

COVID -19 Challenges

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Chunyao Wang

Medical Intensive Care Unit
Peking Union Medical College
Hospital
China

xiaowudie@outlook.com

Personal Experience With Severe COVID-19 After 66 Days in Wuhan

COVID-2019 has become a worldwide pandemic. After working in Wuhan as intensive care physicians for 2 months, we have gained significant experience and would like to share our experience about daily care and supportive therapies for severe COVID-19 patients with our colleagues all over the world. The goal is for all of us to gain victory over COVID-19.

Oxygen Therapy: Divided by Phenotypes or Stages?

According to the SSC guidance (Alhazani et al. 2020), respiratory support for COVID-19 patients included non-invasive support and invasive mechanical ventilation. As mentioned in Gattinoni et al. (2020), COVID-19 was divided into two different phenotypes factitiously. For type L, the respiratory mechanics showed high compliance, low V/Q ratio and was less recruitable, while type H showed low compliance and was more recruitable. Thus, oxygen therapy, according to the author, was different in these 2 types: for type H, the strategy was similar to severe ARDS, while for type L, the main principle was to maintain adequate CO₂ level rather than to facilitate low tidal volume method, or just follow the ventilation strategy for patients with interstitial lung disease, since the CT scan showed interstitial lesions.

However, we noticed in our daily practice that the two phenotypes may be just different stages of the same disease. Since we worked in a special ICU for COVID-19, we admitted patients from other general wards and high dependency units. After reviewing the CT scan in other teams, we noticed the process from type L to type H. Daily images other than x-ray should be performed to access the exact process.

Lung ultrasound, including the PLAPS (posterolateral alveolar and/or pleural syndrome-point (Lichtenstein 2016), might be a useful choice. According to Rouby et al. (1998), the learning curve of the lung ultrasound seemed to be flat, and the skill was easily grasped, thus it was quite suitable for daily monitoring during the outbreak of such a disaster like COVID-19.

We agreed to utilise different oxygen therapies for different radiological manifestations in different stages rather than different phenotypes of COVID-19, and bedside lung ultrasound might be an alternative to CT scan for daily monitoring of COVID-19 process.

Intubation and ECMO: More Aggressive, More Efficient?

Almost all the guidance about the treatment of severe COVID-19 recommended unhesitating alteration from non-invasive oxygen therapy, such as high flow nasal cannula or non-invasive ventilation, to intubation. However, we noticed the median days between onset of respiratory failure to intubation is about two weeks in our patients, while the duration of NIV usually exceeded 10 days. The exact indication of intubation was not published as a consensus, but we suggested less than 24 hours for investigation. If no improvement was

observed within 24 hours, intubation should be performed immediately with adequate personal protective equipment. According to one meta-analysis in the period of SARS (Tran et al. 2012), after intubation, the risk of airborne spreading by sputum aspiration decreased, and OR dropped from 13.8 to 0.6.

After intubation, though some centres suggested not routinely performing recruitment manoeuvre and prone ventilation in COVID-19 patients, we found improvement of oxygenation after prone ventilation in patients with consolidation in dependent zones. Xu et al. (2018) reported in patients with acute exacerbation of interstitial lung disease, prone ventilation could also improve oxygenation. For interstitial lung disease-mimic type L phenotypes, prone ventilation might be also a choice.

However, we titrated PEEP by compliance rather than oxygenation, and found some patient's optimal PEEP was 4-6cmH₂O, although recruitable. Thus, daily monitoring of respiratory mechanics was suggested in patients with intubation, and if available, oesophageal pressure and transpulmonary pressure should be monitored, since we also noticed cases of pneumothorax could occur even when tidal volume was less than 350 ml.

According to ELSO guidance (Bartlett et

al. 2020), when meeting one of the following 3 criteria: $\text{PaO}_2/\text{FiO}_2$ (P/F) < 80 mmHg for more than 6 hours, P/F < 50 mmHg for more than 3 hours or pH < 7.25 with $\text{PaCO}_2 \geq 60$ mmHg for more than 6 hours, ECMO was recommended. In our practice, we noticed the ECMO was also delayed according to those criteria. Thus, the weaning of ECMO seemed impossible, especially for elderly patients. The causes of delay were multilingual; shortage of device supply was one of the major reasons. In our unit, we utilised ECCO2R operated by CRRT. Although current issues showed controversy on minimal-flow ECCO2R (Moerer et al. 2019; Schmidt et al. 2018), some of our patients benefited from the manoeuvre; further result of minimal-flow ECCO2R in severe COVID-19 patients was reported by our colleagues and is currently under review.

Although less is more for an unknown disease such as COVID-19, individually aggressive utilisation of currently available methods should be of great importance in daily practice.

Hyperinflammation, Peaceful Coexistence or Vigorous Intervention?

Increased level of serum interleukin-6 (IL-6) and C-reactive protein suggested hyperinflammation during the process of COVID-19. Thus, anti-inflammatory drugs such as steroid, chloroquine and tocilizumab were utilised in different centres, while the results were also controversial. Theoretically, IL-6 can cause macrophage activation-mimic syndrome in COVID-19 patients (McGonagle et al. 2020), and some histological autopsy samples from patients who died from COVID-19 showed bilateral diffuse alveolar damage including oedema, proteinaceous exudate, focal reactive hyperplasia of pneumocytes with patchy inflammatory cellular infiltration, and multinucleated giant cells (Xu et al. 2020), which suggested inflammatory cytokine storm. The block of IL-6 receptors seemed possible to block the pathway of

the storm, and therefore might decrease the severity of COVID-19.

Hyperinflammation was common in sepsis patients (Yadav and Cartin-Ceba 2016). However, anti-inflammatory therapies in septic patients had never shown any improvement. The immune reaction during the process of sepsis consisted of two phases: cytokine storm and immune exhaustion, and the exact boundary of those was difficult to determine, thus theoretical therapy always failed in the real world.

Almost all patients admitted to our unit received steroids in general wards. The average dose was about 1 gram methylprednisolone/kg body weight daily, and the duration was 5–7 days. However, we did not find any improvement in those patients, but due to admission bias, steroids might help in mild to moderate COVID-19 patients.

Interestingly, we had three special cases of immunocompromised patients, including two patients who had received renal transplantation and one with myasthenia gravis. All those patients received tacrolimus regularly before the outbreak of COVID-19, and this was discontinued after diagnosis of COVID-19. Their respiratory manifestations were less severe than other patients, and serum IL-6 remained low-level during the process of COVID-19. The same process was also reported in a patient with systemic sclerosis regularly treated by tocilizumab, and the last dose was given four weeks before being diagnosed with COVID-19 (Mihai et al. 2020). Perhaps prophylactic anti-inflammation rather than post-infected utilisation of anti-inflammatory drugs might be more efficient.

We also noticed different autopsy discoveries from different centres. Autopsy report from Ohio (Barton et al. 2020) showed heterogeneity in two patients, which suggested individualised therapy should be applied, if we could perform lung biopsy during the process of COVID-19.

The beneficial effects of reducing inflammation should be reconsidered when comparing with the potential of immu-

nocompromising effects. Thus, we did not suggest routine use of anti-inflammatory drugs in severe COVID-19 cases.

Since we were focused on severely ill patients with COVID-19, the experience seemed only focused on such patients. Further studies are needed to verify the exact effect of certain therapies like mechanical ventilation or ECMO. Antiviral therapies and anti-inflammation therapies might also have their roles in certain patients or certain conditions, for example, early stage of COVID-19 within two weeks. We believe we can deal with this disease and meet the victory in the near future. ■

Key Points

- An overview of our personal experience in Wuhan from the intensive care unit at Peking Union Medical College Hospital in China.
- COVID-19 was divided into two different phenotypes factitiously but we noticed in our daily practice that the two phenotypes may be just different stages of the same disease.
- We noticed the median days between onset of respiratory failure to intubation is about two weeks in our patients, while the duration of NIV usually exceeded 10 days.
- We found improvement of oxygenation after prone ventilation in patients with consolidation in dependent zones.
- Almost all patients admitted to our unit received steroids in general wards. The average dose was about 1 gram methylprednisolone/kg body weight daily, and the duration was 5–7 days.
- The beneficial effects of reducing inflammation should be reconsidered when comparing with the potential of immunocompromising effects. Thus, we did not suggest routine use of anti-inflammatory drugs in severe COVID-19 cases.

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