COVID 19; challenges to critical care and lessons learnt

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The WHO declaration on 11th March 2020 of COVID 19 as a global pandemic and the forecast by Imperial College, London of 20,000 expected deaths in UK, there was intense pressure on the intensive care units in the UK to increase their capacity and services. This meant that gaining new knowledge to manage this disease with constantly changing strategies was required and was a challenge. The discussion is on the experience gained by the author during the pandemic in UK.

Keywords: COVID 19; ARDS; prone ventilation; PPE; coagulopathy; non-invasive ventilation

Introduction

On the 11th March 2020 WHO declared COVID 19 as a global pandemic following 114 countries reporting cases.[1] As per a model forecasted by Imperial College, London estimations were that about 20,000 deaths were expected in the UK, provided optimal health care can be delivered. It was predicted that the number of deaths could be more than 200,000 in a worst-case scenario mounting an intense pressure especially on ventilated beds.[2] Intensive care units all over the country took over this herculean task in terms of increasing their capacity and services to face the forecasted demand in service. This also involved gaining knowledge in best management strategies for critically ill COVID 19 pneumonitis caused by the SARS-CoV 2 virus. This article focuses about the experience gained during the pandemic in the UK where the author works.

Increase in critical care capacity and services

Level 3 intensive care beds were increased overnight by utilising anaesthetic machines as ventilators. Theatre recovery area was converted to manage ventilated patients. As the patient number rose more ventilated beds were recruited quadrupling the ventilated bed capacity in critical care. However, this led to the problem of running 3 intensive care units in physically distant locations. This was mitigated by converting a large medical ward to manage ventilated patients and relocating all the resources to create 2 ICUs. More ICU ventilators, infusion pumps, drugs, dialysis machines and other equipment were requested from NHS.

Theatre work was limited to emergency operations, maternity and trauma cases stopping all elective work. This gave the opportunity to relocate theatre staff, surgeons, anaesthetists, and trainees to man the ICUs. Intensive care duty hours were changed to 12 hourly sessions with night residential consultant cover. General anaesthetic consultants were invited to join ICU rota after upskilling to work together with intensivists. Trainees who had recent ICU experience were identified across the trust and redeployed to work in critical care areas. Other consultant colleagues who wanted to help facilitated communication with families while the patients were in ICU since no visitors were allowed. A real time video calling system was used to communicate with relatives while maintaining patient confidentiality.

Upskilling

An upskilling leader was appointed and both medical and non-medical staff were given the opportunity for a rapid brainstorm about management of ventilated ICU patients. This was achieved as a series of lectures, webinars, and hands on experience. SOPs created about management for ventilated COVID patients (includes PPE usage, donning and doffing, management of ARDS, intubation and extubation of COVID patients, transfer policy, referring transferring for ECMO, prone ventilation) and

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relevant learning materials were uploaded to the trust intranet.

PPE (Personnel Protective Equipment)

Usage of correct PPE with donning and doffing was a challenging and a daunting task. Only FFP 3 masks were allowed in the critical care setting. This was challenging at first due to rapid surge on demand for FFP masks. However critical care areas had an uninterrupted supply. Despite the difficulty in performing daily work under PPE, all members of the critical care team were committed to provide best patient care while keeping themselves safe. This was of utmost importance as nursing all these patients in rooms with negative pressure ventilation was not practically possible.

New knowledge and experience

Different phenotypes

Very soon it was evident to us that all patients with COVID 19 pneumonitis would not fit in to "typical ARDS" model. This contradicted the suggestion from surviving sepsis campaign that "mechanically ventilated patients with COVID-19 should be managed similarly to other patients with acute respiratory failure in the ICU".[3] Often, in most patients the lung compliance was good during the early stages of the disease. Early and repeated prone ventilation was favoured for most patients however some did not do well with early prone ventilation. Fluid restriction and judicious diuretics administration did not help with ventilatory strategies in some and negatively impacted on the kidney functions. We now know, as described by Prof Gattinoni that there are 2 phenotypes to the disease (type L and H) and clinical behaviour depends on the evolution of the disease.[4] Type L phenotypes were with low elastance, nearly normal compliance, low V/Q ratio, low hypoxic pulmonary vasoconstriction, low lung weight with subpleural ground glass densities seen often only in chest CT scans with low lung recruitability. These patients present as "silent hypoxaemic" with low CO_2 levels and are at high risk of developing "Patient Self-Inflicted Lung Injury" (PSILI) due to high negative intrathoracic pressures maintaining spontaneous ventilation. Type H phenotypes were associated with opposite features to the above with typical ARDS lung features which developed due to disease progression and worsening PSILI.

Coagulopathy

It was experienced that the disease is highly prothrombotic leading to DVTs in multiple areas despite being on prophylactic anticoagulation with mechanical calf compression devices. We had problems in continuation of renal replacement therapy due to clotting of RRT circuits and vascular catheters. CT chest performed in some patients confirmed blood clots related to invasive lines with multiple pulmonary emboli. We now know that despite prophylactic anticoagulation COVID-19 pneumonitis is associated with life-threatening thrombotic complications.[5] The pathophysiology of the viral infection leads to micro and macrovascular thrombi generation in various organs. Higher anticoagulation targets than in usual critically ill patients were suggested and accordingly in our trust tinzaparin 125u/kg was used for all ICU patients for prophylactic anticoagulation unless contraindicated.

Cytokine storm

Some patients developed cataclysmic hyperpyrexia episodes leading to multiorgan shut down and sudden death. The pathophysiology of the disease clearly describes a state of "cytokine storm" involving severe SIRS status provoked by raised IL1, IL6, G-CSF, TNFα and others.[6] Some of such patients showed features of secondary haemophagocytic lympho histiocytosis (HLH) with raised ferritin levels.[7] This was not initially well recognised but as more cases were reported we have used daily serum ferritin levels to monitor patients at risk. Such patients were discussed with rheumatology and high dose methyl prednisolone or IL-1 inhibitors were used as treatment.[7,8]

Patient characteristics

More of non-white, middle aged, male patients with high BMI were noted to have complicated disease requiring critical care admission. This was later confirmed by an ICNARC report that mean age of patients treated in critical care as 60.6 for white ethnicity and 55.6 for non-white ethnicity.[9] About 70% from both ethnicities were male patients and had BMI of >25. The outcome at the end of critical care showed 41% death rate for white ethnicity and 45% for non-white ethnicity. Broader analysis is required to assess the clinical significance of above figures.

Antibiotics
On admission to the ICU empirical antibiotics were added to cover superadded bacterial infections. The antibiotics of choice were co-amoxiclav or piperacillin/ tazobactam with clarithromycin or azithromycin. Trapped sputum from the endotracheal suctioning was sent for bacterial cultures as a part of the septic screening on admission and antibiotics were guided as per culture results. As the number of patients increased, we got the opportunity of having procalcitonin levels measured to guide the antibiotic usage.

Awake Prone Ventilation (APV)
APV was used in all patients with mild/ moderate ARDS who were not intubated. Oxygen was supplemented with either non-invasive ventilation (NIV), nasal high flow oxygen (NHFO) or as non-rebreathing face mask devices. APV was encouraged in all ward patients with supplemented oxygenation. Benefits of awake prone ventilation could be explained by counteracting the pendelluft effect in the lung which increases regional lung stress and strain even in the absence of large tidal volumes.[10,11] It was not clear to us whether APV has delayed the overall outcome in the critical care setting. However, this practice was continued in respiratory wards as tolerable by patients. The sustainability of the beneficial effects of this intervention needs further evidence.

NIV
At the beginning of the pandemic NIV or NHFO therapy was not considered for deteriorating patients due to the risk it carries to health care workers by high risk of aerosol generation. Lack of negative pressure chamber rooms also added to withholding these interventions. Patients were manged in wards and were considered for early intubation as hypoxia worsened. However, as more evidence emerged in the safe use of NIV and NHFO with appropriate PPE minimising the risk for health care workers, these interventions were offered to deteriorating patients.[12] The overall outcome whether they prevented intubation and improved patientmortality or morbidity needs further evaluation.

Tracheostomy
Tracheostomy was offered to patients who required prolonged weaning from mechanical ventilation. However, this was not considered until 14 days had passed since admission to ICU with a negative swab test from endotracheal aspirate. Discussions were made with the relatives, physiotherapy, and ENT teams to decide the optimal timing for the tracheostomy. Those patients who were benefitting from prone position ventilation and high PEEP were delayed from tracheostomy due to safety reasons. All tracheostomies were performed in dedicated operation theatres and no bedside tracheostomies were done despite recognising that bedside procedures are not contraindicated.[13,14] A careful weaning plan which led to successful decannulation was carried out involving respiratory physiotherapists, swallowing and language team and dieticians.

Neurological manifestations
A spectrum of neurological manifestations was noted during the recovery from ARDS. More recovery time was required for patients who were on continuous infusions of morphine and midazolam which was the choice of sedation over propofol and remifentanil due to drug shortages and suspected propofol related infusion syndrome. These neurological manifestations ranged from profound neuromuscular weakness, cerebral infarctions, cerebral haemorrhages, seizures, encephalopathy, and Guillain-Barre syndrome among many others.Many patients developed a degree of delirium during recovery which responded to pharmacological and non-pharmacological interventions. Some required bridging therapy with buprenorphine to prevent acute opioid withdrawal following sedation hold. It is believed now that the virus can invade the nervous system by several routes giving rise to variety of neurological manifestations.[15,16,17,18] However more studies are imperative to understand the CNS effects of the virus. Some severe neurological manifestations (severe intracranial bleeding) contributed to treatment withdrawal and end of life care decision making.

Acute Kidney Injury (AKI)
Several ventilated patients required renal replacement therapy (RRT) for AKI. It is postulated the mechanism for AKI in COVID patients could be multifactorial.[19,20] AKI was associated with high rates of mortality. The practice of judicious usage of diuretics and targeting negative fluid balance for ARDS was soon changed in our unit following consultations with the nephrologists as it was evident that these interventions were worsening the AKI. It was challenging to sustain continuous supply of RRT

fluids, machines, and circuits to meet the demand for RRT. As the patients were recovering from the disease AKI slowly resolved following a polyuric phase. As mentioned earlier blockage of the RRT circuits and clotting of vascular lines were noted before high dose prophylactic anticoagulation.

New trials

Our critical care unit was enrolled for 2 main trials focussed on COVID management. Namely, the "RECOVERY" trial (Randomised Evaluation of COVID 19 Therapy)[21] and the "REMAP-CAP" trial (Randomised, Embedded, Multi-factorial, Adaptive Platform Trial for Community-Acquired Pneumonia).[22] Both the trials have adaptive platforms and are focused on investigating multiple interventions. RECOVERY Trial is investigating on the effectiveness of,

- antivirals (lopinavir-ritonavir)
- low-dose dexamethasone
- hydroxychloroquine
- azithromycin
- tocilizumab (Interleukin 6 inhibitor)
- convalescent plasma therapy.

The REMAP-CAP is investigating on.

- antiviral therapy
- hydroxychloroquine
- corticosteroids (no steroids or fixed duration hydrocortisone for 7 days or shock-dependent hydrocortisone while the patient is in septic shock)
- immune modulators [no immune modulation or interferon-beta-1a or anakinra (interleukin-1 receptor antagonist) or sarilumab (IL-6 receptor antagonist)]
- vit c (no vitamin C or vitamin C 50 mg/kg IV every 6 hours for 16 doses)
- convalescent plasma
- anticoagulation (local standard venous thromboprophylaxis or therapeutic anticoagulation with intravenous unfractionated heparin or subcutaneous low molecular weight heparin)
- antibiotics [(ceftriaxone + macrolide or moxifloxacin or levofloxacin) or (piperacillin-tazobactam + Macrolide) or (ceftaroline + macrolide) or (amoxicillin-clavulanate + macrolide)].

Some of the intervention domains of both the trials were suspended by the Medicine and Health care products Regulatory Agency (MHRA) due to safety reasons. Remdesivir an antiviral used against Ebola virus has been approved by the MHRA to be used in selected patients following application of strict criteria. Many of the above drugs are new to critical care practice and help from other specialists (especially rheumatologists who use immunomodulators in their practice) were much helpful.

Wellbeing management

The disease not only challenged the critical care service in UK, it has mounted an immense pressure on the critical care workers. Prolonged working hours, increased workload, reduced breaks, stepping in to roles beyond normal work pattern, sustaining service with drug and equipment shortages, performing routine tasks under PPE, constantly being vigilant about PPE usage, risk of getting infected, effects of lockdown, witnessing increased daily deaths in critical care, not seeing rapid recovery of patients, lack of treatments or interventions for the disease, witnessing the death of colleagues and loved ones all added to a highly stressful job. However, it was amazing to witness the resilience, motivation, team spirit and stepping into roles with quick adaption from all levels of critical care staff. Staff were approached by wellbeing management teams and psychological help was provided. But the concealed damage that was caused, if any, needs careful evaluation.

Future

COVID 19 has challenged the critical care service globally in terms of resources, personnel, and management strategies.[23] Scientific community was flooded with low quality information and anecdotal treatment modalities. Critical care community awaits eagerly for high quality evidence-based guidance which would make a difference in the management of critically ill COVID 19 patients. Is this something achievable soon? Only time could tell.

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