

low <14 cm H₂O [48]. Avoiding ventilator disconnections is critical to prevent atelectasis and loss of PEEP. Paralytics inducers should be used only if PaO₂/FiO₂ <150 mmHg. Prone ventilation lasting longer than 12 hours a day, and conservative fluid management (ARDS strategy in patients without hypoperfusion) are strongly recommended [48, 123].

Antivirals

Oseltamivir (75 mg BID every 12 hours PO, orally), Ganciclovir (250 mg BID every 12 hours IV, intravenously) ribavirin, Lopinavir/Ritonavir tablets (400/100 mg BID every 12 hours PO, orally) [48] have all been used in efforts to decrease viral load, and to avoid the probability of respiratory complications in several studies [2, 7, 12–14].

Remdesivir, a broad spectrum antiviral [124] that inhibits RNA dependent RNA- polymerase, was successful in the control of *in vitro* SARS-CoV-2 [12, 125, 126], and it is hypothesized that it could be efficacious for prophylaxis and therapy of human coronavirus infections [48]. The first dosage under investigation for treatment of COVID-19 was 200 mg intravenously (IV) on day 1 followed by 100 mg IV daily for up to 10 days, infused over 30–60 minutes [127]. More recent studies have demonstrated there is no clinical difference between the administration of the same dosage for 5 or 10 days [128].

Steroids

The WHO report results from a clinical trial in the United Kingdom where the use of dexamethasone showed promising, lifesaving results for critically ill COVID-19 patients. In the study, preliminary findings showed that mortality was reduced by one-third for patients on ventilators, and one-fifth for patients on oxygen [120].

Anticoagulants

COVID-19 can induce an immune-thrombotic and disseminated intravascular coagulation, which can explain for thrombosis on a consumptive basis [121]; however, the thrombotic effects of COVID-19 are not completely understood [122].

A non-randomized retrospective study of 351 patients evaluated preemptive administration of prophylactic anticoagulants versus therapeutic anticoagulants. The average age of the participants in

the study was 64.7 years old, with a distribution of 58.6% male and 41.4% female. A 93.5% of the sample group were on enoxaparin, 14.8% on heparin, and some were on both medications. The results showed a difference in in-hospital mortality among COVID-19 patients and those with significantly elevated C-Reactive protein (CRP) levels (>200 mg/L) [122]. The most common causes of death between patients were refractory acute respiratory failure with hypoxia, shock, and multi-organ system failure. Thrombosis could point the etiology of death, but it could also be attributed to direct viral end-organ damage or to a viral systemic inflammatory response syndrome. The study showed no prevention in the progression of disease with a therapeutic dosage of anticoagulation [122].

The risk of mortality was 2.3-fold higher for patients on therapeutic anticoagulants compared to the ones just taking them prophylactically, after controlling other variables. Even for patients with elevated CRP levels, there was no clinical improvement in administering preemptive therapeutic anticoagulation. The study recommends considering the risks and benefits for the patient, as well as a cautious approach in the use of anticoagulation in the management of COVID-19 patients who require them [122].

Convalescent plasma

In an uncontrolled study of 5 critically ill patients with COVID-19, who were receiving mechanical ventilation, antivirals, and methylprednisolone with an age range of 36–65 years old, the use of convalescent plasma containing neutralizing antibody resulted in clinical improvement of symptoms, ARDS resolution, and weaning of mechanical ventilation, with an increase in the levels of SARS-CoV-2 antibodies [129].

Monoclonal antibodies

Specific neutralizing monoclonal antibodies, either against receptor-binding domain of spike protein or those binding to ACE2, could effectively block SARS-CoV-2 virus entry. Several monoclonal antibodies have yielded promising results in neutralizing SARS-CoV and MERS-CoV *in vitro* or *in vivo* [130].

Anti-malarial

The combination of Hydroxychloroquine (HCQ) (600 mg/day)/Azithromycin (500 mg/day) has been