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General Medicine

UTILITY OF ROCHE COCKTAIL IN THE MANAGEMENT OF COVID 19 CASES

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ABSTRACT **Background:** Role of various drugs in the management of COVID 19 remains controversy. In order to through light on the same, this study was conducted to assess the duration of hospital stay and outcome of cases those who were treated with Roche cocktail (Casirivimab and Imdevimab). **Methods:** This study was conducted as a cross sectional study in the Department of general medicine in Thanjavur Medical College and hospital, Thanjavur, a tertiary care Government teaching hospital during the period of September 2021. All these cases were treated with Casirivimab and imdevimab (Roche Cocktail) and their outcome and duration of hospital stay were assessed. **Results:** The mean duration of symptoms was 2.4±1.6 days. The severity of illness was mild, moderate and severe among 30%, 54% and 16% of the cases respectively. The duration of hospital stay was 1-7 days for 94% of the cases and more than a week among 6% of the cases. Mean duration of stay in hospital was 5.4±3.6 days. Also there were no mortality reported. **Conclusion:** In comparison to the severity of COVID 19 infection, the average length of stay in hospital was longer. However, when compared to other trials where cases were not treated with cocktail, the mean length of stay in hospital was reduced in our study with the use of Roche cocktail. As a result, large-scale, comparative randomised controlled trials are required to further confirm the efficacy of the Roche combination.

KEYWORDS : Roche cocktail, COVID 19, casirivimab and imdevimab

INTRODUCTION

Monoclonal antibodies are a group of antibodies that are all similar and have a high affinity and specificity for a single epitope. When used for prophylaxis (respiratory syncytial virus) or therapy of certain viral infections, they have been found to be safe and effective (Ebola virus disease).[1] Monoclonal antibodies are hypothesised to have clinical efficacy in viral infections by attaching directly to free virus particles and neutralising their capacity to infect host cells. The crystallisable fragment part of monoclonal antibodies may bind to viral antigens expressed on the surface of infected cells and trigger antibody-dependent phagocytosis and cytotoxicity.[2]

The viral transmembrane spike glycoprotein binds to angiotensin-converting enzyme 2 on the surface of host cells to initiate SARS-CoV-2 infection.[3] As a result, neutralising antibodies are drawn to the spike glycoprotein's receptor-binding domain.[4] Monoclonal antibodies targeting the spike receptor binding region were quickly identified from humanised mice and peripheral B cells of recovered patients following the emergence of SARS-CoV-2.[5,6] Anti-SARS-CoV-2 spike protein neutralising monoclonal antibodies have demonstrated in-vivo efficacy in both therapeutic and preventive settings in mouse and non-human primate models, with reductions in viral load and lung pathology.[7,8]

Casirivimab and imdevimab (Roche Cocktail) are two non-competing human IgG1 anti-SARS-CoV-2 monoclonal antibodies that bind exclusively to the receptor binding region of SARS-spike CoV-2's glycoprotein, preventing viral entrance into host cells.[9] Instead of a single antibody, a mixture of antibodies that bind to non-overlapping epitopes is used to reduce the risk of antiviral efficacy loss due to naturally circulating viral variations or the formation of escape mutants under drug pressure.[10]

In a clinical trial in adult outpatients with SARS-CoV-2 infection and factors associated for severe COVID-19, the combination of casirivimab and imdevimab was well tolerated and, as compared to placebo, lowered viral load in the upper airway, shortened the time to symptom resolution, and decreased the composite outcome of COVID-19-related hospitalisation or all-cause mortality.[11] The combination of casirivimab and imdevimab has also been proven to protect previously uninfected household contacts of infected patients from contracting SARS-CoV-2.[12] In adult outpatients with SARS-CoV-2 infection, other anti-spike monoclonal antibody products have also showed antiviral and therapeutic effects.[13]

The US Food and Drug Administration has granted Emergency Use Authorization for bamlanivimab with etesevimab, casirivimab and imdevimab, and sotrovimab in outpatients with mild to moderate COVID-19. Casirivimab and imdevimab in combination have been approved by the European Medicines Agency for treatment in patients who are at high risk of advancing to severe COVID-19 but do not require oxygen therapy. A preliminary finding from a short trial[14] of casirivimab and imdevimab in COVID-19 patients requiring low-flow oxygen was consistent with a therapeutic benefit in seronegative patients. With these in view this study was conducted to assess the duration of hospital stay and outcome of cases those who were treated with Casirivimab and Imdevimab.

MATERIALS

This study was conducted as a cross sectional study in the Department of general medicine in Thanjavur Medical College and hospital, Thanjavur, a tertiary care Government teaching hospital during the period of September 2021. Patients with COVID 19 cases, from both genders were included in the study. Patients already treated with antiviral drugs for the management of COVID 19 infection and immune-compromised cases were excluded from the study. A total of 50 RTPCR positive COVID 19 cases who presented to department of general medicine during the study period were included in the study. All these cases were treated with Casirivimab and imdevimab (Roche Cocktail with 1200 mg each) and their outcome and duration of hospital stay were assessed. All the cases were assessed for detailed history and clinical examination. Data was entered and analyzed using SPSS.

RESULTS

In this study maximum of 42% of the cases were between 51-60 years of age, 18% of the cases were between 61-70 years of age, 16% of the cases were in the age range of 41-50 years of age. in the age range of less than 40 years and more than 70 years 12% cases were found in each age group. Based on the gender of the participants 60% were males and 40% were females.

Table 1: Background characteristics of the study participants

Variables	Frequency	Percentage
Age groups		
≤ 40 years	6	12.0
41-50 years	8	16.0
51-60 years	21	42.0
61-70 years	9	18.0
>70 years	6	12.0
Total	50	100.0

Sex		
Male	30	60.0
Female	20	40.0
Total	50	100.0

Among the patients with COVID-19 54% of them were known to have Diabetes mellitus, systemic hypertension was found among 52% of the cases, 10% of the patients had CAD. Other chronic diseases like Hypothyroid, PostCABG, Uro Sepsis, Breast Disease and Old cerebrovascular accident was recorded among 6%, 88%, 2% and 2% cases in this current study.

Table 2: Proportion of cases based on chronic illness

Variables	Frequency	Percentage
Diabetes mellitus		
Present	27	54.0
Absent	23	46.0
Total	50	100.0
Systemic hypertension		
Present	26	52.0
Absent	24	48.0
Total	50	100.0
Coronary artery Disease		
Present	5	10.0
Absent	45	90.0
Total	50	100.0
Other chronic illnesses		
Hypothyroid	3	6.0
Post CABG	44	88.0
Uro Sepsis	1	2.0
Breast Disease	1	2.0
Old cerebrovascular accident	1	2.0
Total	50	100.0

In this study among patients who were treated with antibody cocktail drug, 44% of the cases had symptoms more than 4 days duration while 56% of the cases had symptoms less than 3 days. The mean duration of symptoms was 2.4±1.6 days. The severity of illness was mild, moderate and severe among 30%, 54% and 16% of the cases respectively. The duration of hospital stay was 1-7 days for 94% of the cases and more than a week among 6% of the cases. Mean duration of stay in hospital was 5.4±3.6 days and mean duration of stay in hospital with respect to severity of COVID infection is given in table.

Table 3: Duration of symptoms, severity of illness and hospital stay among the cases

Variables	Frequency	Percentage
Duration of symptoms		
≥ 4 days	22	44.0
<3 days	28	56.0
Total	50	100.0
Severity of illness		
Mild	15	30.0
Moderate	27	54.0
Severe	08	16.0
Total	50	100.0
Duration of stay in hospital		
1-7 days	47	94.0
>7 days	03	06.0
Total	50	100.0
Severity of COVID 19	**Duration of stay in hospital (in days)**	
	Mean	SD
Mild	2.4.	1.1
Moderate	3.1	1.5
Severe	6.3	4.3

An adverse event followed by antibody cocktail drug among COVID-19 cases was noted in only two percentages of cases however the rest free from adverse events. There was no mortality among patients treated with antibody cocktail drug in our study.

Table 4: Adverse events and mortality among the study

Variables	Frequency	Percentage
Adverse events		
Present	01	2.0
Absent	49	98.0
Total	50	100.0
Mortality		
Absent	50	100.0

DISCUSSION

In this study the mean duration of symptoms was 2.4±1.6 days. The severity of illness was mild, moderate and severe among 30%, 54% and 16% of the cases respectively. Mean duration of stay in hospital was comparatively more with respect to severity of COVID 19 infection.

However, Abani O et al[15] reported that the monoclonal antibody combination of casirivimab and imdevimab reduced 28-day mortality in patients who were seronegative (and so had not developed their own humoral immune response) at baseline but not in those who were seropositive at baseline in patients admitted to hospital with COVID-19. Weinrich DM et al[11] in their study stated that when compared to placebo, the REGEN-COV antibody combination (casirivimab plus imdevimab) significantly reduced Covid-19-related hospitalisation or all-cause death. In all dosing arms, the median time to resolution of Covid-19 symptoms was 4 days shorter than in the placebo group. REGEN-efficacy COV's was constant across subgroups, including those with SARS-CoV-2 serum antibody positivity at the start. REGEN-COV lowered viral load faster than placebo. Serious adverse events were more common in the placebo group (4.0%) than in the 1200mg (1.1%) and 2400mg (1.3%) groups, while grade 2 infusion-related reactions were uncommon (0.3 percent in all groups). They concluded that REGEN-COV therapy was well-tolerated and reduced Covid-19-related hospitalisation or all-cause death, as well as symptom resolution and viral load reduction.

In another study, Brien O et al[12] reported that in cases with a baseline viral load of >107 copies/mL, the time-weighted average daily reduction in viral load was significantly larger in the REGEN-COV combination 2400mg+8000mg group than placebo through day 7. Compared to placebo, REGEN-COV lowered the proportion of patients with one COVID-19–related MAV; relative risk reduction; treatment effect was more significant in patients with one risk factor for hospitalisation. The occurrence of adverse events was consistent between groups. They concluded that treatment with REGEN-COV effectively reduced viral load and COVID-19–related MAVs in COVID-19 outpatients enrolled before the extensive dissemination of delta and omicron variants. Also, Yasutaka K et al[16] stated that the use of an antibody cocktail treatment was connected to a decrease in the need for additional medical interventions. The finding of the 51 cases shows that antibody cocktail therapy is linked to lessening hospital strain, which is linked to better medical management for public health care in the Covid-19 pandemic era.

Marco F et al[17] reported that there were 165 patients in the trial, with 105 of them infected with the VOC Alpha and 43 with the VOC Gamma. There were no differences in the primary outcome between patients treated with bamlanivimab/etesevimab or casirivimab/imdevimab in the Alpha group. In the Gamma group, however, patients treated with bamlanivimab/etesevimab reached the primary goal at a higher rate than those treated with casirivimab/imdevimab. The Gamma variant and days from beginning of symptoms to mAbs infusion were independently related with a greater risk of hospitalisation or mortality in multivariate Cox regression analysis, whereas casirivimab/imdevimab was protective. They concluded that bamlanivimab/etesevimab should be used with caution in cases infected with the SARSCoV-2 Gamma form due to the significant risk of illness progression. Zitek T et al[18] found that 3.0% of completely vaccinated patients required hospital admission within 28 days, compared to 6.2 percent of unprotected patients. Aside from that, no statistically significant variations in univariate outcomes were found. In terms of the primary outcome, their multivariate regression analysis indicated that full immunisation was linked with a statistically significant reduction in hospitalisation within 28 days for patients receiving casirivimab/imdevimab for COVID-19, with an odds ratio of 0.19.

The monoclonal antibodies casirivimab and imdevimab were used to treat COVID-19 in pregnant women, according to Mayer C et al[19]. They found that two unvaccinated pregnant women, one in the second trimester and the other in the third trimester, both had moderate COVID-19 and satisfied the criteria for outpatient care. They were given casirivimab and imdevimab to reduce the chance of serious

illness. Neither had a bad pharmacological reaction, and neither developed a serious illness. Monoclonal antibodies, such as casirivimab and imdevimab, licenced under emergency use permission, should be evaluated in unvaccinated pregnant women with mild-to-moderate COVID-19 to reduce the risk of severe disease, they found. Phan AT et al[20] found that using a monoclonal antibody combination of casirivimab and imdevimab to lower viral load in infected seronegative non-hospitalized patients effectively reduced viral load. However, there is little evidence that REGN-COV2 can be used in an inpatient context. We discuss the case of a 45-year-old man with confirmed SARS-CoV-2 infection, mild dyspnea, and symptoms that progressively worsened over a week. After a single low-dose regimen of REGN-COV2 infusion while in the hospital, the patient's symptoms improved dramatically, and he was discharged without further medical issues.

CONCLUSION

In this study among the cases the mean duration of stay in hospital was comparatively more with respect to severity of COVID 19 infection. However when compared to other studies where cases were not treated with cocktail, in this study, with the use of Roche cocktail, the mean duration of stay in hospital was reduced. Hence, in order to prove the efficacy of Roche cocktail further, large scale, comparative randomized controlled trials are needed.

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