ORIGINAL RESEARCH PAPER
Volume - 12 | Issue - 08 | August - 2023 | PRINT ISSN No. 2277 - 8179 | DOI : 10.36106/ijsr
INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

EARLY MECHANICAL VENTILATION IN A CASE OF SEVERE COVID-19 WITH ACUTE RESPIRATORY DISTRESS SYNDROME

Internal Medicine

Dr. Jessica Pereira MD, Consultant Physician, Galaxy Hospital, Duler, Goa
Dr. Bernadette Prabhu Dabholkar MD, Consultant Anesthetist, Galaxy Hospital, Duler, Goa

ABSTRACT

This is a case of a 41 year old male patient who presented in the last week of April 2023 with severe respiratory distress and was found to be Covid-19 positive. He was put on early mechanical ventilatory support and treated with steroids, antibiotics, Remdesivir and Tocilizumab and had a successful recovery. This case is presented to highlight that even though Covid-19 is no longer considered a global emergency by the World Health Organisation, we should not let our guard down as early detection and prompt action can save patients even with severe Covid-19.

KEYWORDS

Covid-19, respiratory distress, ARDS, mechanical ventilation, Tocilizumab

INTRODUCTION

Covid-19 was initially recognised in Wuhan, China, in December 2019[1], and was a devastating pandemic till May 2023. On 5th May 2023, the WHO declared that Covid-19 is no longer a global health emergency. Covid-19 is caused by the Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2)[1]. Severe Covid-19 represents the viral pneumonia leading to Acute Respiratory Distress Syndrome (ARDS). Covid-19 infection can be confirmed by rapid antigen tests or by detection of viral RNA in nasopharyngeal secretions using a specific RT-PCR test[1]. Management includes adequate ventilation, steroids , immunosupressants and optimisation of therapy for comorbidities.

CASE REPORT

A 41 year old male presented with a history of cough for 10 days, which had increased in severity over 4 days andfever for 3 days with fatigue and body ache during this period. He complained of breathlessness since the past 2 days, with progressive worsening on the day of presentation. He had no chest or abdominal pain and no jaundice, rash or bleeding tendencies. He was a diabetic for the past 2 years on oral hypoglycaemic agents with a fair control of blood sugars. He had no addiction to either alcohol or drugs and was a non-smoker. The patient had taken Ciprofloxacin 500 mg BD for 2 days and Paracetamol for fever prior to presentation. The patient had received 2 doses of the Covishield vaccine in 2021.

The patient was hemodynamically stable at presentation and respiratory rate of 26/min. His oxygen saturation was 84% on room air. Besides a few scattered crepitations on auscultation of the lung fields, the rest of the systemic examination revealed no abnormalities. A random blood sugar check showed a value of 397 mg % and his electrocardiogram tracing was normal.

Within half an hour his respiratory distress worsened to a respiratory rate of 36 to 38/min and saturation dropped to 76% on room air and 86% on a facemask at 8L of oxygen.

The patient was admitted in the intensive care unit. He was initiated on non-invasive ventilation in the continuous positive airway pressure (CPAP) mode immediately after admission in ICU. With an Fi02 of 100%, the oxygen saturation came up to 91 to 93% but the respiratory rate remained around 34 to 36/min.

Prior to presenting to our hospital the patient had already done blood investigations on the previous day. These included hemoglobin and total counts which were normal and platelet count of 1.1 lakh / cu mm. The smear for malarial parasites and rapid kit tests were negative as was the dengue NS1 antigen and IgM antibody. A WIDAL for typhoid and rapid antigen test for Covid-19 were also negative. A urine sample examined revealed sugars 4+ , no pus cells or albumin. HbA1c was 7.3%. Renal and liver function tests were within normal limits except for a raised SGOT and SGPT of 102 and 158 IU/L respectively.. An RTPCR for Covid-19 had been sent but the report was awaited.

After being admitted in the ICU an urgent arterial blood gas (ABG) analysis and bedside chest radiograph were done. The ABG was suggestive of hypoxia and chest radiograph showed bilateral fluffy opacities consistent with acute respiratory distress syndrome (ARDS). [FIGURE 1]

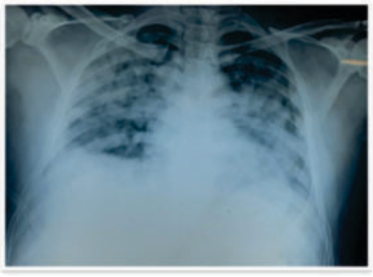

Figure 1 : Chest Radiograph (AP) Showing Bilateral Fluffy Opacities

A urine sample tested negative for the presence of ketones.The INR was 1.

As the patient had respiratory distress even after a trail of non-invasive ventilation and a chest radiograph suggestive of ARDS, the patient was intubated (within 2 hours of admission). He was sedated and curarized. The ventilator was set to volume-controlled ventilation (VCV) mode with 100% FiO2 and a positive end expiratory pressure (PEEP) of 7 cm H2O. Post intubation, the Sp02 was 93 to 94% and blood pressure was maintained. The chest radiograph was repeated after intubation which showed worsening of the existing shadows over all lung fields [FIGURE 2]. Based on this, the PEEP was increased to 9 cm H2O and sp02 maintained at around 95 to 96%.There was improvement in pO2 on ABG post intubation. Blood and endotracheal aspirate cultures were collected.

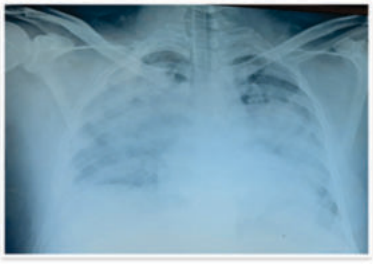

Figure 2 : Chest Radiograph (AP) After Intubation Showing Worsening Of Existing Lung Shadows To All Lung Fields

The patient was started on IV methylprednisolone 40mg IV 8 hourly, LMWH (Enoxaparin) 0.6 ml SC 12 hourly, antibiotics : Azithromycin + Piperacillin-Tazobactum, antivirals : Oseltamivir, mucolytics, insulin infusion and other supportive measures. At this time, there was no confirmatory positive report of Covid-19 and hence the patient was

being treated along the lines of any severe viral pneumonia.

The patient's vital parameters were stable all night. However by 6am next day, the Sp02 started dropping to 75 to 80% even on maximal ventilator support. The patient had profuse secretions and despite repeated suctioning and nebulisations there was no improvement. He was also beginning to develop visible respiratory distress. It was decided to perform an urgent tracheostomy. Even after he was tracheostomised, sP02 was around 85 to 88%. The antibiotics were upgraded to IV Teicoplannin and Meropenem.

At around 10 am, the RTPCR report for covid-19 was obtained which was positive! A blood sample was collected for CRP, ferritin, d-dimer, IL-6 and procalcitonin levels. The CRP value was 435mg/L (normal: 0 to 6 mg/L), the rest of the reports were expected after 2 days. The patient was started on IV Remdesivir (200mg IV loading dose on day 1, followed by 100mg IV once a day for 4 days). Considering the patient to be in cytokine storm in view of his deteriorating status, a single dose of IV Tocilizumab (400mg IV) was given. Around 5 hours after this dose, Sp02 improved to 98 to 99% and remained stable all night.

The chest radiograph was repeated the next day (day 3) [FIGURE 3].

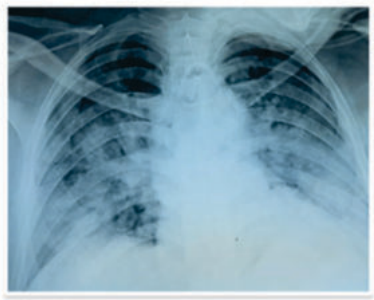

Figure 3 : Chest Radiograph (AP) After Tocilizumab Showed Improvement (Day 3)

We performed serial arterial blood gas analysis and were able to gradually reduce the FiO2 to 45% and PEEP to 3cm H_2O over the next 24 hours. The patient tolerated this reduction in ventilatory settings very well, without any hemodynamic compromise during this time. However, our efforts at further weaning were hampered by a sudden drop in blood pressure to ~ 70 mmHg (systolic) on the evening of the fourth day. There was no improvement after a fluid challenge of 1 L.A central line was passed via right internal jugular vein and further fluids given to achieve adequate central venous pressure. Despite this, the patient required both Dopamine and Noradrenaline infusions to raise the pressure up. These were carefully titrated over 2 and half days (day 4, 5 and 6) and stopped on the 6th day.

Over these days we repeated a few blood investigations and also obtained the pending reports. The creatinine was normal, SGOT and SGPT were mildly raised, total counts 13,400 /cu mm and CRP had reduced to 14.8 mg/L. 2d ECHO was normal with an ejection fraction of 60%. A sonography of the abdomen showed only a fatty liver. Ferritin was 1655ng/ml (normal: 30 to 400 ng/ml). D-dimer was raised to 3.87 ug/ml (normal: < 0.5 ug/ml) and IL-6 to 66.3 pg/ml (normal: < 7 pg/ml). Procalcitonin was marginally high at a value of 0.67 ng/ml (normal: < 0.5 ng/ml).

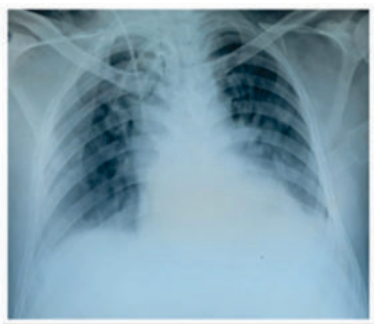

Figure 4 : Chest Radiograph (AP) Showed Good Clearing Of The Lung Opacities (Day 7)

Over the course of the 6th day, we reduced the sedation and started alternating the patient on volume controlled ventilation vs. synchronised intermittent mandatory ventilation (SIMV) modes. The next day (day 7) we put him on CPAP mode which the patient tolerated well with PEEP 0.. Sp02 did not drop below 95%. The chest radiograph on day 7 showed good clearing of the lung opacities. [FIGURE 4]

The patient was put on a T-piece at 6 L of oxygen for a few hours on the 8th day. After this, he was given a trial of spontaneous breathing on room air. He had no respiratory distress or drop in saturation. He was shifted out of the ICU. Meropenem and Teicoplannin were stopped and antibiotics were downgraded. Chest physiotherapy was given. The central line was removed. The patient was mobilised on the same day.

On the 9th day the tracheostomy was partially closed and by the next day (day 10) fully closed and the tube was removed. The patient started walking with support on the 10th day. We further reduced the dose of the steroids. Anticoagulants were converted into oral form, ie : Rivaroxaban 10mg once a day. Over the next 2 days (day 11 and 12) medications were reduced further.

A HRCT scan of the thorax done on the 11th day revealed sub-pleural dependant atelactasis in both lower lobes. There were no cavities, nodules, bronchiectasis or fibrosis. Due to the rapid progression of the patient's illness we were unable to shift the patient for scan earlier.

The patient was able to walk without any support by the 12th day and he was discharged the next day! He was advised oral medications at discharge: Methylprednisolone in tapered doses over 14 days, Rivaroxaban 10 mg once a day for 1 month, antibiotics for 5 days, multivitamins, hepato-protective agents and oral hypoglycemic agents plus insulin for blood sugar control.

The patient was followed up over 3 months in May,June and July 2023. At his first follow up visit 10 days after discharge he reported having hoarseness of voice which gradually returned to normal with speech therapy. However, he had a good exercise tolerance and no other symptoms.. Over 3 months, the patient had no complications, he ensured strict sugar control and was doing well without any residual effects of a severe Covid-19 infection.

DISCUSSION

Covid-19 was initially recognised in Wuhan, China, in December 2019[1,2,3,5,6,10,11,12], and was a devastating pandemic that took millions of lives. On 5th May 2023, the WHO declared that Covid-19 is no longer a global health emergency of concern. Covid-19 is caused by the SARS-CoV-2 virus[1,2,3,4,5,10]. It is spread by droplets generated by sneezing or coughing[2]. It affects mainly the respiratory system with minor involvement of other organs[3]. Patients are either asymptomatic or present with symptoms such as sneezing, coughing, breathlessness, fatigue and fever, approximately 2 to 4 days following infection[4,10]. Infection can be confirmed by rapid antigen tests or by detection of viral RNA in nasopharyngeal secretions using a specific RT-PCR test[1].

ARDS is a serious complication of Covid-19 with a high mortality rate[4,6,10,11,12] and requires early recognition and prompt comprehensive management[1,2,3]. Typical or non-Covid-19 ARDS is diagnosed when a patient meets the Berlin 2012 ARDS diagnostic criteria[1,3,4] of (i) acute hypoxemic respiratory failure; (ii) presentation within 1 week of worsening respiratory symptoms; (iii) bilateral airspace disease on chest radiograph, computed tomography or ultrasound that is not fully explained by effusions, lobar or lung collapse, or nodules; and (iv) cardiac failure is not the primary cause of acute hypoxemic respiratory failure. The differences in Covid-19 ARDS include (i) a later onset at around 8 to 12 days compared to one week in the Berlin criteria[1,2,3,4] ; (ii) normal or high lung compliance[2,3,4,8,9] compared to classical ARDS. The rest of the criteria are similar. Our patient satisfied all these criteria. Covid-19 ARDS was divided into 3 categories based on oxygenation index on PEEP≥5 cm H_2O : mild (200mmHg≤PaO_2/FiO_2<300mmHg) / moderate (150mmHg≤PaO_2/FiO_2<200mmHg) / severe (PaO_2/FiO_2<150mmHg)[3,4].

Monitoring the patient's respiratory rate and SpO_2 can help to judge the clinical progress and allows early recognition of ARDS. Any patient who has a respiratory rate ≥ 30 breaths/min or $SpO_2 \leq 92\%$[1] will require further evaluation.

The basic pathology in ARDS is diffuse alveolar damage[1,4] in the lung with hyaline membrane formation in the alveoli in the acute stage, ad

oedema and then fibroblast proliferation in the organising stage[1]. Induction of a cytokine storm is believed to be the inciting factor[2], with the release of pro-inflammatory cytokines[4,10,11], such as IL-1, IL-6, IL-7, IL-10, granulocyte-colony stimulating factor, tumor necrosis factor α etc.This increase of inflammatory cytokine levels is related to the severity and prognosis of the disease. There is injury mainly to the alveolar epithelial cells[4] and endothelial cells are less damaged with less exudation[3] .Coagulation dysfunction is also common, and is detected by elevated D-dimer levels[1], and in severe cases there can be microvascular thrombosis[1,4].

Covid-19 ARDS outcomes appear worse than ARDS from other causes[1] .Poorer outcomes are seen in the elderly; patients with comorbidities[1,3,4,6,10] such as hypertension, cardiovascular disease and diabetes mellitus, kidney disease; and raised D-dimer levels[1,4].

Laboratory investigations include leucocyte counts, D-dimer, SGOT, SGPT , lactate dehydrogenase, C-reactive protein (CRP), Interleukin 6 and procalcitonin levels, some or all of which are raised in ARDS[4]. Radiologically, there are dense bilateral multifocal patchy shadows or ground-glass opacities with consolidations which may evolve over time to form fibrotic bands[1,3,4,6].

Ventilation is the most important strategy in treating Covid-19 ARDS[1,4,8,9]. Prone ventilation (at least 16 hours/day[8]) appears to be of benefit as it improves aeration of the lung[1,5,6,7,9] and V/Q inequalities[8,9] as collapsed alveoli in dependent lung zones are recruited[9]. High flow nasal oxygen is preferred for moderate but can be safe in some severe patients.Non invasive ventilation may also be used. The timing of invasive mechanical ventilation is very important. The lung protective ventilation strategy used in Covid-19 ARDS differs from typical ARDS by involving a higher tidal volume target upto 8mL/kg and lower positive end expiratory pressure levels[1,4,9] while the reverse is often used in non-Covid ARDS[1,4]. The aim should be to mitigate ventilator induced ling injury[8].Volume control remains the most common ventilation mode during the initial days[8]. Applying PEEP mitigates the risk of atelectotrauma by preventing the cycling opening and closing of unstable alveoli and improving lung compliance by increasing the number of open alveoli[8,9].Median PEEP used in studies was ≥10 cmH_2O[8]. PEEP above a certain level might be harmful by increasing dead space and reducing venous return and cardiac output leading to reduced oxygen delivery[9]. Neuromuscular blockade is advised for all intubated patients[1,3] to improve patient-ventilator synchrony[8]. Extracorporeal membrane oxygenation is reserved for rescue[1,5] in selected patients with refractory hypoxia not responding to conventional ventilation[8].

Adjunctive measures include corticosteroids[1,4,5,12],anticoagulants, antivirals like Remdesivir [1,2,11] or immunosuppressive therapy like Tocilizumab[10,11] and fluid resuscitation[7,12]. Methylprednisolone[3] or dexamethasone[11] are the preferred steroids and shorten duration of invasive mechanical ventilation and lower mortality by reducing inflammation and fibrosis[3]. Remdesivir is a nucleoside analog that inhibits RNA-dependent RNA polymerase[12]. Treatment with Remdesivir was associated with lower mortality, lower rate of ICU admission, and shorter time of hospitalization if used early in the disease before the onset of the cytokine storm[12]. However, it may also be used in advanced disease with symptom onset upto 10 days prior.Tocilizumab is a humanized monoclonal antibody drug[10] which selectively and competitively binds to solubles expressing the IL-6 receptor (IL-6) and then blocking the signalling caused by IL- 6[10]. 4–8 mg/kg is administered a single dose which may be repeated as required[10]. Tocilizumab has reduced mortality and improved clinical manifestations[10,11]. The optimal time to prescribing it is in beginning of inflammation and at first signs of dropping O_2 saturation[10]. In the initial stages of the pandemic, Hydroxychloroquine[10], Azithromycin[10], Lopinavir–Ritonavir[1,2,10] plus subcutaneous interferon□β 1b[1,10] were tried but over time their benefit was doubtful and use gradually decreased.

CONCLUSION

With this case report, we can conclude the following about severe Covid-19 cases:

1) If a patient is not maintaining oxygen saturation on non-invasive ventilation, invasive ventilation shouldn't be delayed and can prove to be lifesaving in patients with ARDS. 2) Tracheostomy can be done to reduce dead space if the patient is de-saturating on maximal ventilator support. 3) Start weaning from the ventilator as early as possible (as per patient's tolerance. 4) Use Tocilizumab early in severe and progressive disease (within 24 to 48 hours). 5) CT scans are not a must prior to initiating treatment. Severity can be judged clinically. 6) Anti-fibrotic agents are not routinely indicated in all cases of severe Covid pneumonia. They should be started only if there is significant fibrosis on the CT scan of the thorax and not only for a consolidation or ground glass opacities.

Early identification of ARDS and treatment helps to improve prognosis and reduce mortality.

REFERENCES

1. Gibson P, Qin L, Puah SH. COVID□19 acute respiratory distress syndrome (ARDS): clinical features and differences from typical pre□COVID□19 ARDS. Med J Aust. 2020 Jul; 213(2): 54–56.e1. doi: 10.5694/mja2.50674
2. Aslan A, Aslan C, Zolbanin NM, Jafari R. Acute respiratory distress syndrome in COVID-19: possible mechanisms and therapeutic management. Pneumonia. 2021 Dec 6;13(1):14. doi: 10.1186/s41479-021-00092-9
3. Li X, Ma X. Acute respiratory failure in COVID-19: is it "typical" ARDS? Crit Care 24, 198 (2020). doi: 10.1186/s13054-020-02911-9
4. Krynytska I, Marushchak M, Birchenko I, Dovgalyuk A, Tokarskyy O. COVID-19-associated acute respiratory distress syndrome versus classical acute respiratory distress syndrome (a narrative review). Iran J Microbiol. 2021 Dec; 13(6): 737–747. doi: 10.18502/ijm.v13i6.8072
5. Park MH, Kim AJ, Lee M, Kim YS, Soo J. Case Report of Patients with Acute Respiratory Distress Syndrome Caused by COVID-19: Successfully Treated by Venovenous Extracorporeal Membrane Oxygenation and an Ultra-Protective Ventilation. Medicina 2020, 56(11), 570; doi: 10.3390/medicina56110570
6. Ng M K, Ngo J, Patel A, et al. (May 21, 2020) A Case Report of Rapidly Lethal Acute Respiratory Distress Syndrome Secondary to Coronavirus Disease 2019 Viral Pneumonia. Cureus 12(5): e8228. doi:10.7759/cureus.8228
7. Bellani G, Pham T, Laffey J. Missed or delayed diagnosis of ARDS: a common and serious problem.Intensive Care Medicine volume 46,1180–1183 (2020)
8. Kondili E, Makris D, Georgopoulos D, Rovina N, Kotanidou A, Koutsoukou A. COVID-19 ARDS: Points to Be Considered in Mechanical Ventilation and Weaning. J Pers Med. 2021 Nov; 11(11): 1109. doi: 10.3390/jpm11111109
9. Lepper P, Muellenbach R. Mechanical ventilation in early COVID-19 ARDS. eClinicalMedicine volume 28, 100616, November 2020. doi:https://doi.org/10.1016/j.eclinm.2020.100616
10. Samaee H, Mohsenzadegan M, Ala S, Maroufi S, Moradimajdc S. Tocilizumab for treatment patients with COVID-19: Recommended medication for novel disease. Int Immunopharmacol. 2020 Dec; 89: 107018. doi: 10.1016/j.intimp.2020.107018
11. Salama C, Han J, Ph.D, Yau L, Reiss W et al. Tocilizumab in Patients Hospitalized with Covid-19 Pneumonia. N Engl J Med 2021; 384:20-30. Jan 7, 2021.doi: 10.1056/NEJMoa2030340.
12. Boglione L, Dodaro V, Meli G, Rostagno R, Poletti F et al.Remdesivir treatment in hospitalized patients affected by COVID-19 pneumonia: A case-control study. JMedVirol. 2022 Aug;94(8):3653-3660. doi:10.1002/jmv.27768