response to possible questions during the research.

To collect data from research participants, a semi-structured questionnaire was administered that contained questions about age, sex, type of vaccination schedule, type of

adverse reaction after vaccination and use of medications to prevent or treat these reactions. Participants were monitored by telephone for 30 days to check the occurrence of adverse reactions and the use of related medications.

Data were analyzed using Jamovi® software version 2.3. A descriptive analysis of categorical variables was carried out, including 'adverse reaction' (yes/no), 'type of adverse reaction', 'use of medication' (yes/no), 'sex' (male/female) and 'type of vaccination schedule' (homologous/heterologous). The absolute distribution and percentages were calculated. Furthermore, the continuous numerical variable, 'age', was summarized using the mean, median and standard deviation. For the analyses, 95% confidence intervals (95% CI) were considered.

After descriptive analysis, the multiple logistic regression model was adjusted to assess in more detail whether the association between independent variables including "adverse reaction", "sex", "age" and "type of vaccination schedule" influence the probability of "Medication Use" after vaccination. In this sense, adjustment measures for the global model were obtained to guarantee the adequate quality of the proposed model (R^2cs 0.0546).

The results of the multiple logistic regression model were analyzed considering coefficients and p values less than or equal to 0.05 ($p \leq 0.05$). Odds ratios were calculated to assess how the chances of 'Medication Use' change for each change in the independent variables."

Results and Discussion

The sample analyzed consisted of 150 individuals living in Rio Branco, Acre, who received doses of the vaccine against COVID-19. The age range of participants ranged from 18 to 58 years, the mean age was 24.5 years (SD: ± 7.13) and the median was 22, which suggests a relatively young distribution with the majority of ages below 30 years.

Regarding the characterization by sex, it is noted that 91 individuals (60.7%) were female, while 59 individuals (39.3%) were male (95% CI 0.5237-0.685 and 0.3147- 0.476 respectively).

With regard to post-vaccination adverse reactions, 18 cases (12.0%) without adverse reactions and 132 cases (88.0%) that presented adverse reactions to the vaccine were identified, considering the total of 150 individuals analyzed (IC 95% 0.0727-0.183 and 0.8170-0.927 respectively). The adverse reactions reported by individuals are in line with previous studies, mainly highlighting the occurrence of local pain and swelling at the injection site [14,15].

Table 2 presents a detailed analysis of the symptoms reported by participants in relation to adverse reactions after vaccination against COVID-19, considering gender differences. Pain at the application site was the most common symptom reported by both sexes, with 42.9% of women and 44.1% of men mentioning this local discomfort. This result is consistent with the general experience of discomfort at the vaccine site [16].

The experience acquired in previous vaccinations and the possible manifestation of adverse reactions seems to have a decisive influence on an individual's decision to seek additional booster doses, especially in cases where such reactions are mild or do not even occur [17].

In this context, it is important to consider that prior guidance, which outlines expectations regarding immunization, has the power to mitigate anxiety raised by incorrect information or negative beliefs about adverse reactions [17,18].

When analyzing the different vaccination schemes adopted, it was found that 54 individuals (36.0%) received the heterologous scheme, while 96 individuals (64.0%) received the homologous scheme (95% CI 0.2833-0.442 and 0.5577- 0.717 respectively). The immunogenicity of both regimens has been positively described, however, individuals who receive heterologous regimens demonstrate superior immunological responses in terms of maintaining long-lasting humoral immunity. This is true even for people who have not received full vaccination or who have been partially vaccinated [18–20].

However, regardless of the type of regimen adopted, these individuals remain susceptible to adverse reactions that are generally mild and temporary, which demonstrates the safety of the various vaccines against COVID-19 [21,22].

With regard to the use of medication after vaccination, it is important to note that, of the 150 participants, 70% did not report using medication, while 45 participants, 30%, mentioned having used medication for adverse reactions to the vaccine (CI 95 % 0.6199-0.772 and 0.2280-0.380 respectively) (Table 1) reinforcing the idea that adverse reactions, when present, are tolerable.

Table 1. Profile of study participants according to gender, adverse reaction to the COVID-19 vaccine, type of vaccination schedule, and use of medication, Rio Branco, Acre, 2023.

	Level	N	Total	%	p value	95% Confidence Interval Lim. Inferior	95% Confidence Interval Lim. Superior
Sexo	Female	91	150	60,7	0.011	0.5237	0.685
	Male	59		39,3	0.011	0.3147	0.476
Adverse reaction post COVID-19 vaccination	No	18	150	12	< .001	0.0727	0.183
	Yes	132		88	< .001	0.8170	0.927
Type of vaccination schedule	Heterologous	54	150	36	< .001	0.2833	0.442
	Homologous	96		64	< .001	0.5577	0.717
Medication Use	No	105	150	70	< .001	0.6199	0.772
	Yes	45		30	< .001	0.2280	0.380

Headache was observed in 22% of women and 10.2% of men. Headache is a multifaceted symptom, often associated with inflammatory responses from the immune system, which can vary in intensity and duration. The difference in prevalence between sexes may suggest different immune response profiles after vaccination [8] and is also an important finding and similar to previous studies [23–26].

Fever was reported by 8.8% of women and 11.9% of men. This response, also linked to the activation of the immune system, was observed in similar proportions between the sexes. Fever is a sign that the immune system is active, responding to the introduction of the vaccine antigen [15,27].

Table 2. Reported symptoms related to observed reactions according to gender

Adverse reactions	Female N (%)	Male N (%)
Pain at the application site	39 (42,9)	26 (44,1)
Headache	20 (22)	6 (10,2)
Tiredness	8 (8,8)	8 (13,6)
Fever	8 (8,8)	7 (11,9)
Dizziness	1 (1,1)	1 (1,70)
Other symptoms	6 (6,6)	2 (3,4)
No reactions	9 (9,9)	9 (15,3)
Total	**91 (100)**	**59 (100)**

These results highlight the heterogeneity of responses to adverse reactions to vaccination between different sexes [28]. It is important to highlight that, despite variations in

the proportions of symptoms, all of which are expected and mild [25], there were no reports of serious adverse reactions.

Table 3 presents the classes of medications used by participants after vaccination against COVID-19 due to adverse reactions. The analgesics/antipyretics category represents the most prevalent therapeutic choice, with 80.4% of participants reporting their use. These medications, known to relieve pain and reduce fever, appear to be a common choice to mitigate possible mild side effects after immunization, results similar to previous studies [7,18,29,30] that showed that participants predominantly used paracetamol, with ibuprofen as the second medication of choice, in this case as an anti-inflammatory.

Anti-inflammatories were mentioned by 8.7% of participants. Although this proportion is lower, it is important to consider that the choice of anti-inflammatories may be motivated by specific symptoms, such as swelling and redness.

Table 3. Characteristics related to the use of medications after vaccination

Drug Classes	N (%)
Analgesic/antipyretic	37 (80,4)
Anti-inflammatory	4 (8,7)
Antibiotic	3 (6,5)
Antibiotic/analgesic/anti-inflammatory	2 (4,3)
Total	**46 (100)**

The results revealed that the presence of adverse reactions after vaccination is a factor associated with the use of medications. Individuals who reported adverse reactions to vaccination were significantly more likely to use medication after vaccination (Odds Ratio = 7.9895, $p < 0.05$), meaning they are almost 8 times more likely to use medication compared to those who reported no adverse reactions.

However, the other variables studied, including 'Sex' (Odds Ratio = 0.5491, $p > 0.05$), 'Age' (Odds Ratio = 1.0236, $p > 0.05$) and 'Type of vaccination schedule (Odds Ratio = 1.0680, $p > 0.05$), did not show significant associations with 'Medication Use'.

These findings have important implications for understanding the factors that influence post-vaccination behavior and may provide relevant guidance for interventions and counseling for individuals. However, it is important to highlight that it cannot be said that the adverse reaction directly causes the use of medications, as the regression analysis does not establish causality, only association.

However, self-medication can pose a significant risk to individual health in many cases as seen during the COVID-19 outbreak [31,32], including when seeking to mitigate adverse reactions to the vaccine.

While it is understandable that people seek relief from mild and/or moderate symptoms, it is essential to remember that not all medications are appropriate or indicated [33]. Therefore, self-medication, even when aimed at mitigating temporary discomfort, can trigger unforeseen side effects, unwanted drug interactions and, in extreme cases, serious health complications.

Conclusion

Adverse reactions following vaccination against COVID-19 are significantly associated with medication use. Those who experienced adverse reactions were almost 8 times more likely to turn to medication. However, gender, age and vaccination schedule did not demonstrate a significant influence on the use of medications.

It is crucial to maintain vigilance regarding the therapeutic choices made by people after vaccination, considering the possible occurrence of adverse reactions. Additionally, it is important to promote public policies and communicate to healthcare professionals the relevance of targeted and personalized post-vaccination strategies.

These approaches not only have significant implications for understanding the factors that shape post-vaccination behavior but can also offer important guidelines for individual interventions and counseling.

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