

Safety Profile of Acellular Pertussis Vaccines: A Statistical and Epidemiological Analysis

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Perfil de Seguridad de las Vacunas Acelulares Contra la Tos Ferina: Un Análisis Estadístico y Epidemiológico

RESUMO:

Objetivo: Foi efetuado uma análise sobre trabalhos de cunho observacional os quais mensuraram as taxas de eventos adversos de vacinas celulares e acelulares contra essa doença. **Método:** A busca foi realizada em bases como PubMed, Scopus, Cochrane, Embase e LILACS, utilizando descritores controlados e palavras-chave relacionadas a coqueluche, e eventos adversos a vacina. **Resultados:** Vacinas acelulares tiveram menores taxas de incidência. **Conclusão:** Viu-se que a segurança desse modelo de vacina é um bom preditivo quanto ao uso desses imunobiológico.

DESCRIPTORES: Coqueluche; Vacinação; Reações Adversas.

ABSTRACT

Objective: An analysis was conducted on observational studies that measured the rates of adverse events of cellular and acellular vaccines against this disease. **Method:** The search was performed in databases such as PubMed, Scopus, Cochrane, Embase and LILACS, using controlled descriptors and keywords related to pertussis and adverse events to the vaccine. **Results:** Acellular vaccines had lower incidence rates. **Conclusion:** It was seen that the safety of this vaccine model is a good predictor of the use of these immunobiologicals.

DESCRIPTORS: Whooping cough; Vaccination; Adverse reactions.

RESUMEN

Objetivo: Se realizó un análisis de estudios observacionales que midieron las tasas de eventos adversos de vacunas celulares y acelulares contra esta enfermedad. **Método:** La búsqueda se realizó en bases de datos como PubMed, Scopus, Cochrane, Embase y LILACS, utilizando descriptores controlados y palabras clave relacionadas con la tos ferina y eventos adversos a la vacuna. **Resultados:** Las vacunas acelulares presentaron tasas de incidencia más bajas. **Conclusión:** Se observó que la seguridad de este modelo de vacuna es un buen predictor del uso de estos inmunobiológicos.

DESCRIPTORES: Tos ferina; Vacunación; Reacciones adversas.

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INTRODUCTION

Pertussis is a transmissible respiratory infection caused by the bacterium *Bordetella pertussis*, whose occurrence and severity are typically higher in neonates and infants. Although vaccination programs are classically the main primary prevention measures, pertussis continues to be an important public health problem, as it remains endemic in many localities, and increases in incidence rates cause epidemics that appear cyclically at intervals of three to five years, so it is important to keep the population protected based on primary prevention measures such as vaccination campaigns¹.

There are currently two types of pertussis vaccines, usually combined with diphtheria and tetanus antigens (dTpa), namely whole-cell vaccines (wP) and acellular vaccines (aP). Whole-cell vaccines are made up of a suspension of the entire inactivated *B. pertussis* organism, while acellular vaccines contain purified components of the bacterium, such as inactivated pertussis toxin, alone or in combination with other components, such as filamentous hemagglutinin, fimbrial antigens and pertactin. Both vaccines have relative protective efficacy, but whole-cell vaccines have been associated with a series of adverse reactions².

Regarding the epidemiological situation, it can be inferred that the increase

in the incidence of *B. pertussis* infection since 2011 and the recent implementation of dTpa in the National Vaccination Schedule for Pregnant Women highlight the relevance of pertussis today, while more recent factors such as low vaccination coverage, especially among children, have proved to be a critical factor in controlling this disease. Studies that carried out a longitudinal profile of vaccination coverage in Brazil confirmed the downward trend in vaccination coverage, alerting us to the need for strategies to improve this scenario and reduce vaccine hesitancy¹⁻³.

Conclusions range from the population's lack of awareness of the threat of re-emergence of vaccine-preventable diseases, more implicit attention to minor side effects and the influence of anti-vaccine propaganda on social media.

Given the worrying scenario of pertussis in Brazil, this study aims to assess the frequencies of adverse events to acellular and whole-cell vaccines, and to evaluate them from a statistical perspective based on epidemiological studies involving sample trials using both vaccines.

METHODOLOGY

An analytical review was carried out with the aim of assessing the risk factors associated with the prevalence and/or incidence of adverse events from vac-

cines in use by the Unified Health System (SUS) and their implications for the safety of these immunobiologicals. To this end, measures of association applied in observational cohort and case-control studies, such as the Odds Ratio (OR) and Relative Risk (RR), were considered in the observed studies, and the quality analyses of the studies were calculated using the Mantel-Haenszel (MH) fixed model, considering the following components for calculation: Y_j (desired effect) = $\theta M + \epsilon_j$ (where ϵ_j is the random error of the study, and θM is the effect common to all studies). In addition, the Higgins and Thompson models were used, $I^2 = (Q - gl) / Q \times 100$, where Q is based on Cochran's Q test ($Q = \sum w_i(\theta_i - \theta)^2$ which presents the null hypothesis that the studies that make up the review are homogeneous).

A complementary analysis inferred morbidity rates and their respective confidence intervals for adverse reactions seen in the literature based on epidemiological trials that compared users of wP and aP vaccines.

The tests used had a cut-off point of 0.05% and all statistical analyses were carried out using the JASP software, version 0192 (2024).

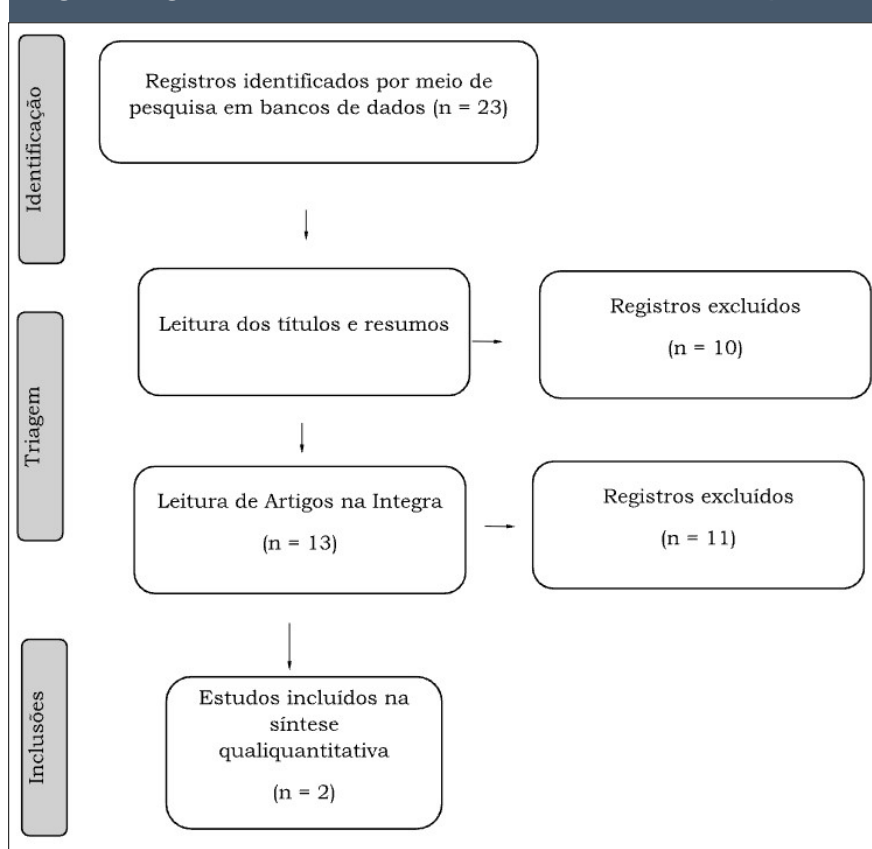
The systematic review process was based on the Cochrane Model (Cochrane Handbook for Systematic Reviews of Interventions version 6.1, 2020), and also followed the recom-

recommendations established by the PRISMA protocol (Preferred Reporting Items for Systematic Reviews and Meta-Analyses). The databases evaluated were PUBMED, BVS / BIREME, SCOPUS, Web of Science and EMBASE. The search strategy used to select the papers was as follows: "vaccination" OR whooping cough OR "adverse reactions". The selection criteria were articles that included patients with a description of adverse reactions between vaccines, classified as cohort studies, case-control studies, clinical trials or case series. The search was carried out between June and December 2024 and complemented with the use of a computer tool called Publish or Perish (www.harzing.com), which uses the Google Scholar search engine to search the databases according to the search strategy adopted, while verifying the scientific coefficients of the articles by evaluating their impact factors and h-index. The inclusion criteria were articles that identified the relevance of the incidence rates of adverse reactions to both vaccines. Information materials, partial e-books and articles that did not cover the subject proposed by the study were excluded. The articles found were categorized in ascending order based on the h-index and impact factor cut-off above 4 citations. The data obtained from this categorization was analyzed for literature review and grouped for literature review⁴.

RESULTS

Initially, 23 articles were identified that met the previously established search strategy. After reading the abstracts and titles, 10 papers were eliminated because they did not discuss the subject proposed for this review, leaving 13 articles. Then, based on a careful reading of the full text of the remaining papers, a sample of 2 papers was obtained which met all the criteria previously established (Figure 1).

Figure 1 - Organizational chart of the article identification and exclusion process.



Source: Author, 2025.

Two articles were retrieved by the search systems, which showed that observational studies compared the prevalence of adverse events associated with wP and aP vaccines. The heterogeneous set of studies ($p < 0.05$) refuted the null

hypothesis and ensured the variability of the data and the validation of the results. The identification of moderators of the observed effects and the reduction of biases inferred in the tests can be seen in Table 1.

Table 1 Q-test and I2test values in the analysis of the 2 articles evaluating the outcome of complications between the different types of vaccines.

	Test Q	p-value	I ²
Coefficient	1,73	<0,05	77%
Heterogeneity residue test	1,15	<0,05	

Source: Own authorship, 2025.

Table 2 shows the analysis of the prevalence rates of adverse events between the whole-cell and acellular vac-

cines and their respective confidence intervals.

indicate that the perceived safety of acellular vaccines favors return for subsequent doses, highlighting the importance of continuously monitoring and reviewing immunization programs to optimize both safety and public acceptance.

Vaccine acceptance is a challenge that requires the attention of health professionals, whose active listening and guidance are essential to clarify doubts and strengthen confidence in vaccines. Communication about the efficacy and safety of vaccines, along with information on how to deal with possible adverse reactions, plays a key role in achieving and maintaining vaccination coverage that guarantees protection against outbreaks of vaccine-preventable diseases. Therefore, strengthening and expanding efforts to raise awareness and educate the population must remain pillars of immunization policies.

The limitation of our study was the low number of articles based on observational epidemiological surveys, which shows the need to expand discussions on health surveys with a larger sample size among the Brazilian population. Pertussis vaccination coverage is still below the national target of 95%. This scenario calls for continued efforts to raise this figure by understanding the variables implicit in this situation, thus ensuring the minimization of cyclical epidemics, the risk of re-emergence of this disease and the constitutional guarantee of public vaccination safety.

Table 2 Odds ratio values implying the rates of serious adverse events between both vaccines observed in observational studies between 2014 and 2021.

Authors	OR	CI (95%)*	p-value
Zhang et al, 2014 ⁵ .	1,86	[0,85- 2,07]	0,07
Elas et al, 2021 ⁶ .	4,23	[1,72- 9,35]	0,03

*The confidence interval was calculated with the standard error (SEa) corrected for stratification: $\sqrt{p(1-p)/n}$ and with 95% confidence = $p' - 1.96 \times \text{SEPa}$; $p'' + 1.96 \times \text{SEPa}$.

Source: own authorship, 2025.

DISCUSSION

The heterogeneity of the studies was fundamental to the construction of this analysis, as it guaranteed the variability of the data and the validation of the results seen in the studies identified.

The comparative analysis carried out in 2014 evaluated the differences between acellular and whole-cell vaccines and in terms of efficacy, no significant difference was observed between them (OR 1.86). However, in terms of safety profile, acellular vaccines showed superiority (CI 0.85). These vaccines have fewer adverse reactions, although according to the authors there is an increase in reactions from the

first to the third dose, these rates are still lower than those observed with whole-cell vaccines. In the 2021 study carried out in El Salvador, there was a significant difference in the occurrence of these events between the two types of vaccines, the results indicated that the rate of effects following vaccination with cell vaccines (OR of 4.23) exceeded the rate expected by the WHO of 6 cases per 100,000 doses as of April 2019, reaching a peak of 9.2 cases in September of the same year.

CONCLUSION

Acellular vaccines have had a significant reduction in adverse events compared to whole-cell vaccines, a factor that positively impacts confidence and adherence to the vaccination schedule. Although both vaccines have guaranteed efficacy, studies

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