



**Contents include:**

Brief summary:

- As yet unpublished Chinese multicenter trial shows efficacy of chloroquine phosphate in treatment of COVID-19

Articles reviewed:

- Chloroquine is a potent inhibitor of SARS coronavirus infection and spread (Virology Journal)
  - NOTE: This is a basic science paper related to SARS, not COVID-19. Given the similarities between the two viruses and likely related mechanism, however, I felt that it was relevant and important given the press and excitement about a potential treatment.
- Prevalence and impact of cardiovascular metabolic diseases on COVID-19 in China (Clinical Research in Cardiology)

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Unpublished data reported to demonstrate efficacy of chloroquine phosphate in treatment of COVID-19

- Per a letter published in Bioscience Trends, chloroquine will be recommended as treatment for COVID-19 in the next version of the Chinese guidelines
- Report based on audio transcript (only available in Chinese) describing a multicenter study with manuscript in process
- [https://www.jstage.jst.go.jp/article/bst/14/1/14\\_2020.01047/article](https://www.jstage.jst.go.jp/article/bst/14/1/14_2020.01047/article)

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| <b>Article Title:</b> | Chloroquine is a potent inhibitor of SARS coronavirus infection and spread   |
| <b>Authors:</b>       | Vincent M, Bergeron S, Benjannet S et al   |
| <b>Full Citation:</b> | Vincent M, Bergeron S, Benjannet S et al. (2005). Chloroquine is a potent inhibitor of SARS coronavirus infection and spread. <i>Virology J.</i> 2:69. |

**Background:**

Chloroquine is particularly active on diseases infections which utilize the Golgi vesicles and other low pH organelles – this is why it has been so widely used in therapies for malaria, amoebiasis, HIV, and autoimmune diseases. The SARS-CoV buds in the Golgi apparatus allowing for the ‘spike’ glycoprotein to be incorporated into the virion. Given this mechanism of entry, chloroquine was hypothesized to be a potential therapy for SARS.

**Study Question:**

Does chloroquine have antiviral effects against the novel coronavirus responsible for SARS? Is it effective for prophylaxis and/or therapy?

**Methods:**

In vitro cell cultures (Vero E6 cells) were repeatedly utilized with chloroquine as a pretreatment or therapy at multiple different concentrations. Given similarity in mechanism, the experiments were repeated with NH4Cl (ammonium chloride)

**Results:**

- Chloroquine pretreatment 20-24h prior to exposure prevented SARS-CoV infection in a dose-dependent way
- Immediate chloroquine administration after virus adsorption significantly reduced infection and prevented spread – it also did so after being added several hours after viral adsorption
- NH4Cl inhibits SARS-CoV infection in a similar dose-dependent way, likely through a similar mechanism
- Neither chloroquine or NH4Cl decreased ACE2 receptors expression, but it appears that both drugs affect terminal glycosylation – unclear what role this plays
- Neither chloroquine or NH4Cl affected the expression of the viral spike protein

**Conclusions:**

- Chloroquine and possible NH4Cl are likely to be effective for both prophylaxis and treatment of SARS based on in vitro experiments
- The mechanism of effect is not entirely clear, but is likely related to ACE2 terminal glycosylation and pH changes in the Golgi apparatus which interfere with viral replication

**Perspective:**

Chloroquine was studied in vitro for use in SARS, but given the short duration of the epidemic was never studied in clinical trials. Given the similarity in virus structure to the coronavirus causing COVID-19, there is hope that chloroquine may be effective as a prophylactic and/or therapeutic option.

**Summary Written by:**

Katherine B. Saliccioli MD

**Topic Areas:** SARS, coronavirus, chloroquine

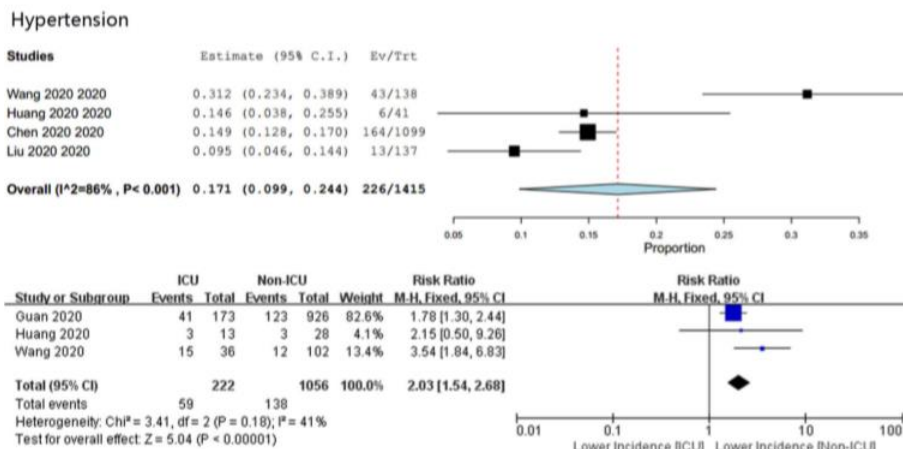
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| <b>Authors:</b>       | Li B, Yang J, Zhao F et al.  |
| <b>Full Citation:</b> | Li B, Yang J, Zhao F et al. (2020). Prevalence and impact of cardiovascular metabolic diseases on COVID-19 in China. <i>Clin Res Cardiol</i> . Published online 11 March 2020 at <a href="https://link.springer.com/article/10.1007%2Fs00392-020-01626-9">https://link.springer.com/article/10.1007%2Fs00392-020-01626-9</a> |

**Review design:**

Meta-analysis of 6 studies including 1527 patients. Summarized prevalence of CV and metabolic disease in COVID-19 and compared comorbidities for ICU/severe vs milder cases

**Key points to remember:**

- HTN, cardio/cerebrovascular disease, and diabetes were all highly prevalent in COVID-19 patients, although the prevalence varied between studies
- HTN and DM prevalence was similar to the general Chinese population overall – this is different than has been reported in individual studies, which suggested HTN was a RF for developing symptomatic COVID-19
- Cardio/cerebrovascular disease prevalence was higher than the general Chinese population
- There were higher incidences of HTN, cardio/cerebrovascular disease, and DM in more severely ill patients than in those less ill due to COVID-19
- While there is conflicting data about whether certain individual comorbidities affect the likelihood of developing COVID-19, they were definitively associated with more severe illness



**Summary written by:**

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**Topic Areas:** COVID-19, hypertension, cardiovascular disease, cerebrovascular disease, diabetes