EVALUATION OF THE NOTIFICATION PROFILE OF ADVERSE EVENTS RELATED TO CHLOROQUINE AND AZITHROMYCIN BEFORE AND DURING THE COVID-19 PANDEMIC

Thalyta dos Santos Alencar [1]
Amanda Fernandes Borges de Araújo [1]
Aline de Araújo Freitas [2]
Emerith Mayra Hungria Pinto [3]

ABSTRACT

This study evaluated the profile of adverse event notifications related to the use of Chloroquine and Azithromycin before and during the COVID-19 pandemic. The pandemic led to massive prescribing of these drugs, even without solid scientific evidence proving their efficacy against SARS-CoV-2. Using data from the VigiMed system, adverse event notifications were analyzed for the periods from January 2018 to December 2019 (pre-pandemic) and from March 2020 to December 2021 (pandemic). The results showed a significant increase in notifications during the pandemic, highlighting the severity of adverse effects associated with the indiscriminate use of these drugs. This study emphasizes the importance of evidence-based medical practices and rigorous pharmacovigilance to avoid unnecessary risks to public health. The conclusions reinforce the need for public policies focused on health education and the prevention of self-medication, especially in scenarios of health crises.

Keywords: Chloroquine, Azithromycin, COVID-19, Pharmacovigilance

INTRODUCTION

The COVID-19 pandemic, which began in December 2019, caused a global public health crisis, triggering an urgent search for effective treatments. In this context, drugs such as chloroquine and azithromycin were widely used, despite the lack of concrete evidence about their efficacy against SARS-CoV-2 (CHEN, 2020).

Chloroquine, traditionally used in the treatment of malaria and autoimmune diseases, such as systemic lupus erythematosus and rheumatoid arthritis, presented side effects ranging from mild gastrointestinal symptoms to severe

ophthalmological damage, such as retinopathy associated with high doses and prolonged use (WALKER, 2020; CHARY, 2020; FURTADO, 2020). Azithromycin is a macrolide antibiotic used in various bacterial infections. The drug is associated with adverse effects such as gastrointestinal, neurological, and hepatic disorders (JOHNSTON, 2021).

With the massive and often indiscriminate use of these medications during the pandemic, there was a significant change in the profile of adverse event notifications, which raises the need for a detailed and comparative evaluation between the pre-pandemic and pandemic periods (SAID, 2022; JOHNSTON, 2020; DANZA, 2015).

Therefore, given the dissemination of the "COVID kit," the present study aims to evaluate adverse events during the pre-pandemic and pandemic periods.

METHODOLOGY

The study adopted a cross-sectional design with a descriptive-exploratory and analytical approach. Data were collected from the VigiMed system, a platform of the Brazilian Health Regulatory Agency (Anvisa) intended for pharmacovigilance, where adverse events related to drugs and vaccines are reported.

Adverse events related to Chloroquine and Azithromycin in VigiMed between January 1, 2018, and December 31, 2019 (pre-pandemic period) and between March 1, 2020, and December 31, 2021 (pandemic period) were analyzed. Adverse reactions were categorized according to the Medical Dictionary for Regulatory Activities (MedDRA), used by VigiMed.

RESULTS

The results indicated substantial differences in the profile of adverse event notifications for Chloroquine and Azithromycin between the pre-pandemic (2018-2019) and pandemic (2020-2021) periods. During the pre-pandemic period, notifications related to Azithromycin were mainly concentrated on cutaneous reactions (rashes, pruritus) and gastrointestinal disorders (nausea, diarrhea), with serious events such as hospitalizations due to anaphylactic reactions representing

8.82% of cases. For Chloroquine, visual disorders, such as retinopathy (92%), and gastrointestinal disorders (51.7%) were predominant, with a low number of serious events (1.44%).

With the pandemic, there was a sharp increase in notifications; adverse events reported for azithromycin increased from 34 to 269, an increase of 691.18%, and those for chloroquine from 139 to 765 notifications, representing an increase of 450.36%. The pandemic period was also associated with a change in the type of adverse events reported. For Azithromycin, in addition to cutaneous (32.34%) and gastrointestinal reactions (41.17%), serious complications such as cardiac arrhythmias (12.63%) and hepatotoxicity (2.65%) emerged. In the case of Chloroquine, in addition to visual and gastrointestinal disorders, there was a significant increase in cardiac arrhythmias (28.62%) and neurological disorders such as seizures and tremors (82.61%).

Azithromycin, an antibiotic often prescribed in combination with chloroquine, was widely used in the hope of reducing lung inflammation associated with COVID-19. However, according to Furtado (2020) and Danza (2015), the indiscriminate use of azithromycin led to an increase in serious adverse events, including hepatotoxicity and cardiac arrhythmias, due to its potential to prolong the QT interval when administered together with other cardiotoxic drugs.

The scientific literature also suggests that the rapid dissemination of unverified information, often exacerbated by social media and statements from public figures, contributed to the widespread adoption of these treatments without the support of robust scientific evidence (WALKER, 2020). As highlighted by Santos *et al* (2024), the infodemic - an epidemic of misinformation - was a critical factor that led to unnecessary and potentially dangerous prescribing of medications such as chloroquine and azithromycin, resulting in a considerable increase in complications and serious adverse effects.

CONCLUSION

The results obtained in this study revealed a significant increase in notifications of adverse events related to the use of Chloroquine and Azithromycin

during the COVID-19 pandemic, compared to the pre-pandemic period. This increase is indicative of the indiscriminate and often inappropriate use of these drugs, driven by the urgency to find effective treatments for COVID-19, despite the lack of robust scientific evidence supporting their efficacy. The analysis of the data suggests that massive prescribing and self-medication, motivated by unfounded recommendations, contributed to a higher incidence of adverse reactions, including some of a serious nature.

ACKNOWLEDGEMENTS

We would like to express our deep gratitude to UniEvangélica for the support of our research project.

REFERENCES

CHARY, M.A. *et al*. COVID-19: Therapeutics and Their Toxicities. **Journal of Medical Toxicology,** v. 16, p. 284-294, 2020.

CHEN, N. *et al*. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. **Lancet**, v. 395, n. 10223, p. 507-513, 2020.

DANZA, A. *et al*. Hidroxicloroquina no tratamento das doenças autoimunes sistêmicas. **Revista Médica do Chile**, v. 144, n. 2, p. 232-240. Chile, 2015.

FURTADO, H.M.R. *et al*. Azithromicin in addition to standard of care versus standard of care alone in the treatment of patients admitted to the hospital with severe COVID-19 in Brazil (COALITION II): a randomised clinical trial. **Lancet**, v. 396, p. 959-967, 2020

JOHNSTON, C. *et al*. Hydroxychloroquine with or without azithromycin for treatment of early SARS-CoV-2 infection among high-risk outpatient adults: A randomized clinical trial. **EClinical Medicine,** v. 33, 2021.

SAID, S.A.A. *et al.* Monoterapia versus politerapia de enoxaparina e hidroxicloroquina para o tratamento de COVID-19: um ensaio clínico controlado randomizado. **Pharmacy Practice**, v. 21, n. 1, p. 1-7, 2023.

SANTOS, A. C. *et al.* Investigação original: reações adversas a medicamentos usados para a COVID-19 em cinco países da América Latina. ***Revista Panamericana de Saúde Pública, Washington,*** v. 47, n. 1, p. 45-58, 2023. Disponível em: https://doi.org/10.26633/RPSP.2023.0047. Acesso em: 28 ago. 2024.

WALKER, P.G.T. *et al.* The impact of COVID-19 and strategies for mitigation and suppression in low-and middle-income countries. ***Science***, v. 369, n. 6502, p. 413-422, 2020.