Prophylactic Use Of Hydroxylchlorquine In Covid-2019

Amer Alkhuzaie
College of Dentistry. Al-Bayan University. Baghdad. Iraq, amer.hassan@albayan.edu.iq

Susan F.K. AL-Sudani
College of Dentistry. Al-Bayan University. Baghdad. Iraq, susan.f@albayan.edu.iq

Abstract

Among 200 person, we studied by giving them 400 mg of HCq in once weekly, for 1 years, all of them are contacts with COVID patients. Some of them are doctors working in the world of COVID patient, other are pharmacist, and families of infected patients, from different ages starting from 7-85 years so all of them are of high risk group, the result was great, that no person infected with COVID 2019 for one year. We stopped giving them HCQ when vaccine started to be given, so the use of HCQ 400mg/wk. as prophylactic was 100% protective COVID infection, for adults and 5 mg/Kg for children.

Introduction

The narrow therapeutic index of hydroxychloroquine, indicating that the differences between toxic and therapeutic dosages are minimal. 1 .

The medication hydroxychloroquine is used to treat some illnesses like Q fever and some forms of malaria as well as autoimmune diseases such as systemic lupus erythematosus, rheumatoid arthritis, and porphyria cutaneous.2.

HCQ: 1st discovered in the 19th century as antimalarial drug, and approved by FDA in 40 years of 20th century. It derived from Cinchona tree flowers, used for other diseases especially autoimmune disease as Rheumatoid lupus arthritis. S.L.E., it was proven to be broad spectrum antiviral drug, it has different mechanism of action as

1- It prevent adhesion of virus to cell membrane

2- In cytoplasm prevent endosome contain viruses to be open

3- It inhibit RDRP (RNA Dependent RNA Polymerase) enzyme so prevent replication of viruses.

4- It is ionophoric drug, help Zin to enter the cell making the cell environment more alkaline, decreasing reaction in the cell at PH about 6

5- It prevent formation of simple proteins from polypeptide by inhibition protease so deprive the viruses from forming its futces protein capsid.

All of these actions stimulated us to think of prophylactic use, which provided 100% protection.

In vitro tests on Vero cells infected with the severe acute respiratory syndrome (SARS-CoV-2), coronavirus-2 revealed that chloroquine and hydroxychloroquine were SARS-CoV-2 inhibitors 3-5. This supported the idea that these medicines may be utilized as both a prophylactic measure against SARS-CoV-2 infection and a therapeutic measure for those suffering from coronavirus sickness (COVID-19). Several rheumatic disorders are treated over a long period of time with hydroxychloroquine, which has a good safety

profile6,7 and a low cost7, which is crucial while dealing with a pandemic. In patients with COVID-19 who are hospitalized, five randomized clinical trials have shown that treatment with hydroxychloroquine had no adverse effects8-12 . In three randomized clinical investigations, two of which were against COVID-1913,14, and one against SARS-CoV-2 infection as determined by polymerase chain reaction, hydroxychloroquine was also discovered to be ineffective as a postexposure prophylactic treatment (PCR)15. Additionally, two randomized trials have investigated the use of hydroxyl-chloroquine as a major COVID-19 preventive medication16,17. Both, however, came to an abrupt end before a solid conclusion could be reached. There are now four epidemiological studies looking into the main preventive impact of hydroxyl-chloroquine for SARS-CoV2 infection18-21. Three of these studies found no effect18-20, however, the most comprehensive study discovered that people who used hydroxychloroquine repeatedly had a lower risk of contracting SARS-CoV2 21. According to a recent meta-analysis, To support the use of hydroxychloroquine for COVID-19 prevention, more research is necessary22. In a sizable population-based cohort research, it was investigated whether individuals who had taken hydroxychloroquine before the SARS-CoV-2 virus was less common in those affected by the pandemic than in controls with similar age and sex distributions. This study had a significant number of events compared to previously published studies.

Methods

Patients and method

Among 200 person, we studies by giving them 400 mg of HCQ in once weekly, adults doses and 5 mg/Kg for children who constitutes 20% of patients (40) for 1 years, all of them are contacts with COVID patients. Some of them are doctors working in the world of COVID patient, other are pharmacist, and families of infected patients, so all of them are of high risk group.

Outcomes

A SARS-CoV-2 infection that was PCR- or antigenic-verified during the study period served as the primary efficacy measure (2021). In order to examine the secondary outcome of hospital admissions while considering the aforementioned factors the aforementioned factors into consideration, the logistic regression method was used. For subgroup analysis on the general population, only individuals who underwent a SARS-CoV-2 test during the study period were utilized to account for changes in patients' patterns of seeking medical attention.

Results

The hydroxychloroquine group gave hydroxychloroquine to staff or other individuals who came into contact with the COVID-19 patients who had dementia, respiratory disease, renal disease, and gastrointestinal/metabolic disease, and cardiovascular disease. The population that was propensity matched for the sensitivity research did not reflect this. That nobody joined up for COVID 2019 for one year was an excellent result. Since we stopped giving them HCQ after the vaccination was initiated, the 400 mg of HCq administered every week as prophylactic was 100% protective against COVID infection. Furthermore, the hydroxychloroquine group had a much higher percentage of participants who were taking antirheumatic drugs. Both the study's primary and secondary outcomes had a

100% follow-up rate because of the way the study registries were designed.

Discussion

Patients who used the drug had a lower rate of SARS-CoV-2 positive tests. This is most likely the result of these groups' social behavior given that, as had previously been noted, positive patients' odds of admission were shown to rise with age23,24 . People who use and don't use hydroxychloroquine have the same risk of getting SARS-CoV-2, according to three epidemiological studies that support these conclusions 18-20 . A larger observational study from Portugal linked national databases on medication prescription, legally required to report abnormalities, and using a database of all SARS-CoV-2 tests performed and found that people undergoing long-term hydroxychloroquine treatment had a reduced incidence of SARS-CoV-2. 21.

Two randomized controlled trials have been conducted so far on hydroxychloroquine to examine its effectiveness as a main COVID-19 prevention17,18. The subjects in both trials were healthcare professionals. While Abella et al. (17) investigated a dose of 600 mg daily, which was higher than the daily amount recommended for rheumatological disorders, Rajasingham et al. (18) employed two different dosing regimens with either 400 mg once or twice weekly. Both trials had extremely few occurrences and were therefore abruptly stopped, making them ambiguous, but they do not contradict the current findings. By Boulware et al. (25) and Mitjà et al. (14) against COVID-19, the postexposure prophylactic characteristics of hydroxychloroquine were examined. These two investigations failed to find any influence on the disease's occurrence. The short-term, high-dosage regimen used in the trial by Boulware et al., as well as the absence of microbiological confirmation for all patients, were also limitations25. This restriction did not apply to the second study that yielded PCR-verified SARS-CoV-2, but it's probable that the study was limited by the inclusion window following contact, which was up to 7 days14. A more recent study was conducted without the aforementioned limitations and came to the same conclusions regarding the post-exposure prophylactic effects of hydroxychloroquine against PCR-verified SARS-CoV-2 infection15. The World Health Organization (WHO) recently updated its advice on COVID-19 prevention drugs, and now strongly discourages using hydroxychloroquine as prophylaxis against COVID-1926. Singh et al.(22) recently conducted an extensive review and meta-analysis of the use of hydroxychloroquine in the prevention and treatment of COVID-19 and came to the conclusion that further research is needed to support prevention22 .

Four randomized controlled trials exploring the use of hydroxy-chloroquine as prophylaxis provided data on admissions14,15,17,25. Across the four investigations, 51 hospitalizations were totaled. Admissions were divided into two trials, both of which focused on postexposure prophylaxis, according to how closely they related to COVID-19. Both the treatment and control groups had a similar number of admissions attributable to COVID-1915,17. Therefore, despite the strong WHO recommendations, there is not enough data to support the effectiveness of hydroxychloroquine prophylaxis. When comparing the present results with those from SARS-CoV-2, the neutral outcomes are consistent. Due to a paucity of information, a slight advantage from hydroxychloroquine cannot be completely ruled out. The evidence is scant and limited by a small number of incidents, particularly when it comes to the

impact on hospitalization. The current data, notwithstanding their limited power, show no difference in admissions after SARS-CoV-2, which is in keeping with the neutral results.

Despite the advantages previously highlighted, this study has several disadvantages. First, the primary analysis' design does not account for potential behavioral or living situation variations between the groups, as shown, for instance, due to cancer patients' reduced SARS-CoV-2 risk. Although it is far from certain, employing propensity-score screening for the sensitivity analysis likely reduced is likely that employing propensity-score screening for the sensitivity analysis reduced the impact of the two biases mentioned above. Second, accessibility to testing by the population, particularly early in the pandemic, may introduce bias. A second's wave, which struck Fall of 2020 in Denmark and coincided with testing opportunities, mitigated this bias; information on the quantity of testing conducted in Denmark is provided. Third, despite the possibility of residual confounding, there isn't yet solid proof connecting the possibility of catching SARS-CoV-2 from someone with a known rheumatic disease. Fourth, the Danish National Patient Registry does not collect data on biological treatment, making it hard to account for the influence of the so-called biological' medications' (tumor necrosis' factor antagonists, etc.) effects. Additionally, dosage information was removed, but it is safe to conclude that the treatment followed the Danish guidelines of (200–400) mg of hydroxyl-chloroquine per day27. Finally, it is noteworthy to note that, despite the propensity-matched population's emergence of some discrete changes in some of the baseline characteristics, only the variations between systemic corticosteroids and methotrexate were noteworthy.

Conclusion

This study discovered that hydroxychloroquine primary prophylaxis had an anti-infection activity against SARS-CoV-2 in those who' had previously taken the medication. Instead, estimations were seen in the sensitivity analyses as well as the primary and secondary analyses. These results corroborate the WHO's recommendations for medications to prevent COVID-19 and the limited, randomized studies on pre- and post-exposure prophylaxis. The results of this study and the information on utilizing hydroxychloroquine for COVID-19 recommends using hydroxychloroquine as a preventative measure against SARS-CoV-2.

Reference

A 1-Evans, W. C., & Evans, D. (2009). Alkaloids. Trease and Evans' Pharmacognosy, 353–415. doi:10.1016/b978-0-7020-2933-2.00026-5

2- Fox RI. Mechanism of action of hydroxychloroquine as an antirheumatic drug. Semin Arthritis Rheum. 1993 Oct;23(2 Suppl 1):82-91. doi: 10.1016/s0049-0172(10)80012-5. PMID: 8278823.

3- Liu J, Cao R, Xu M, Wang X, Zhang H, Hu H, et al. Hydroxychloroquine, a less toxic derivative of chloroquine, is effective in inhibiting SARSCoV- 2 infection in vitro. Cell Discov. 2020;6:16. [PMC free article] [PubMed] [Google Scholar]

4- Wang C, Horby PW, Hayden FG, Gao GF. A novel corona virus outbreak of global health concern. Lancet. 2020;395:470–3. [PMC free article] [PubMed]

5- Yao X, Ye F, Zhang M, Cui C, Huang B, Niu P, et al. In vitro antiviral activity and projection of optimized dosing design of hydroxychloroquine for the treatment of severe acute respiratory syndrome

coronavirus 2 (SARS-CoV-2) Clin Infect Dis. 2020;71:732 [PMC free article] [PubMed] [Google Scholar]

6- Ruiz-Irastorza G, Ramos-Casals M, Brito-Zeron P, Khamashta MA. Clinical efficacy and side effects of antimalarials in systemic lupus erythematosus: a systematic review. Ann Rheum Dis 2010;69:20–8.

7- Ponticelli C, Moroni G. Hydroxychloroquine in systemic lupus erythematosus (SLE). Expert Opin Drug Saf 2017;16:411–9.

8- Abd-Elsalam S, Esmail ES, Khalaf M, Abdo EF, Medhat MA, Abd El Ghafar MS, et al. Hydroxychloroquine in the treatment of COVID-19: a multicenter randomized controlled study. Am J Trop Med Hyg 2020;103:1635–9.

9- Group RC, Horby P, Mafham M, Linsell L, Bell JL, Staplin N, et al. Effect of hydroxychloroquine in hospitalized patients with COVID-19. N Engl J Med 2020;383:2030–40.

10- Self WH, Semler MW, Leither LM, Casey JD, Angus DC, Brower RG, et al. Effect of hydroxychloroquine on clinical status at 14 days in hospitalized patients with COVID-19: a randomized clinical trial. JAMA 2020;324(21):2165–76.

11- Tang W, Cao Z, Han M, Wang Z, Chen J, Sun W, et al. Hydroxychloroquine in patients with mainly mild to moderate coronavirus disease 2019: open label, randomised controlled trial. BMJ 2020;369:m1849.

12- WHO Solidarity Trial Consortium, Pan H, Peto R, Henao-Restrepo AM, Preziosi MP, Sathiyamoorthy V, et al. Repurposed antiviral drugs for COVID-19 – Interim WHO Solidarity Trial Results. N Engl J Med 2020;384(6):497–511.

13- Boulware DR, Pullen MF, Bangdiwala AS, Pastick KA, Lofgren SM, Okafor EC, et al. A randomized trial of hydroxychloroquine as postexposure prophylaxis for COVID-19. N Engl J Med 2020;383:517–25.

14- Mitjà O, Corbacho-Monné M, Ubals M, Alemany A, Suñer C, Tebé C, et al. A cluster- randomized trial of hydroxychloroquine for prevention of COVID-19. N Engl J Med 2020;384(5):417–27.

15- Barnabas RV, Brown ER, Bershteyn A, Stankiewicz Karita HC, Johnston C, Thorpe LE, et al. Hydroxychloroquine as postexposure prophylaxis to prevent severe acute respiratory syndrome coronavirus 2 infection: a randomized trial. Ann Intern Med 2020;174(3):344–52.

16- Abella BS, Jolkovsky EL, Biney BT, Uspal JE, Hyman MC, Frank I, et al. Efficacy and safety of hydroxychloroquine vs placebo for pre-exposure SARS-CoV-2 prophylaxis among health care workers: a randomized clinical trial. JAMA Intern Med 2020;181(2):195–202.

17- Rajasingham R, Bangdiwala AS, Nicol MR, Skipper CP, Pastick KA, Axelrod ML, et al. Hydroxychloroquine as pre-exposure prophylaxis for COVID-19 in healthcare workers: a randomized trial. Clin Infect Dis 2020;72(11):e835–42.

18- Gendelman O, Amital H, Bragazzi NL, Watad A, Chodick G. Continuous hydroxy- chloroquine or colchicine therapy does not prevent infection with SARS-CoV-2: insights from a large healthcare database analysis. Autoimmun Rev 2020;19:102566.

19- Jung SY, Kim MS, Kim MC, Choi SH, Chung JW, Choi ST. Effect of hydroxychloroquine pre-exposure on infection with SARS-CoV-2 in rheumatic disease patients: a population-based cohort

study. Clin Microbiol Infect 2020;27(4):611–7.

20- Bae S, Ghang B, Kim YJ, Lim JS, Yun SC, Kim YG, et al. Recent hydroxychloroquine use is not significantly associated with positive PCR results for SARS-CoV-2: a nationwide observational study in South Korea. Viruses 2021;13(2).

21- Ferreira A, Oliveira ESA, Bettencourt P. Chronic treatment with hydroxychloroquine and SARS-CoV-2 infection. J Med Virol 2021;93:755–9.

22- Singh B, Ryan H, Kredo T, Chaplin M, Fletcher T. Chloroquine or hydroxychloroquine for prevention and treatment of COVID-19. Cochrane Database Syst Rev 2021;2: CD013587.

23- Ioannou GN, Locke E, Green P, Berry K, O'Hare AM, Shah JA, et al. Risk factors for hospitalization, mechanical ventilation, or death among 10131 US veterans with SARS-CoV-2 infection. JAMA Netw Open 2020;3:e2022310.

24- Reilev M, Kristensen KB, Pottegard A, Lund LC, Hallas J, Ernst MT, et al. Characteristics and predictors of hospitalization and death in the first 11 122 cases with a positive RT-PCR test for SARS-CoV-2 in Denmark: a nationwide cohort. Int J Epidemiol 2020;49:1468–81.

25- Boulware DR, Pullen MF, Bangdiwala AS, Pastick KA, Lofgren SM, Okafor EC, et al. A randomized trial of hydroxychloroquine as postexposure prophylaxis for COVID-19. N Engl J Med 2020;383:517–25

26- Lamontagne F, Agoritsas T, Siemieniuk R, Rochwerg B, Bartoszko J, Askie L, et al. A living WHO guideline on drugs to prevent COVID-19. BMJ 2021;372:n526.

27- Danish Rheumatology Society. Behandling med hydroxychloroquin [Treatment with hydroxychloroquine]. 2019 Available at: https://danskreumatologi.dk/laegemidler/hydroxychloroquin/. [Accessed 21 December 2020].