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Evaluation of the safety profile of the quadrivalent vaccine against human papillomavirus in the risk of developing autoimmune, neurological, and hematological diseases in adolescent women in Colombia

Ivette Maldonado [a b], Nicolas Rodríguez Niño [a], Carlos F. Valencia [c], Daniela Ortiz [c], Nathalia Ayala [b], Liz D'silva [b], Santiago Castro Villarreal [c], Diego Salazar [c], Catalina Lozano [c], Daniela Angulo [c d]

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Abstract

Background

Cervical cancer eradication is one of the main goals for 2030 by the World Health Organization, which can only be achieved with high vaccination rates against Human Papilloma Virus. In Colombia, more and better scientific evidence is required to increase confidence in vaccination. The objective of this study is to evaluate the safety profile of the quadrivalent vaccine against HPV in the risk of developing autoimmune, neurological, and hematological diseases in adolescent women in Colombia.

Methods

We designed a cohort study based on national HPV vaccination records and incident diagnostic data for the diseases of special interest during 2012 and 2021. We included adolescent women between 9 and 19 years old and compared vaccinated and non-vaccinated cohorts using an Inverse Probability of Treatment Weighting (IPWT) method for each scenario disease and follow-up period (180 and 360 days).

Findings

The Odds Ratio (OR) of developing diseases of interest was estimated during two follow up periods, 180 and 360 days after the follow-up index date (Vaccination Day). The OR for developing rheumatoid arthritis was 4·4; CI95% (1·74 – 11·14), juvenile idiopathic arthritis was 2·76 IC95% (1·50 – 5·11), idiopathic thrombocytopenic purpura was 2·54 IC95% (1·28 – 5·02) and thyrotoxicosis was 2·86 IC95% (1·03 – 7·95), when comparing the vaccinated versus unvaccinated population. However, the temporal distribution of cases incident did not reveal a clear difference between the cohorts, since the rate of appearance of new cases has a constant linear behavior for the two groups.

Interpretation

For rheumatoid arthritis, juvenile idiopathic arthritis, idiopathic thrombocytopenic purpura, and thyrotoxicosis; the application of the vaccine had an effect on the development of the disease. Nevertheless, our results should be interpreted with caution and be further studied, considering that the biological plausibility of the events occurred without a clear temporal pattern in relation to the exposure to the vaccine.

Introduction

In August 2020, the World Health Organization proposed a global strategy to accelerate the elimination of cervical cancer, whose goal is to achieve and maintain an incidence rate lower than four cases per 100.000 women / year.[1] Developed countries like Sweden, Australia and the United Kingdom have an incidence rate of 5·6 to 10·4 cases per 100.000 women / year. Colombia has a rate that exceeds 14 cases per 100.000 women / year, making it one of the main causes of death for women in this country.[2].

This high burden of disease of cervical cancer in Colombia is due to multiple factors: lack of an efficacious screening program, lack of timely access to the health system in remote areas, widespread public misinformation regarding primary prevention in the adolescent population,[2], [3] and mistrust that intensified in 2014 due to a massive psychogenic reaction after immunization in a school population in a rural region, with multiple symptoms that led to the assumption of adverse events secondary to vaccination. [4] This caused a drastic drop in the global vaccination rate that varied from 98 % in the first dose in 2012, going through the worst stage in 2016 with 6 % and finally reaching 28 % in 2020.[5].

There is strong scientific evidence worldwide that defines the quadrivalent vaccine against human papillomavirus (qHPV vaccine) as safe and effective.[6] However, lack of local studies that support this evidence, could be one of the factors that explain the low vaccination rates. The aim of this study is to provide information about the safety profile of the vaccine in Colombia.

Section snippets

Data sources

The RIPS (Individual Records for the Provision of Health Services, in Spanish), contain individual records of access to health services in Colombia and are composed mainly of the datasets of medical consultations, hospitalizations, medical procedures, and emergencies.[7] For this study, the Ministry of Health provided us with access to a subset of de-identified RIPS datasets which contain all records of de-identified patients with at least one record associated to an ICD-10 code of any of the…

Results

For the first dose analysis, we compared a sample of 55,114 vaccinated women versus 370,800 unvaccinated adolescents. Regarding the analysis of second dose, we compared 35,801 vaccinated women versus 370,793 unvaccinated adolescents. The overall statistics of the vaccinated and unvaccinated groups in both, first and second doses, analysis are shown in Table 1.

For the propensity score estimation models in both analysis (first and second doses), we selected the Boosting classification model,…

Discussion

This study is based on data from 1,953,196 adolescent women exposed to the HPV vaccine in the context of a national vaccination plan over nearly a decade. Of the total number of the population in the PAI database, only 2·8% (55,144) was registered in the RIPS database, which is why it was considered the exposed cohort to be included in the statistical approximation to estimate the causal relation.

64 possible analysis scenarios were considered, based on the combination of: (i) the 16 diseases,…

Conclusion

From the total universe of 36 diseases, we used a statistical approximation to evaluate the safety profile of the qHPV vaccine on the development of 16 diseases of interest. We estimated the effect of the vaccine using a quasibinomial regression model with binary response weighted by the inverse probability of treatment. Additionally, we used a two-step analytical strategy to identify diseases that require additional verification to analyze. First, we found that only for four diseases:…

CRediT authorship contribution statement

Ivette Maldonado: Conceptualization, Data curation, Formal analysis, Funding acquisition, Investigation, Methodology, Project administration, Resources, Supervision, Validation, Visualization, Writing – original draft, Writing – review & editing. **Nicolas Rodríguez Niño:** Conceptualization, Data curation, Formal analysis, Funding acquisition, Investigation, Methodology, Project administration, Resources, Software, Supervision, Validation, Visualization, Writing – original draft, Writing – review…

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that

could have appeared to influence the work reported in this paper.…

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