Retrospective Review: Convalescent Plasma & Dexamethasone may be Effective in Treatment of Acute Respiratory Distress Syndrome Secondary to COVID-19

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BACKGROUND

The outbreak of COVID-19 disease due to novel coronavirus (SARS-CoV-2), leading to severe acute respiratory distress syndrome (ARDS), was first documented in late December 2019 in Wuhan, China. Following this, international spread occurred rapidly.[1] Preliminary data has been released and multiple studies are ongoing, including the SOLIDARITY and RECOVERY trials, concerning potential treatment regimens for COVID-19.[2-3] However, there is currently insufficient evidence to declare a general first line treatment regimen for COVID-19. This retrospective analysis may suggest treatments that warrant further study or provide supporting evidence for management evaluated in other trials. In this study, we will describe our initial institutional practices and outcomes, focusing on mortality and length of stay data.

METHODS

- **Trial design**: This study is a retrospective chart review conducted at a single medium-sized community hospital in Amarillo, TX
- **Study subjects:** This retrospective chart review studied patients who were admitted to our institution between March 14, 2020 and June 9, 2020 with a laboratory-confirmed COVID-19 diagnosis. Patients were excluded from this analysis if they died prior to hospital admission (in the emergency department) or if they were still admitted at study cutoff date.
- **Treatment groups:** Patients were assigned to groups based on therapeutic modalities administered for the treatment of COVID-19. Treatment approaches analyzed will include convalescent plasma, remdesivir, hydroxychloroquine + azithromycin, tocilizumab, lopinavir/ritonavir + ribavirin, dexamethasone, and supportive care. The supportive care group will include patients who are not treated with any of the treatment regimens identified by the treatment arms.
- **Outcomes:** The primary outcome of the study was the incidence of in-hospital mortality. Secondary outcomes included total hospital length of stay and total intensive care unit length of stay.
- **Data collection**: All data was collected from our institutional EMR
- **Statistical analysis**: To derive each treatment group, propensity matching was used to match patients to members of the supportive care group based on the following baseline characteristics: mSOFA score, gender, age, BMI, and presence of at least one COVID-19 associated comorbidity. The propensity match analysis was run in a one to one manner using an optimal algorithm with a tolerance of 0.001. All matches were matched in a one to one manner. All values are reported as means or percentages with a standard deviation. Continuous data was analyzed with an unpaired student's t-test. Nominal data was analyzed with a chi-square test or a Fisher's exact test for groups with a small sample size (N < 5). For mortality data, a hazard ratio (HR) was calculated. Ninety-five percent confidence intervals (CI) were also calculated. Statistical significance was determined using a two-sided alpha of 0.05

RESULTS

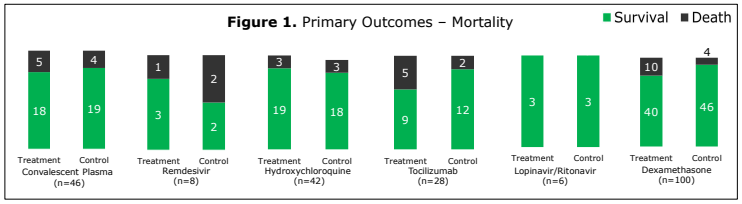

Figure 1. These findings did not find statistical significance in utilization of convalescent plasma, remdesivir, hydroxychloroquine, tocilizumab, lopinavir/ritonavir, or dexamethasone (p>0.05 for all treatment groups and effects on mortality)

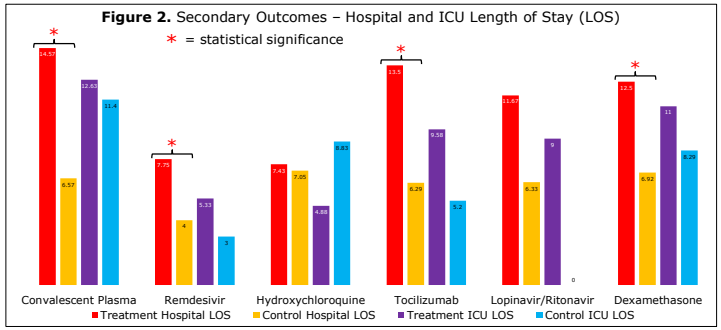

Figure 2. These findings demonstrated significant differences for length of stay in the hospital setting for convalescent plasma (p < 0.05), remdesivir (p < 0.05), tocilizumab (p<0.05), and dexamethasone (p<0.05) but not for hydroxychloroquine or lopinavir/ritonavir (p>0.05); these findings did not demonstrate significant differences for length of stay in the ICU setting for convalescent plasma, remdesivir, hydroxychloroquine, tocilizumab, lopinavir/ritonavir, or dexamethasone (p>0.05 for all treatment groups and effects on ICU LOS)

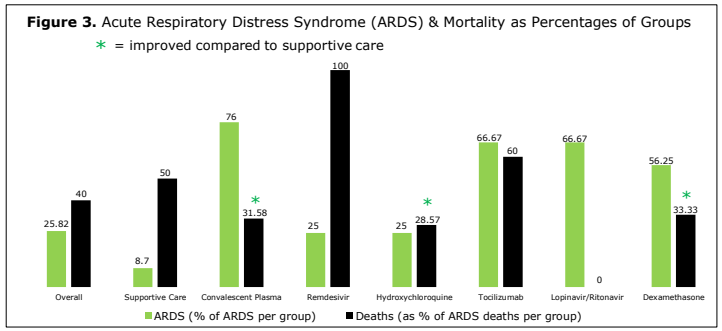

Figure 3. This figure demonstrates the percentage of ARDS in each treatment group and percentage of mortality within the ARDS patients per treatment groups. Overall (n = 213), this study had 55 patients with ARDS and 22 patients died due to ARDS. Supportive care group (n=115) had 10 patients with ARDS and 5 ARDS deaths, convalescent plasma group (n=25) had 19 patients with ARDS and 6 ARDS deaths, remdesivir group (n=4) had 1 patient with ARDS and 1 ARDS death, hydroxychloroquine group (n=28) had 7 patients with ARDS and 2 ARDS deaths, tocilizumab group (n=15) had 10 patients with ARDS and 6 ARDS deaths, lopinavir/ritonavir group (n=3) had 2 patients with ARDS and 0 ARDS deaths, and dexamethasone group (n=64) had 36 patients with ARDS and 12 ARDS deaths.

DISCUSSION

In patients with ARDS, there was a trend toward mortality improvement in patients treated with convalescent plasma or dexamethasone.

- **Convalescent plasma**: Recent data from a Chinese study found that convalescent plasma therapy versus standard therapy did not affect clinical improvement in COVID-19.[4] In our study, there were more patients diagnosed with ARDS in the convalescent plasma group versus the supportive care group, which may account for the significantly increased difference in hospital LOS. It is worth noting when compared to supportive care in ARDS mortality (50%), there was improvement with convalescent plasma (32%).
- **Remdesivir**: Recent data from the ACTT-1 trial suggested that remdesivir may be effective in reducing recovery time in hospitalized COVID-19 patients.[5] Our study did not show any difference in mortality, this may have been due to our small sample size (due to date range of our study). The significant increase in hospital LOS observed in this study may be due to utilization of remdesivir for patients in more critical condition.
- **Hydroxychloroquine (+/- azithromycin)**: Recent data from a French study suggested that hydroxychloroquine may reduce viral load,[6] while data from the SOLIDARITY trial led to the cessation of the hydroxychloroquine in the study.[2] Our study did not find any evidence to suggest that hydroxychloroquine worsens outcomes nor evidence to suggest that hydroxychloroquine improves outcomes.
- **Tocilizumab**: Recent data from a retrospective cohort study found no significant improvement in recovery time or invasive ventilation duration.[7] While our study did not show significant improved mortality or ICU LOS, there was a significant increase in hospital LOS – but tocilizumab was often administered further along in the progression of COVID-19 when physicians suspected cytokine storm.
- **Lopinavir/ritonavir (+ribavirin)**: Recent data from the LOTUS trial demonstrated no statistical improvement in recovery time, mortality, or viral load with lopinavir/ritonavir.[8] Our study did not show a difference in mortality or hospital LOS between the three treatment patients and propensity-matched controls.
- **Dexamethasone**: Recent data from the RECOVERY trial suggested that dexamethasone may be effective in reducing mortality in patients requiring respiratory support.[3] Our study did not confirm these findings, possibly due to smaller sample size and lack of assessment on required level of respiratory support. Instead, the significantly increased hospital LOS in these patients may have been due to the utilization of dexamethasone in ARDS patients. However, when compared to supportive care in ARDS mortality (50%), there was improvement with dexamethasone (33%).

Limitations: small sample sizes across treatment groups which may lead to weaker statistical power, utilization of mSOFA in propensity matching which is limited by the unknown nature of this pandemic and isolated respiratory symptoms in COVID-19 disease, and utilization of LOS as secondary outcomes of this study leading to significant differences but does not account for severity of disease

CONCLUSION

Although our study suggests potential benefit in patients with severe COVID-19 treated with convalescent plasma or dexamethasone, further data in prospective, randomized trials is necessary to effectively guide decision-making.

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