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To Identify the Effectiveness of Immunoglobulin Therapy in Covid 19

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ABSTRACT

A worldwide health emergency was declared in January 2020 by the WHO Emergency Committee due to rising case notification rates at Chinese and international locations. COVID-19 patients typically go through three clinical stages: the acute or pneumonia stage, the viremia stage, and the recovery stage. The lymphocyte count in the early phase of the disease (1-14 days) is normal or slightly low, which could be the pathogenesis of COVID-19. When viremia occurs, however, significant lymphopenia occurs in the late phase (7-14 days after symptoms appear). Furthermore, during the early stage, B lymphocytes are reduced. Antibody detection in patients' serum is one of the COVID-19 diagnostic methods. The length of hospital stay was significantly lower for the control group than that of the intervention group (P-value = 0.003). In our study we concluded that the length of hospital stay was decreased in the IVIG group when compared with that of the NON IVIG group(p-value = 0.0001). We also performed unpaired t-test for CRP, D-Dimer, lymphocytes, duration of fever. The unpaired t-test is used to compare the mean percentage reduction of two independent groups. From our study the effectiveness of intravenous immunoglobulin therapy over non IVIG therapy in covid 19 patients has been observed. The recovery rate in patients who received ivig therapy was fast when compared to non-IVIG patients. There is much difference in CRP and lymphocyte levels in IVIG pts after two follow ups. The duration of fever and length of hospital stay decreased in patients receiving IVIG therapy which shows that the IVIG treatment was effective in covid-19 patients than non-IVIG treated patients.

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INTRODUCTION

A worldwide health emergency was declared in January 2020 by the WHO Emergency Committee due to rising case notification rates at Chinese and international locations. On the Johns Hopkins University website and other forums, the case detection rate may be followed virtually instantly and changes regularly. China is currently carrying a heavy burden of disease and mortality as of the middle of February 2020, although the incidence in other Asian nations, in Europe, and in North America is still relatively low.

Coronaviruses are positive single-stranded, enclosed, big RNA viruses that can infect a variety of animals in addition to humans. By cultivating the viruses from cold patients, Tyrell and Bynoe published the first description of coronaviruses in 1966. They were given the name coronaviruses based on their shape as spherical virions with a core shell and surface projections resembling a solar corona [1]. Coronaviruses are classified into four subfamilies: alpha, beta, gamma, and delta. Gamma and delta viruses are thought to have their origins in pigs and birds, but alpha and beta coronaviruses are thought to have their origins in mammals, particularly bats. Among the seven coronavirus subtypes that can infect people, beta coronaviruses can result in serious illness and even death, whereas alpha coronaviruses only produce infections that are asymptomatic or minimally symptomatic.SARSCoV2 is a beta-coronavirus that belongs to the B lineage and is closely related to the SARS-Co virus [2, 3].

Pneumonia was the first clinical sign of the SARSCoV2-related disease COVID-19, allowing case detection. Recent reports also mention gastrointestinal symptoms and asymptomatic infections, particularly in young children [4]. So far, observations indicate a mean incubation period of five days [5] and a median incubation period of three days (range: 0-24 days) [6]. The proportion of people infected with SARSCoV2 who remain asymptomatic throughout the infection has yet to be determined. Clinical manifestations of the disease, consisting of fever, cough, nasal congestion, fatigue, and other signs of upper respiratory tract infections, usually begin in less than a week in symptomatic patients. In approximately 75% of patients, the infection can progress to severe disease, with dyspnea and severe chest symptoms resembling pneumonia, as detected by computed tomography on admission [6].

Pneumonia typically develops during the second or third week of symptomatic infection. Reduced oxygen saturation, blood gas deviations, changes visible through chest X-rays and other imaging techniques, with ground glass abnormalities, patchy consolidation, alveolar exudates, and interlobular involvement, eventually indicating deterioration, are all prominent signs of viral pneumonia. Lymphopenia appears to be common, with elevated inflammatory markers (C-reactive protein and pro-inflammatory cytokines). The nucleocapsid protein (N), spike protein (S), small membrane protein (SM), and membrane glycoprotein (M) are encoded by the major four structural genes, with an additional membrane glycoprotein (HE) occurring in the HCoVOC43 and HKU1 betacoronaviruses. At the whole genome level, SARSCoV2 is 96 percent identical to a bat coronavirus [5].

However, there is a shortage of efficient therapeutic approaches. Antiviral and oxygen therapy, as well as organ and symptomatic support, including mechanical breathing, even extracorporeal membrane oxygenation (ECMO) of cardiac support, and continuous renal replacement therapies, are the main clinical therapeutic options for critical COVID-19 (CRRT) [7]. The therapeutic effectiveness of these tactics is not yet clear. Though the underlying mechanisms are still unknown, several clinical testing and postmortem findings have indicated that the inflammation and immunological response brought on by the viral infection is the primary cause of the disease's progression and bad prognosis [8, 9]. In critically ill COVID-19 patients, an unchecked immune response to SARS-CoV-2 infection leads to a systemic hyperinflammatory response. As a result, immunotherapies based on immunomodulation and inflammatory cytokine neutralisation could lessen lung damage caused by inflammation. One of the main therapy options is targeted intravenous immunoglobulin (IVIG) [7].

Immunologic Mechanisms of Using IVIG in Covid-19 Patients

COVID-19 patients typically go through three clinical stages: the acute or pneumonia stage, the viremia stage, and the recovery stage. The lymphocyte count in the early phase of the disease (1-14 days) is normal or slightly low, which could be the pathogenesis of COVID-19. When viremia occurs, however, significant lymphopenia occurs in the late phase (7-14 days after symptoms appear). Furthermore, during the early stage, B lymphocytes are reduced. Antibody detection in patients' serum is one of the COVID-19 diagnostic methods. The majority of evidence suggests that a higher level of SARS-2-COVID-IgG is a marker of severe disease (for unknown reasons at the moment), and that antibody levels are more diagnostic than therapeutic. Inflammatory pathways are inhibited by IVIG therapy, such as decreased production of IL-6, TNF, T-cell activation, matrix metalloproteinase 9 activity, and IL-12/23p40 in macrophages. On the other side, anti-inflammatory systems are activated, leading to a rise in macrophages, PPAR-gamma, and IL-10 production in the gut, among other things [8]. The expression of the TLR-4 toll-like receptor is decreased concurrently. It has been found that these IVIG effects on the inflammatory storm do not lead to a greater tendency for patients to develop immunosuppression [9]. Additionally, dendritic cell maturation may

be prevented by IVIG, along with a decrease in IL-12 expression and an increase in IL-33, IL-4, and IL-13 production.

Aims and Objectives

To determine the effectiveness of immunoglobulin therapy in covid-19 patients by using the data on hospital stay.

METHODOLOGY

Study Design

A retrospective study of 300 patients (200 cases of IVIG and 100 cases of non-IVIG)who satisfied the inclusion criteria were recruited into the study.

Inclusion Criteria

1. Patient with lab-confirmed covid-19.
2. Age 18 years and above.

Exclusive Criteria

1. Studies with insufficient data.
2. Studies with control groups.

Study Procedure

1. The study enrolled a total of 300 patients who met inclusion criteria. A suitable data collection form was created.
2. All relevant data for the study were collected and documented in an adequately defined data collection form, including demographic characteristics (age, gender), comorbidities (HTN, DIABETES), primary outcomes (drugs), secondary outcomes (duration of fever, length of hospital).
3. Ms excel was used to evaluate data.

Sources of Data

Patient case profiles.

RESULTS

The percentage decrease in CRP levels of female patients who received intravenous immunoglobulin therapy received and non IVIG therapy which are taken at 2 stages- follow-up 1 and follow-up 2, and their decreased percentage was measured.

The unpaired t-test is used to compare the mean percentage reduction of two independent groups. The unpaired t-test is done to find out the significance between the percentage decrease in CRP levels of IVIG and NON-IVIG received female patients and it is provided to be statistically significant (p=0.0175). as represented in Table 1.

The percentage decrease in CRP levels of male patients who received intravenous immunoglobulin therapy received and non IVIG therapy which are taken at 2 stages follow-up 1 and follow-up 2, and their decreased percentage was measured.

The unpaired t-test is used to compare the mean percentage reduction of two independent groups. The unpaired t-test is done to find out the significance between the percentage decrease in CRP levels of IVIG and NON-IVIG received male patients and it is provided to be statistically significant (p= 0.001), as shown in Table 2.

The D DIMER levels in female patients who received intravenous immunoglobulin therapy received and non IVIG therapy which are taken at 2 stages- follow up 1 and follow up 2, and their decrease in percentage was measured.

The unpaired t-test is used to compare the mean percentage reduction of two independent groups. The unpaired t-test is done to find out the significance between the d dimer levels of IVIG and NON-IVIG received female patients and is provided to be statistically not significant (p= 0.8723), as shown in Table 3.

The D DIMER levels in male patients who received intravenous immunoglobulin therapy and non IVIG therapy which are taken at 2 stages- follow up 1 and follow up 2, and their decrease in percentage was measured.

The unpaired t-test is used to compare the mean of reduction percentage of two independent groups. The unpaired t-test is done to find out the significance between the d dimer levels of IVIG and NON-IVIG received male patients and it is provided to be statistically not significant (p= 0.5387), as shown in Table 4.

The lymphocyte values in female patients who received intravenous immunoglobulin therapy and NON-IVIG therapy which are taken at 2 stages- follow up 1 and follow up 2, and their increased percentage was measured.

The unpaired t-test is used to compare the mean percentage increase of two independent groups. The unpaired t-test is done to find out the significance between the lymphocyte's levels in IVIG and NON-IVIG received female patients and it is provided to be statistically highly significant (p=0.000), as shown in Table 5.

Table 1: T-Test for CRP Levels of IVIG AND Non-IVG Female Patients

	Sample Size	Mean	Standard Deviation	p-value
IVIG	29	22.75	45.1	
Non IVIG	39	45.16	30.7	0.0175

Table 2: T-Test for CRP Levels of IVIG and Non-IVIG Male Patients

	Sample Size	Mean	Standard Deviation	p-value
IVIG	38	19.6	36.9	
Non IVIG	81	48.9	47.3	0.0010

Table 3: T-Test for D Dimer Levels of IVIG and Non-IVG Female Patients

	Sample Size	Mean	Standard Deviation	p-value
IVIG	29	7.1	26.9	
Non IVIG	45	8.14	27.2	0.8723

Table 4: T-Test for D Dimer Levels of IVIG and Non-IVG Male Patients

	Sample Size	Mean	Standard Deviation	p-value
IVIG	38	9.27	29.6	
Non IVIG	79	13.27	34.3	0.5387

Table 5: T-Test for Lymphocyte Values in Female Patients who Received IVIG and Non-IVG Therapy

	Sample Size	Mean	Standard Deviation	p-value
Sample 1	53	-0.27	13.73	
Sample 2	29	18.4	12.8	0.0001

Table 6: T Test for Lymphocyte Values in Male Patients who Received IVIG and Non-IVG Therapy

	Sample Size	Mean	Standard Deviation	p-value
IVIG	38	-0.71	15.2	
Non IVIG	86	15.98	7.9	0.0001

Table 7: T Test for Duration of Fever in IVIG vs Non-IVIG

	Sample Size	Mean	Standard Deviation	p-value
Non-IVIG	56	6.73	1.757546	
IVIG	37	4.18	2.141455	0.0001

Table 8: T Test for Length of Hospital Stay in IVIG vs Non-IVIG

	Sample Size	Mean	Standard Deviation	p-value
Non-IVIG	144	7.14	2.472361	
IVIG	67	4.78	1.63135	0.0001

The lymphocyte levels in male patients who received intravenous immunoglobulin therapy and NON-IVIG therapy which are taken at 2 stages-follow up 1 and follow up 2, and their increased percentage was measured.

The unpaired t-test is used to compare the mean percentage increase of two independent groups. The unpaired t-test is done to find out the significance between the lymphocyte's levels of IVIG and NON-IVIG treated male patients and it is provided to be statistically significant (p= 0.0001), as shown in Table 6.

The unpaired t-test is used to compare the mean percentage increase of two independent groups. The unpaired t-test is done to find out the significance between the duration of fever in IVIG and NON-IVIG received patients and it is provided to be statistically highly significant (p=0.0001), as shown in Table 7.

The unpaired t-test is used to compare the mean percentage increase of two independent groups. The unpaired t-test is done to find out the significance between the Length of hospital stay in IVIG and NON IVIG received patients and it is provided to be statistically highly significant (p=0.0001), as shown in Table 8.

DISCUSSION

In the study conducted by P. Tabarsi et al. The length of hospital stay was significantly lower for the control group than that of the intervention group (P-value = 0.003). In our study we concluded that the length of hospital stay was decreased in the IVIG group when compared with that of the NON IVIG group(p-value = 0.0001). We also performed unpaired t-test for CRP, D-Dimer, lymphocytes, duration of fever. The unpaired t-test is used to compare the mean percentage reduction of two independent groups. The unpaired t-test is done to find out the significance between the percentage decrease in CRP levels of IVIG and NON-IVIG received female patients and it is provided to be statistically slightly significant (p=0.0175). The unpaired t-test is done to find out the significance between the percentage decrease in CRP levels of IVIG and NON-IVIG received In male patients also it is provided to be statistically slightly significant (p-value = 0.001). D -dimer levels of IVIG and NON-IVIG is found to be non significant in both male (p= 0.5387) and female (p= 0.8723). The unpaired t-test is done to find out the significance between the percentage decrease in LYMPHOCYTES levels of IVIG and NON-IVIG received female patients and it is provided to be statistically highly significant (p=0.0001). The unpaired t-test is done to find out the significance between the percentage decrease in LYMPHOCYTES levels of IVIG and NON-IVIG received male patients and it is provided to be statistically significant (p=0.0001). The unpaired t-test is done to find out the significance between the duration of fever in IVIG and NON-IVIG received patients and it is provided to be statistically significant (p=0.0001).

Study Limitations

First the study is limited by its retrospective single-centre design. second our study had a small study sample which is attributable to restrictions imposed by the study design of a retrospective study at a single centre. Third, the clincal followup duration was short which might influence the reliability of results. Further large scale studies will be required to evaluate the implication of these results.

Because of these limitations, the effectiveness of intravenous immunoglobulin therapy in covid affected patients maybe not significantly related and likely to be influenced by the study limitations. However, these findings should be confirmed in larger population of patients.

CONCLUSION

From our study the effectiveness of intravenous immunoglobulin therapy over non IVIG therapy in covid 19 patients has been observed. The recovery rate in patients who received ivig therapy was fast when compared to non-IVIG patients. There is much difference in CRP and lymphocyte levels in IVIG pts after two follow ups. The duration of fever and length of hospital stay decreased in patients receiving IVIG therapy which shows that the IVIG treatment was effective in covid-19 patients than non-IVIG treated patients.

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Conflict of Interest

The authors declare that there is no conflict of interest.

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