INPLASY

Investigating The Potential of Inhaled Hydroxychloroquine (HCQ) for The Treatment of SARS-CoV-2 Infection: A Systematic Review

INPLASY202450029

doi: 10.37766/inplasy2024.5.0029

Received: 07 May 2024

Published: 07 May 2024

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ADMINISTRATIVE INFORMATION

Support - Lestari Covid.

Review Stage at time of this submission - Completed but not published.

Conflicts of interest - None declared.

INPLASY registration number: INPLASY202450029

Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 07 May 2024 and was last updated on 07 May 2024.

INTRODUCTION

Review question / Objective How effective is hydroxychloroquine in preventing and/or treating SARS-CoV-2-related cases when delivered via oral and inhalation?

Condition being studied COVID-19.

METHODS

Search strategy A web-based search on three selected online database search engines (EBSCO, Scopus, and Web of Science) from January 2020 until June 2023. The search conducted included studies published in the English language and containing keywords in the title and abstract. The search terms used in various combinations of keywords mentioned in the title or abstract were: "hydroxychloroquine", "oral", "inhale*", and "SARS-CoV-2". These keywords were then expanded by two-way synonyms to variant the terms with the same meaning. Search features including Boolean operator, phrase searching, truncation, and wildcard were applied to each database.

Participant or population This study included COVID-19 patients with varying levels of severity, ranging from mild to severe, and covered both hospitalized and non-hospitalized care settings. Healthcare workers, who were at heightened risk due to their direct exposure to infected individuals, were also included as participants, often receiving hydroxychloroquine as a preventive measure (either pre-exposure or post-exposure). Additionally, individuals who had been in close contact with COVID-19 patients or were considered high-risk were assessed to determine the effectiveness of hydroxychloroquine in

preventing infection or reducing symptoms upon exposure. The review encompassed a range of study designs, which include the randomized controlled trials and observational studies, to comprehensively analyse the safety and efficacy of hydroxychloroquine administered orally or via inhalation.

Intervention The intervention in this study involved administering hydroxychloroquine (HCQ) to individuals either orally or via inhalation. The goal was to evaluate the effectiveness of these different delivery methods for treating SARS-CoV-2 infection or preventing infection in those at high risk or in close contact with COVID-19 patients. The study compared the outcomes of oral HCQ treatment with inhaled HCQ treatment across various groups of patients, healthcare workers, and close contacts, assessing each intervention's safety and efficacy.

Comparator The comparator in this study was typically a control group that did not receive hydroxychloroquine (HCQ) treatment or received a placebo. In some studies, the comparator group consisted of participants receiving standard care without HCQ or those given a placebo, enabling a direct comparison of the effects and outcomes of HCQ administered orally or via inhalation against a non-HCQ treatment. This approach helped determine the relative efficacy and safety of HCQ in treating SARS-CoV-2 infections or preventing infection in at-risk individuals.

Study designs to be included Randomized controlled studies, Retrospective studies, Observational studies, Non-randomized study, Retrospective observational case-controlled study, and clinical trial.

Eligibility criteria The eligibility criteria for the systematic review are as follows:
Inclusion Criteria:
1. Population: The study included patients infected with SARS-CoV-2, or those who had recently come into contact with COVID-19 patients.
2. Intervention/Exposure: Only studies that examined hydroxychloroquine (HCQ) monotherapy, either through oral or inhalation delivery, were considered.
3. Comparison: The studies had to compare HCQ treatment effects with a control group or placebo.
4. Outcome: The studies needed to report outcomes related to the virus's progression, symptom severity, hospitalization, mortality rates, or adverse events linked to HCQ treatment.
5. Language: Only research published in English was included.

Exclusion Criteria:
1. Studies that focused on HCQ combined with other medications.
2. Studies that evaluated HCQ for conditions other than SARS-CoV-2.
3. Reports that didn't include original research data, such as reviews, editorials, letters, guidelines, and conference papers.
4. Publications in languages other than English.

Information sources EBSCO, Scopus, and Web of Science.

Main outcome(s)
1. Dose of administration
2. Hydroxychloroquine for prophylaxis
3. Hospitalization and death
4. Viral shedding.

Quality assessment / Risk of bias analysis Three researchers independently assess the reliability of each study using The Joanna Briggs Institute (JBI) Critical Appraisal tool. The reliability was evaluated according to nine criteria, each yielding a score of zero or one. One score was obtained for each criterion if the study was affirmative in the next questions: (1): Was the sample frame appropriate to address the target population? (2): Were study participants sampled in an appropriate way? (3): Was the sample size adequate? (4): Were the study subjects and the setting described in detail? (5): Was the data analysis conducted with sufficient coverage of the identified sample? (6): Were valid methods used for the identification of the condition? (7): Was the condition measured in a standard, reliable way for all participants? (8): Was there appropriate statistical analysis? (9): Was the response rate adequate, and if not, was the low response rate managed appropriately? Any clash in agreements that arose between the authors was resolved through discussion, or by further discussion with the fourth reviewer.

Strategy of data synthesis The included studies were presented in a summary table of important key points: year, study design, patient care, number of patients (HCQ-treated and control), severity of infection, intervention, and primary and secondary outcomes of the studies. From the table, all studies were compared according to several points: dose administration, hydroxychloroquine for prophylaxis, hospitalization, and death, and hydroxychloroquine effect on viral shedding.

Subgroup analysis Subgroup analysis involved different risk groups (hospitalized v. nonhospitalized v. healthcare worker), level of

severity (mild v. moderate v. severe), treatment plan (pre-exposure v. post-exposure), different dosage schemes (e.g. 7 days, 10 days, 2 weeks), and different dosage strength (e.g. 200 mg, 400 mg, 800 mg).

Sensitivity analysis None.

Language restriction English only.

Country(ies) involved Malaysia.

Keywords Hydroxychloroquine; Oral; Inhale; SARS-CoV-2.

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