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LETTER TO THE EDITOR

Administration of chloroquine and hydroxychloroquine through feeding tubes: that was then and this is now

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TO THE EDITOR,

In March 2020, we sent you a short communication entitled "*Administration of chloroquine or hydroxychloroquine through feeding tubes: new challenges in times of coronavirus pandemic*" which was then published in this Journal in early April 2020[1]. Back then, Brazil started to face the new coronavirus (SARS-CoV-2) pandemic. Additionally, we were one of the countries that responded to the call of the World Health Organization (WHO) to participate in multicentric studies of pharmacological treatments that showed promise against the infection during other coronavirus epidemics[2-4]. Chloroquine and hydroxychloroquine are two of those promising medications and were tested in different multicentric studies, such as the Solidarity Trial, developed by the WHO, which involved more than 100 different countries; the DisCoVeRy study, by France; the RECOVERY and COPCOV studies, by the United Kingdom; and the Clinical Research Coalition, developed in 30 countries, including Brazil[2,4-8].

At that time, chloroquine and hydroxychloroquine were also beginning to be used as off-label options in different Brazilian settings, including hospitals that participated in scientific studies and other health care institutions, where a rapidly growing number of patients required critical care and intubation[3]. It was clear that these patients would be unable to receive oral solid dosage forms by mouth and would have a demand for drug administration through feeding tubes and extemporaneous compounding[1,9]. As the world waited for the results of multiple randomized controlled trials and the number of hospitalizations and deaths from COVID-19 increased, we, as researchers and pharmacists, felt the need to help our fellow healthcare workers properly administer chloroquine or hydroxychloroquine through feeding tubes, which was reported in the previous publication[1].

That was then. Now, in November 2021, even though the world, and especially Brazil, has experienced far too many losses, researchers and health care workers are facing different and better situations. To date, it has been possible to access not only randomized controlled trials,

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but also well-conducted meta-analyses and living systematic reviews on the use of various medications to treat of prevent COVID-19[10,11]. In this context, based on cumulative evidence, the scientific community is aware that the use of chloroquine or hydroxychloroquine to treat or prevent COVID-19 is not effective and can now focus on what actually is[12-16].

It is unfortunate that this drug repositioning strategy was not possible, as many lives could have been saved if those affordable medications had proven effective. Nonetheless, it is important to emphasize that dealing with the adverse events that follow the use of chloroquine or hydroxychloroquine, such as cardiac and liver dysfunction and gastrointestinal effects, has always been a challenge[17,18]. There was no difference during the pandemic, when inappropriate use led to a significantly high number of adverse events reported to the Brazilian regulatory agency (Anvisa - Agência Nacional de Vigilância Sanitária). From March to August 2020, hydroxychloroquine was the medication most frequently involved in adverse event reports, accounting for more than 59% of the total national reports in Brazil. Hydroxychloroquine and chloroquine were the only two medications that were shown to be associated with the occurrence of severe adverse events during the same period of time[19].

However, managing these potentially severe adverse events will remain a problem for years to come. This is not because people will still use hydroxychloroquine or chloroquine to treat prevent COVID-19 (we certainly hope not), but rather because they are still important therapeutic options for malaria, rheumatoid arthritis, and lupus[17,18]. One of the many safety challenges still involves their administration through feeding tubes. This challenge has been described in the literature long before the pandemic caught us off guard, and will probably continue to be addressed by other authors around the world, especially in developing countries, such as Brazil, that still have high malaria burdens[20].

In this context, we believe that, although our previously published study has to be read in a different scientific light, its content is still important for guiding safe practices where the use of chloroquine and hydroxychloroquine remain necessary for appropriate evidence-based therapeutic indications.

REFERENCES

1. Nascimento MMG, Santos SR, Rezende CP, Araújo RLB. Administration of chloroquine or hydroxychloroquine through feeding tubes: new challenges in times of coronavirus pandemic. Rev Cienc Farm Basica Apl. 2019;40:e640.
2. Saesen R, Huys I. COVID-19 clinical trials: see it big and keep it simple. BMJ Evidence-Based Medicine. 2021;26(4):147-8. http://dx.doi.org/10.1136/bmjebm-2020-111447.
3. World Health Organization – WHO. Timeline: WHO's COVID-19 response [Internet]. Geneva: WHO; 2021. [cited 2021 Oct 19]. Available from: https://www.who.int/emergencies/diseases/novel-coronavirus-2019/interactive-timeline?gclid=CjwKCAjwrKr8BRB_EiwA7eFapkO88lYCG_hjMzo871HRU0N1jNcOUEtYvYXk8lRw-NUrQwgb2fvLPRoCSYwQAvD_BwE#event-67
4. World Health Organization – WHO. "Solidarity" clinical trial for COVID-19 treatments [Internet]. Geneva: WHO; 2020. [cited 2021 Oct 19]. Available from: https://www.who.int/emergencies/diseases/novel-coronavirus-2019/global-research-on-novel-coronavirus-2019-ncov/solidarity-clinical-trial-for-covid-19-treatments
5. Ader F. Protocol for the DisCoVeRy trial: multicenter, adaptive, randomized trial of the safety and efficacy of treatments for COVID-19 in hospitalized adults. BMJ Open. 2020;10(9):e041437. http://dx.doi.org/10.1136/bmjopen-2020-041437. PMid:32958495.
6. University of Oxford. COPCOV. Chloroquine/ hydroxychloroquine prevention of coronavirus disease (COVID-19) in the healthcare setting; a randomised, placebo-controlled prophylaxis study [Internet]. 2020 [cited 2021 Oct 19]. Available from: https://www.copcov.org/
7. COVID-19 Clinical Research Coalition. Global coalition to accelerate COVID-19 clinical research in resource-limited settings. Lancet. 2020;395(10233):1322-5. http://dx.doi.org/10.1016/S0140-6736(20)30798-4. PMid:32247324.

8. RECOVERY Collaborative Group. Randomised evaluation of COVID-19 therapy [Internet]. 2020 [cited 2021 Oct 19]. Available from: https://www.recoverytrial.net/
9. Benzi RLJ. Extemporaneous compounding for the drugs that may be used in COVID-19 treatment. Rev Cienc Farm Basica Apl. 2019;40:e651.
10. Cappelletti P, Bizzaro N, Dorizzi RM. How COVID-19 is changing research, publishing, and guidelines. Riv Ital Med Lab. 2020;16(2):79-82.
11. Jones CW, Woodford AL, Platts-Mills TF. Characteristics of COVID-19 clinical trials registered with ClinicalTrials.gov: cross-sectional analysis. BMJ Open. 2020;10(9):e041276. http://dx.doi.org/10.1136/bmjopen-2020-041276. PMid:32948577.
12. De Crescenzo F, et al. Comparative effectiveness of pharmacological interventions for Covid-19: a living systematic review and network meta-analysis [Internet]. 2021 [cited 2020 Oct 2019]. Available from: https://www.deplazio.net/farmacicovid/index.html
13. Hernandez AV, Roman YM, Pasupuleti V, Barboza JJ, White CM. Update alert 3: hydroxychloroquine or chloroquine for the treatment or prophylaxis of COVID-19. Ann Intern Med. 2020;173(11):W156-7. http://dx.doi.org/10.7326/L20-1257. PMid:33085507.
14. Juul S, et al. Interventions for treatment of COVID-19: second edition of a living systematic review with meta-analyses and trial sequential analyses (The LIVING Project). PLoS One. 2021;16(3):e0248132. http://dx.doi.org/10.1371/journal.pone.0248132.
15. Pan American Health Organization. Ongoing living update of potential COVID-19 Therapeutics Options: summary of evidence - rapid review [Internet]. Estados Unidos, 2021 [cited 2021 Oct 19]. Available from: https://iris.paho.org/handle/10665.2/52719
16. Siemieniuk RA, et al. Drug treatments for COVID-19: living systematic review and network meta-analysis. BMJ. 2020;370:m2980. http://dx.doi.org/10.1136/bmj.m2980. PMid:32732190.
17. Brasil. Ministério da Saúde. Secretaria de Ciência, Tecnologia e Insumos Estratégicos. Departamento de Assistência Farmacêutica e Insumos Estratégicos. Formulário terapêutico nacional 2010: Rename 2010. 2ª ed. Brasília: Ministério da Saúde; 2010.
18. IBM Micromedex® [Internet]. Colorado: IBM Watson Health; 2020 [cited 2021 Oct 19]. Available from: https://www.micromedexsolutions.com
19. Melo JRR, Duarte EC, Moraes MV, Fleck K, Silva ASDNE, Arrais PSD. Adverse drug reactions in patients with COVID-19 in Brazil: analysis of spontaneous notifications of the Brazilian pharmacovigilance system. Cad Saude Publica. 2021;37(1):e00245820. http://dx.doi.org/10.1590/0102-311x00245820. PMid:33503163.
20. Bezerra JMT, Barbosa DS, Martins-Melo FR, Werneck GL, Braga EM, Tauil PL, Carneiro M. Changes in malaria patterns in Brazil over 28 years (1990-2017): results from the Global Burden of Disease Study 2017. Popul Health Metr. 2020;18(Suppl. 1):5. http://dx.doi.org/10.1186/s12963-020-00211-6. PMid:32993671.

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