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The Effectiveness of Remdesivir versus Ruxolitinib as Covid-19 Supportive Management: Systematic Review, Meta-Analysis

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ABSTRACT

The treatment regimen in severe Covid-19 patients has several types of therapies. However, there is uncertainty about which therapies are more effective in the covid-19 weight category. In June 2020, the study was conducted with keyword search [REMDESIVIR] [RUXOLITINIB] [COVID19] in 2010-2020 using PUBMED.gov. This study used rct (randomization controller trial) method with the theme: the comparison of the effectiveness use of Remdesivir with Ruxolitinib on Covid-19. From the results of the analysis using forest plot obtained, there was a significant difference in the administration of Remdesivir therapy with Ruxolitinib on the improvement from covid-19 on day 7 (1.26 CI 95% 0.41 to 3.86) and day 14 (RR 1.26 CI 95% 0.41 to 3.86). Ruxolitinib therapy is more effective than Remdesivir applied for Covid-19 patients.

Keywords: *"Covid-19, Remdesivir, Ruxolitinib, Systemic Review, Meta-Analysis"*

1. INTRODUCTION

On March 11, 2020, WHO announced the SARS pandemic. COVID-19 has common signs and symptoms including fever, cough and shortness of breath. The longest incubation period is 14 days and the average is about 5-6. In severe cases of COVID-19 it can cause pneumonia, acute respiratory syndrome, kidney failure, and even death. COVID-19 patients can develop into severe pneumonia with acute hypoxia syndrome and accompanied by multiorgan failure. At this time there is no approved therapy as COVID-19 therapy, but antiviral therapy has the potential in clinical evaluation of patients associated with increased concentrations of proinflalamation cytokine plasma. Therefore, supportive therapy is needed to improve the condition of Covid 19 patients (Wu Z, McGoogan JM., 2020).

2. RESEARCH METHODS

2.1. Search Strategy

This research is a Systematic Review using Prisma method (Preferred Reporting Items for Systematic Reviews and Meta-analyses). Research was conducted systematically with the correct stage of research. Systematic Review procedure comprised of several steps which were 1) Preparation of Background and Purpose, 2) Research Question, 3) Searching for the Literature 4) Selection Criteria 5) Practical Screen 6) Quality Checklist and Procedures 6) Data Extraction Strategy, and 7) Data Synthesis Strategy. Journal search was conducted in June 2020 with journal search using RCT method (randomization controller trial) for research using pubmed.gov search system with [Remdesivir keyword] [RUXOLITINIB] [COVID19]. After the pubmed.gov search, researchers obtained 285 journals. This study has research criteria so that 283 journals in the Excellus (do not meet the criteria) and 2 journals in inclusion (meet the criteria) can be seen in Figure 1.

2.2. Research Criteria

The inclusion criteria were in the form of positive Covid-19, Remdesivir, Ruxolitinib and research using RCT method (randomization controller trial). Fever was defined by individual study authors. Exclusion criteria involved patients who have heavy comorbid, not random.

2.3. Extraction and Quality Assessment of Articles

Searches were obtained in the form of journals, then collected by one person by providing an assessment according to the content of each study based on the established inclusion and exclusion criteria. The assessment of the quality of its methodology used Jadad scores. The journal obtaining the highest score for each RCT journal was 5. Value 3 was an RCT article considered to have good methodology quality. Then, it was conducted data extraction of each study for the name of the first researcher, the year of publication, the type of study, the type of therapy, the length of therapy, the total number of samples, the number of treatment samples, the number of control samples, the age of the sample, the country, the length of monitoring, the diagnosis criteria, the outer size, blinding and the loss to follow up (seen in table 1).

Table 1. Assessment of the RCT articles quality according to Jadad scores

No	Criteria	Wang, Yeming., *et al.*, 2020	Cao, Yang., *et al.*, 2020
1	Is it randomized?	1	1
2	Is the randomization method clearly stated?	1	1
3	What is double blind research?	1	2
4	Is the method of blinding clearly stated?	0	0
5	Is there an explanation for dropping out?	0	0
	Total score	3	2

As a result of the next data analysis, it is identified which supportive therapy is more effective between Remdesivir or Ruxolitinib so that it can be seen whether the data have already collected proves that supportive therapy is more effective.

2.4. Limitations

This study has limitations. The quality of the study varied. Randomize was sufficient in all experiments. The analysis did not identify a link between the quality of the drug and the risk of side effects.

The risk of bias might occur in this study, e.g. patients with severe pneumonia who have other infectious diseases, different ages or others that cause inappropriate effects.

2.5 Data analysis

Statistical analysis used SPSS software version 23 (trial). Therapy was declared effective by measuring Relative Risk (RR) using revman (trial) test. The normality test was < 0.05 so that a non-parametric test was administered which was kruskal-walls. A 95% confidence interval (IK) limit was used for indicating a large range of therapeutic effects.

3. RESULTS AND DISCUSSION

Searches using the pubmed.gov search system with the keyword [REMDESIVIR] [RUXOLITINIB] [COVID19] in 2010-2020 found 285 citations (Figure 1). After filtering the title and abstract, it was only derived two studies. Identification was conducted for further examination. Research journals analyzed include, Cao, Yang., et al., 2020., Ruxolitinib in Treatment of Severe Corona Virus Disease 2019 (Covid-19) : A Multicenter, Single Blind, Randomized Controlled Trial., And Wang, Yeming., 2020., Remdesivir In Adults with Severe COVID-19: A Randomised, Double-Blind, Placebo-Controlled, Multicenter Trial.

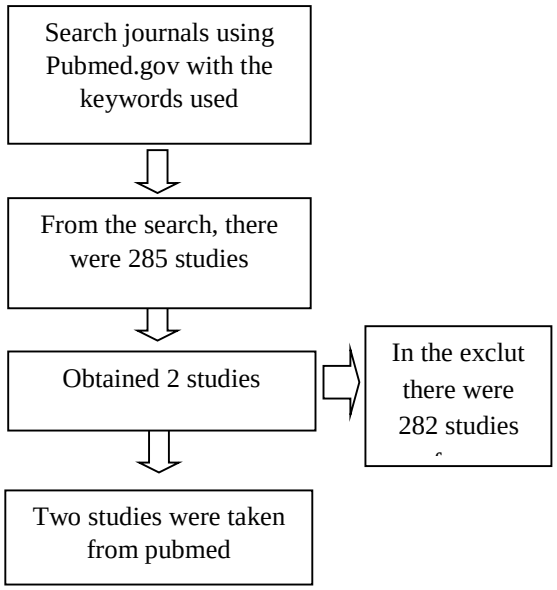

Fig 1. Search diagram

The characteristic data of the study was administered on several articles incorporated into the metanalysis. Then, the quality of the methodology was assessed using Jadad score (table 1). The results of this assessment show that the Jadad score for Wang, Yeming., et al., 2020 is 3, where a value of 3 is a minimum value for a research method RCT was considered to have good methodology quality. As for Cao, Yang., et al., 2020, a score of 2 is considered quite good. Demographic samples in the study were tested for normality and homogeneity. Sample demographics included fever, age, gender, Peripheral White Cell Count, Peripheral Lymphocyte, and serum creatinine. The characteristics can be seen in Table 2.

Table 2. Characteristics of studies

Study characteristics	Wang, Yeming., *et al.*, 2020	Cao, Yang., *et al.*, 2020
Type of study	RCT	RCT
Types of therapy	Covid-19	Covid-19
Number of samples	41	236
Treatment	Remdesivir monotherapy	Ruxolitinib monotherapy
Control	21	78
Measurement time	7,14,21,28 day	7,14,21,28 day
The place	China	Germany
Diagnosis criteria	PCR SpO2 ≤ 92% IMV (invasive mechanical ventilation) or NIV (non-invasive ventilation	PCR SpO2 ≤ 92% IMV (invasive mechanical ventilation) or NIV (non-invasive ventilation
Blinding	Yes	Yes
Length of observation	No	No

In the normality test abnormalities are found in the sex and serum creatinine so that non parametric testing is carried out, namely kruskal wallis. Therefore, it can be interpreted that Ruxolitinib is 1.40 times greater in patients' condition improvement compared to Remdesivir in the 14th hour.Wallis' kruskal test found insignificant results with Wallis' kruskal test found insignificant results with a p> value of 0.05 which meant there was no significant demographic difference.

Table 4. Analysis Kruskalwallis test

	DataFever	Peripheral White Cell Count	Peripheral Lymphocyte	Serum Creatinine	DataSex
Chi-Square	,600	,600	,000	,600	2,667
df	1	1	1	1	1
Asymp. Sig.	,439	,439	1,000	,439	,102

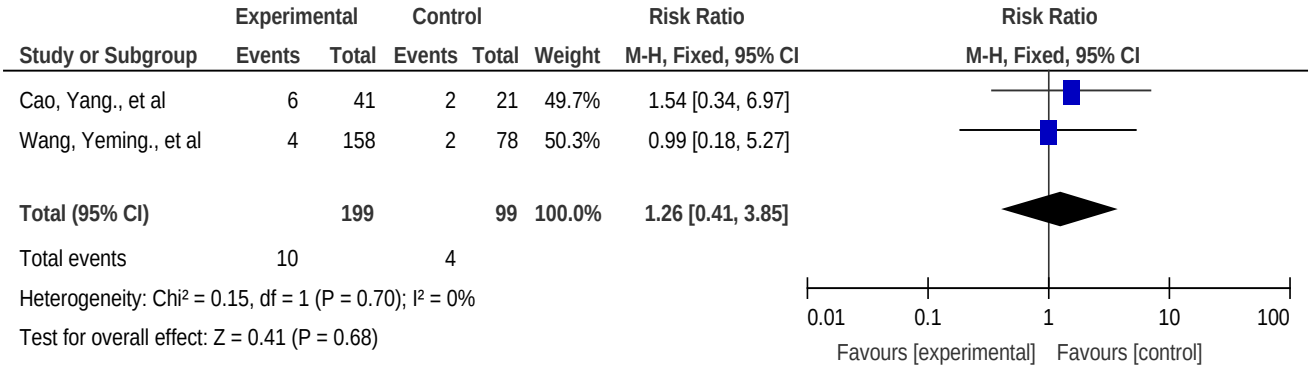

Fig 2. The development of the condition of the Covid patient 19 days 7

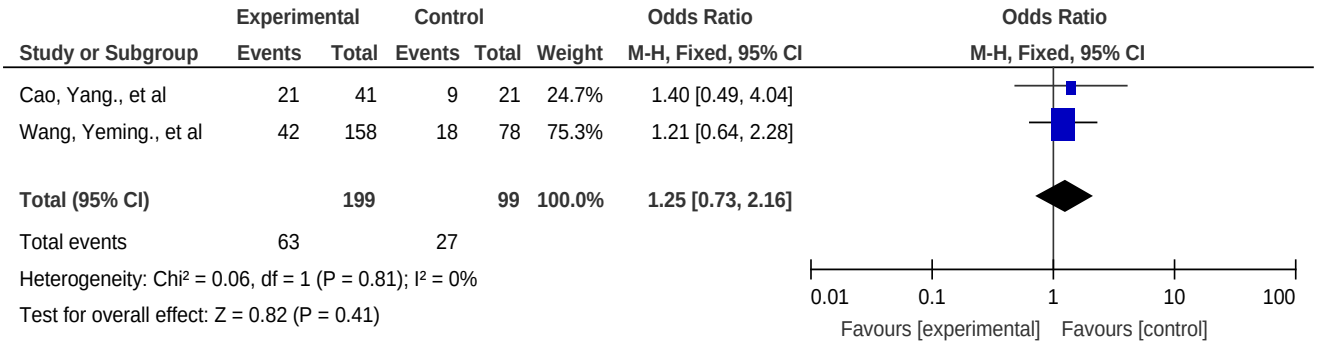

Fig 3. The development of the condition of the Covid patient 19 days 14

4. THE COMPARISON BETWEEN REMDESIVIR AND RUXOLITINIB IN COVID-19 PATIENTS

In this study, the administration of Remdesivir therapy (Wang, Yeming. et al, 2020) and Ruxolitinib (Wang, Yeming. et al; Cao, Yang., et al., 2020) was compared. Risk Ratio Clinical Improvement Rate after being given ruxolitinib suportive therapy (Cao, Yang., et al., 2020) obtained results of RR 1.54, 0.34 to 6.97 with a Risk Ratio of remdesivir of 0.99, 0.18 to 5.27. Thus, it can be interpreted that it was 1.54 times greater in improvement of patient condition compared to Ruxolitinib in the 7th hour (RR 1.26 CI 95% 0.41 to 3.86, 199 participants in both trials)

Meanwhile, administering Remdesivir therapy (Wang, Yeming. et al, 2020) with Ruxolitinib (Wang, Yeming. et al; Cao, Yang., et al., 2020) on the 14th day obtained rr results 1.26 CI 95% 0.41 to 3.86, 199 participants in both experiments. The Risk Ratio Clinical Improvement Rate after being given Ruxolitinib supportive therapy (Cao, Yang., et al., 2020) obtained results RR 1.40, 0.49 to 4.04 and Risk Ratio remdesivir of 1.21, 0.64 to 2.28.

5. CONCLUSION

The results of the analysis of 2 literature discussed above show that there are several languages including clinical improvement day 7, 14, random time of death from Covid-19. Then, it was analyzed using forest plots which

showed significant differences that could improve the clinical improvement comparing between the 7th and 14th days after the therapy was administered. From the results of the analysis using forest plot, there were significant differences in the risk of decreased improvement.

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