

Critical Care COVID-19 Management Protocol

(updated 4-15-2020)

Prophylaxis

While there is very limited data (and none specific for COVID-19), the following “cocktail” may have a role in the prevention/mitigation of COVID-19 disease. While there is no high level evidence that this cocktail is effective; it is cheap, safe and widely available.

- Vitamin C 500 mg BID and Quercetin 250-500 mg BID
- Zinc 75-100 mg/day (acetate, gluconate or picolinate). Zinc lozenges are preferred. After 1-2 months, reduce the dose to 30-50 mg/day.
- Melatonin (slow release): Begin with 0.3mg and increase as tolerated to 1-2 mg at night
- Vitamin D3 1000-4000 u/day (optimal dose unknown).

Mildly Symptomatic patients (at home):

- Vitamin C 500mg BID and Quercetin 250-500 mg BID (if available)
- Zinc 75-100 mg/day
- Melatonin 6-12 mg at night (the optimal dose is unknown)
- Vitamin D3 1000-4000 u/day
- *Optional:* Hydroxychloroquine 400mg BID day 1 followed by 200mg BID for 4 days

Mildly Symptomatic patients (on floor):

- Vitamin C 500mg BID and Quercetin 250-500 mg BID (if available)
- Zinc 75-100 mg/day
- Melatonin 6-12 mg at night (the optimal dose is unknown)
- Vitamin D3 1000-4000 u/day
- Enoxaparin 40-60 mg daily
- *Optional:* Methylprednisolone 40 mg daily
- *Optional:* Hydroxychloroquine 400mg BID day 1 followed by 200mg BID for 4 days
- N/C 2L /min if required (max 4 L/min; consider early t/f to ICU for escalation of care).
- Avoid Nebulization and Respiratory treatments. Use “Spinhaler” or MDI and spacer if required.
- Avoid non-invasive ventilation
- T/f EARLY to the ICU for increasing respiratory signs/symptoms.

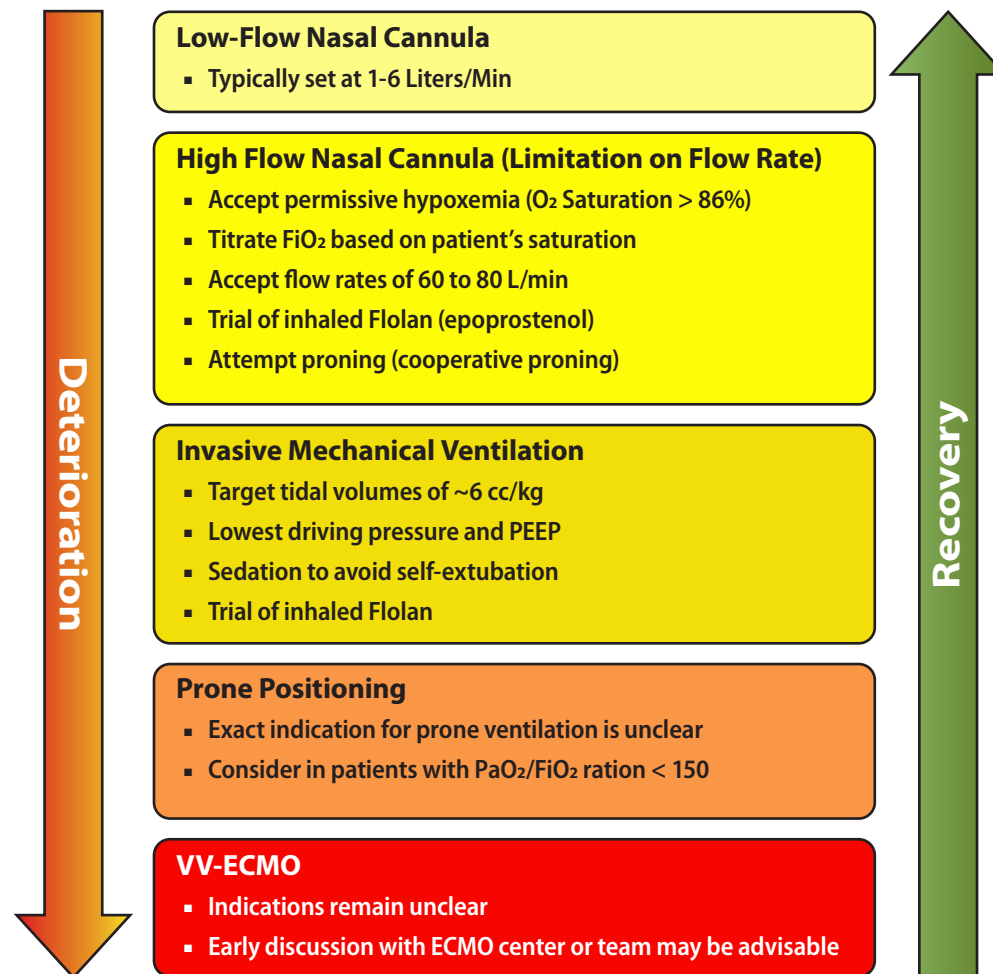
Respiratory symptoms (SOB; hypoxia- requiring N/C \geq 4 L min: admit to ICU):

Essential Treatment (dampening the STORM)

1. Methylprednisolone 80 mg loading dose then 40mg q 12 hourly for at least 7 days and until transferred out of ICU. Alternative approach: Hydrocortisone 50 mg q 6 hourly.
2. Ascorbic acid (Vitamin C) 3g IV q 6 hourly for at least 7 days and/or until transferred out of ICU. Note caution with POC glucose testing (see below).

General schema for respiratory support in patients with COVID-19

TRY TO AVOID INTUBATION IF POSSIBLE



3. Full anticoagulation: Unless contraindicated we suggest FULL anticoagulation (on admission to the ICU) with enoxaparin, i.e 1 mg kg s/c q 12 hourly (dose adjust with Cr Cl $<$ 30mls/min). Heparin is suggested with Cr Cl $<$ 15 ml/min. Alternative approach: Half-dose rTPA: 25mg of tPA over 2 hours followed by a 25mg tPA infusion administered over the subsequent 22 hours, with a dose not to exceed 0.9 mg/kg followed by full anticoagulation. On transfer to floor, consider reducing enoxaparin to 40-60 mg /day. *Note: Early termination of ascorbic acid and corticosteroids will likely result in a rebound effect.*

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Additional Treatment Components (the Full Monty)

4. Melatonin 6-12 mg at night (the optimal dose is unknown).
5. Magnesium: 2 g stat IV. Keep Mg between 2.0 and 2.4 mmol/l. Prevent hypomagnesemia (which increases the cytokine storm and prolongs Qtc).
6. *Optional:* Azithromycin 500 mg day 1 then 250 mg for 4 days (has immunomodulating properties including downregulating IL-6; in addition Rx of concomitant bacterial pneumonia).
7. *Optional:* Atorvastatin 40-80 mg/day. Of theoretical but unproven benefit. Statins have been demonstrated to reduce mortality in the hyper-inflammatory ARDS phenotype. Statins have pleotropic anti-inflammatory, immunomodulatory, antibacterial and antiviral effects. In addition, statins decrease expression of PAI-1
8. Broad-spectrum antibiotics if superadded bacterial pneumonia is suspected based on procalcitonin levels and resp. culture (no bronchoscopy).

Co-infection with other viruses appears to be uncommon, however a full respiratory viral panel is still recommended. Superadded bacterial infection is reported to be uncommon (however, this may not be correct).
9. Maintain *EUVOLEMIA* (this is not non-cardiogenic pulmonary edema). Due to the prolonged "symptomatic phase" with flu-like symptoms (6-8 days) patients may be volume depleted. Cautious rehydration with 500 ml boluses of Lactate Ringers may be warranted, ideally guided by non-invasive hemodynamic monitoring. Diuretics should be avoided unless the patient has obvious intravascular volume overload.
10. Early norepinephrine for hypotension. While the angiotensin II agonist Giapreza™ has a limited role in septic shock, this drug may uniquely be beneficial in patients with COVID-19 (downregulates ACE-2).
11. Escalation of respiratory support (steps); **Try to avoid intubation if at all possible**
 - Accept "permissive hypoxemia" (keep O2 Saturation > 84%)
 - N/C 1-6 L/min
 - High Flow Nasal canula (HFNC) up to 60-80 L/min
 - Trial of inhaled Flolan (epoprostenol)
 - Attempt proning (cooperative repositioning-proning; see Figure)
 - Intubation... by Expert intubator; Rapid sequence. No Bagging; Full PPE. Crash/emergency intubations should be avoided.
 - Volume protective ventilation; Lowest driving pressure and lowest PEEP as possible. Keep driving pressures < 15 cmH2O.

- Moderate sedation to prevent self-extubation
- Trial of inhaled Flolan (epoprostenol)
- Prone positioning
- ?? ECMO < 60 yrs. and no severe commodities/organ failure.

There is widespread concern that using HFNC could increase the risk of viral transmission. There is however, no evidence to support this fear. HFNC is a better option for the patient and the health care system than intubation and mechanical ventilation. CPAP/BiPAP may be used in select patients, notably those with COPD exacerbation or heart failure.

A group of patients with COVID-19 deteriorates very rapidly (see graphic below). Intubation and mechanical ventilation may be required in these patients.

12. Treatment of secondary HLH (increasing Ferritin, CRP and transaminases)
 - "High dose corticosteroids." Methylprednisolone 120 mg q 8 hourly for at least 3 days, then wean accruing to CRP, IL-6, Ferritin etc.
 - Tocilizumab (IL-6 inhibitor) as per dosing guideline.
 - Consider plasma exchange
13. Monitoring
 - Daily: PCT, CRP, IL-6, BNP, Troponins, Ferritin, Neutrophil-Lymphocyte ratio, D-dimer, Mg, CRP and Ferritin are good biomarkers and track disease severity. Thromboelastogram (TEG) on admission and repeated as indicated.
 - In patients receiving IV vitamin C, the Accu-Chek™ POC glucose monitor will result in spuriously high blood glucose values. Therefore, a laboratory glucose is recommended to confirm the blood glucose levels.
 - Monitor QTc interval if using chloroquine/hydrochloroquine and azithromycin and monitor Mg++ (torsades is uncommon in monitored ICU patients)
 - No routine CT scans, follow CXR and chest ultrasound.
 - Follow ECHO closely; Pts develop a severe cardiomyopathy.
14. Post ICU management
 - a. Enoxaparin 40-60 mg s/c daily
 - b. Methylprednisone 40 mg day, the wean slowly
 - c. Vitamin C 500 mg PO BID
 - d. Melatonin 3-6 mg at night