INPLASY PROTOCOL

To cite: Zhao et al. Chloroquine combined with azithromycin in the treatment of novel coronavirus (COVID-19) pneumonia: study protocol for a systematic review and meta-analysis. Inplasy protocol 202110044. doi: 10.37766/inplasy2021.1.0044

Received: 13 January 2021

Published: 14 January 2021

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Support: **NSFC.**

Review Stage at time of this submission: **The review has not yet started.**

Conflicts of interest:
The authors declare that there are no conflicts of interest.

Chloroquine combined with azithromycin in the treatment of novel coronavirus (COVID-19) pneumonia: study protocol for a systematic review and meta-analysis

Zhao, Y[1]; Sun, W[2]; Qi, R[3]; Mi, X[4]; Liao, L[5]; Cheng, M[6]; Zhao, Z[7]; Chen, S[8]; Zhou, J[9]; Chao, G[10]; Hua, B[11].

Review question / Objective: **This systematic review and meta-analysis protocol aims to evaluate the effective and safety of (hydroxy)chloroquine combined with azithromycin to treat COVID-19-related pneumonia. P: Participants who have been diagnosed with pneumonia caused by SARS-CoV-2 infection. I: Chloroquine (hydroxychloroquine) combined with azithromycin. C: Supportive care, placebo, chloroquine or azithromycin alone, or other medications. O: Primary outcomes: Negative rate after treatment and survival rate after treatment and follow-up period.**
Condition being studied: **Coronavirus Disease 2019 (COVID-19) is currently pandemic worldwide, and there is no effective treatment method yet. Chloroquine combined with azithromycin treatment has been used in large quantities of clinical trials for COVID-19 which caught our attention. This systematic review and meta-analysis protocol aims to evaluate the efficacy and safety of chloroquine combined with azithromycin in the treatment of COVID-19.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 14 January 2021 and was last updated on 14 January 2021 (registration number INPLASY202110044).

INTRODUCTION

Review question / Objective: **This systematic review and meta-analysis protocol aims to evaluate the effective and safety of (hydroxy)chloroquine combined with azithromycin to treat COVID-19-related pneumonia. P: Participants who have been diagnosed with pneumonia caused by SARS-CoV-2 infection. I: Chloroquine (hydroxychloroquine) combined with azithromycin. C: Supportive**

care, placebo, chloroquine or azithromycin alone, or other medications. O: Primary outcomes: Negative rate after treatment and survival rate after treatment and follow-up period.

Condition being studied: Coronavirus Disease 2019 (COVID-19) is currently pandemic worldwide, and there is no effective treatment method yet. Chloroquine combined with azithromycin treatment has been used in large quantities of clinical trials for COVID-19 which caught our attention. This systematic review and meta-analysis protocol aims to evaluate the efficacy and safety of chloroquine combined with azithromycin in the treatment of COVID-19.

METHODS

Search strategy: 1 randomized controlled trial.pt. 2 controlled clinical trial.pt. 3 randomized.ab. 4 randomly.ab. 5 placebo.ab. 6 drug therapy.ab. 7 trial.ab. 8 groups.ab. 9 or/1–8. 10 exp animals/ not humans.sh. 11 9 not 10 12 observational study.pt. 13 or/11–12. 14 ("Chloroquine" OR "Chlorochin" OR "Chingamin" OR "Khingamin"OR "Nivaquine" OR "Chloroquine Sulfate" OR "Sulfate, Chloroquine" OR "Chloroquine Sulphate" OR "Sulphate, Chloroquine"OR"Aralen" OR "Arequin" OR "Arechine").ab. 15 ("Hydroxychloroquine" OR "Oxychlorochin" OR "Oxychloroquine " OR "Hydroxychlorochin"OR "Plaquenil" OR "Hydroxychloroquine Sulfate" OR "Hydroxychloroquine Sulfate (1:1) Salt").ab. 16 ("Chloroquine phosphate" OR "chingamin phosphate" OR "unspecified phosphate of chloroquine diphosphate " OR "delagil"OR "khingamin phosphate" OR "arechin" OR "chloroquine phosphate" OR "Resochin" OR "chloroquine diphosphate, (+-)-isomer" OR "chloroquine diphosphate, (-)-isomer" OR "chloroquine bis(dihydrogenphosphate) dihydrate" OR "chloroquine diphosphate, (+)-isomer").ab. 17 (" Azithromycin" OR "Azythromycin" OR "Sumamed" OR "Toraseptol"OR "Vinzam" OR "CP-62993" OR "CP 62993" OR "Zithromax" OR "Azitrocin" OR "Azadose" OR "Ultreon" OR "Zitromax"OR "Azithromycin Dihydrate"OR "Dihydrate, Azithromycin"OR"Azithromycin Monohydrate"OR"Monohydrate, Azithromycin"OR "Goxal"OR "Zentavion").ab. 18 ("COVID 19 virus" OR "COVID-19 virus" OR "SARS-CoV"OR "SARS CoV-2" OR "SARS-CoV-2" OR "SARS2"OR "2019 nCoV" OR "2019 novel coronavirus" OR "COVID-19"OR"COVID 19" OR "2019-nCoV" OR "new coronavirus" OR "novel coronavirus") .ab. 19 or/14–17 . 20 13 and 18 and 19.

Participant or population: Participants who have been diagnosed with pneumonia caused by SARS-CoV-2 infection.

Intervention: Chloroquine (hydroxy-chloroquine) combined with azithromycin

Comparator: Supportive care, placebo, chloroquine or azithromycin alone, or other medications.

Study designs to be included: To assess the clinical efficacy and adverse events of (hydroxy)chloroquine combined with azithromycin for COVID-19.

Eligibility criteria: Randomized controlled trials, quasi-randomized controlled trials and observational studies published in Chinese and English will be included.

Information sources: The following databases will be searched from inception to the present: EMBASE, MEDLINE, the Cochrane Central Register of Controlled Trials (CENTRAL), Web of Science, PubMed, China National Knowledge Infrastructure (CNKI), Wan-fang Database, Technology Periodical Database (VIP).

Main outcome(s): Negative rate after treatment and Survival rate after treatment and follow-up period.

Quality assessment / Risk of bias analysis: We will conduct risk of bias assessment by the Cochrane bias risk assessment tool, and evaluate the quality of observational studies by Newcastle-Ottawa quality assessment scale (NOS). Above steps will be conducted by two independent reviewers. If any inconsistency is

encountered, a third reviewer will be consulted.

Subgroup analysis: We will conduct a subgroup analysis if appropriate number of studies are included to evaluate possible clinical heterogeneity based on the type of study, severity of disease and age.

Sensibility analysis: We will examine the stability of the results by excluding high or unclear risk of bias studies and observe the changes in the results of meta-analysis.

Country(ies) involved: China.

Keywords: Coronavirus; COVID-19; Chloroquine; Azithromycin; Systematic review, Meta-analysis, Protocol.

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Author 1 - Yuwei Zhao.
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Author 8 - Shiqi Chen.
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