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

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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

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**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 "Chinagmin" 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 "Khangamin phosphate" OR "arechin" OR "chloroquine phosphate" OR "Resochin" OR "chloroquine diphosphate, (+)-isomer" OR "chloroquine diphosphate, (-)-isomer" OR "chloroquine bis(dihydrogenphophate) 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 (hydroxychloroquine) 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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