A meta-analysis of intravenous immunoglobulin to control COVID-19 patients

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Citation

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Review question

The aim of this meta-analysis of randomized controlled trials is to evaluate the efficacy and safety of Intravenous immunoglobulin for COVID-19 patients.

Searches

Searched Web of Science, PubMed, Embase, the Cochrane Library, medRxiv for RCTs and observational studies. The search words used included: “Coronavirus Disease 2019” OR “COVID-19” OR “SARS-Cov-2” OR “2019-nCoV Diseases” OR “COVID 19 Virus Infection” AND “Intravenous immunoglobulin,” OR “immunoglobulin,” OR “IVIG”. Search were down on February 17, 2021. The search did not impose restriction on the date between 01.01.2020 to 02.17 2021. No restriction on the geographical location or language of the studies.

Types of study to be included

RCT; retrospective cohort study

Condition or domain being studied

In 2019, a novel coronavirus disease (COVID-19) which caused by the severe acute respiratory syndrome coronavirus 2 (SARS-Cov-2) has aroused an outbreak worldwide. The high infectivity and mortality pose an unprecedented challenge to clinicians. Numerous clinical trials, retrospective studies and observational studies about SARS-Cov-2 disease are underway. Due to the lack of sufficient / significant conclusive evidence, it is difficult to get a consensus on the treatment until now.

The SARS-Cov-2 virus is a member of coronavirus family. Base on the experience of treating previous coronavirus diseases such as severe acute respiratory syndrome (SARS), middle east respiratory syndrome(MERS) and H1N12009, [1] it might be believed that intravenous immunoglobulins (IVIGs) could be used in COVID-19 patients and be one of worthwhile treatments. IVIGs are blood product from healthy donors containing a polyclonal IgG antibodies. They, known for its anti-inflammatory reactions, has been used to treat patients with inflammatory diseases including Kawasaki disease, multiple sclerosis. The controversy over the efficacy of IVIGs for improving in clinical symptoms and mortality, however, has been occurring with the increasing number of patients.

Participants/population

Patients with lab-confirmed COVID-19 , aged 18 years and above

Intervention(s), exposure(s)

Treatment group?IVIg four vials of 5 gm5 IVIg daily for three consecutive days + standard of care

Comparator(s)/control

Another standard of care intervention without Intravenous immunoglobulin or a placebo control group

Main outcome(s)

Treatment duration; morality, mechanical ventilation admission, hospital or ICU duration?

* Measures of effect

Relative risks, odds ratios, standardized mean difference

Additional outcome(s)
Laboratory indicators, number of people getting better

* Measures of effect
Relative risks, odds ratios, standardized mean difference

Data extraction (selection and coding)
We will extract the following data from the randomized controlled studies (RCTs), case-control studies (CCSs), retrospective cohort studies (RCSs):

1) title, author name, publication data,

2) number of patients, study design (including grouping, blinding, etc.),

3) information on interventions)

4) outcome indicators and their measurement,

5) adverse reactions, and adverse events

Data will then be extracted and entered into a pre-defined and piloted microsoft excel database.

The data will be extracted by one reviewer, and independently checked by a second reviewer.

Any discrepancies will be identified and resolved through discussion (with a third author, if necessary).

Risk of bias (quality) assessment
Two authors independently evaluate the quality of the literature. If there are differences in the evaluation results, they will be resolved in consultation with the third author. If the included study is a randomized controlled study, the biased risk assessment tool of the Cochrane Collaboration Network will be used to evaluate the methodological quality of the study, from the aspects of random sequence generation, concealment of allocation schemes, blinding, completeness of outcome data, and selective reporting to assess the risk of bias, there are three types of evaluation results for each item, namely low risk, high risk, and unclear. If the included study is Case-Control Studies (CCSs), Newcastle-Ottawa Scale (NOS) is used to evaluate the methodological quality of the study, and the score is evaluated in terms of patient selection, comparability between groups, and research results. The higher the score, the study higher the quality.

Sensitivity analyses will be conducted to assess the effects of the exclusion of studies at high risk of bias influences the findings.

Strategy for data synthesis
We used RevMan 5.4 to conduct all statistical analysis. Funnel plot was used to assess the possible of publication bias. Statistical heterogeneity was evaluated by The I^2 test. According to the Cochran's Handbook for the systematical reviews of intervention, if I^2 value of 0% to 40%, 30% to 60%, 50% to 90%, 75% to 100% considered as not important, moderate, substantial and considerable level of heterogeneity, respectively. When was I^2 was 0-60?, we used a fix-effect model to pool the results, or else a random-effects model. The select indicators were count data and measurement data. We used either relative risk (RR) or standardized mean difference (SMD) with 95% confidence interval (CI).

Analysis of subgroups or subsets
APACH II score: moderate type, severe type, critical type

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Organisational affiliation of the review
None

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Type and method of review

Meta-analysis, Systematic review

Anticipated or actual start date

12 February 2021

Anticipated completion date

22 March 2021

Funding sources/sponsors

Pwx Group in Department of Pharmacy in the Second Xiangya Hospital Central South University

Conflicts of interest

Language

English

Country

China

Stage of review

Review Ongoing

Subject index terms status

Subject indexing assigned by CRD

Subject index terms

COVID-19; Humans; Immunoglobulins, Intravenous; SARS-CoV-2

Date of registration in PROSPERO

23 February 2021

Date of first submission

21 February 2021

Stage of review at time of this submission

Stage	Started	Completed
Preliminary searches	Yes	No
Piloting of the study selection process	Yes	No
Formal screening of search results against eligibility criteria	Yes	No
Data extraction	No	No
Risk of bias (quality) assessment	No	No
Data analysis	No	No

Revision note

#27 add "Sensitivity analyses will be conducted to assess the effects of the exclusion of studies at high risk of bias influences the findings."

The record owner confirms that the information they have supplied for this submission is accurate and complete and they understand that deliberate provision of inaccurate information or omission of data may be construed as scientific misconduct.

The record owner confirms that they will update the status of the review when it is completed and will add publication details in due course.

Versions

23 February 2021
24 February 2021