

Fleming Inflammation and Cardiovascular Disease SARS-CoV-2 Proposed Treatment Protocol. Initial COVID Hydroxychloroquine Failure Responds to Interferon α -2 β and Tocilizumab

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1. Abstract

Currently there is no established treatment protocol for SARS-2 (CoVid-19). Proponents of hydroxychloroquine (HCQ) argue that early intervention may sufficiently prevent replication of the virus and avoid the need for hospitalization. In instances where viral replication continues and the patient develops CoVid pneumonia (CVP), such patients – particularly with comorbidities – are prone to develop an InflammoThrombotic response similar to cytokine release syndrome (CRS). We present one such patient who failed HCQ treatment and was subsequently treated successfully with an interleukin-6 inhibitor and interferon.

2. Clinical Case

A 73-year old obese (170 cm, 95.4 kg) Cuban male (E.G.) developed fatigue, hyposmia, and dyspnea. He was not aware of any exposure to individuals with CoVid-19. His medical history revealed no other comorbidities other than his age and weight. He was taking no medications. A nasal swab for PCR was obtained and he was started on hydroxychloroquine (HCQ) 200 mg po BID along with 50 mg po elemental zinc daily.

He returned 4-days later with worsening dyspnea and was admitted following FMTVDM [1] imaging to evaluate the severity of corona virus pneumonia (CVP) inflammation. The initial quantification revealed two specific areas in the right lung fields (Figure 1) where an inflammatory response was present.

Following measurements, he was admitted and started on Tocilizumab 762.2 mg IV repeated one time 8-hours later (Treatment arm 7), Interferon alpha-2b 5 million units per nebulizer BID (Treatment arm 9), Atrovent nebulizer treatments q 4-hours, and SQ heparin 5000 Unit q 12-hours per NCT04349410. The patient was initially positioned in the prone position with O2 monitoring. His initial IL-6 level was 16 pg/ml [2], and ferritin 379 ng/ml, with a normal range fibrinogen level.

During the first 48-hours he reported improvement in breathing and was repositioned to a supine position.

Following 72-hours of treatment he underwent repeat FMTVDM (Figure 1) imaging which showed improvement in CVP inflammation, matching his improved symptoms, and follow up blood tests including an IL-6 of 10 pg/ml and ferritin of 224 ng/ml. The initial PCR test for SARS-2 returned positive.

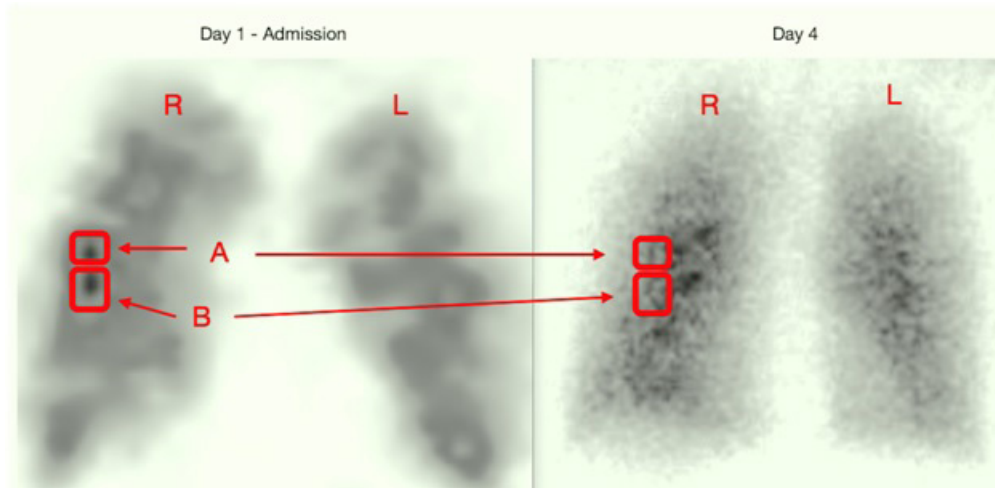


Figure 1: Measurement of SARS-2 Pneumonia (CVP) Inflammation.

Legend: Initial CVP in the right lung measured 170 in region A and 180 in region B. After 72-hours of treatment, improvement was seen with measurements of 125 for region A and 128 in region B. The right (R) and left (L) lung fields are marked accordingly.

The patient continued to improve and was discharged on the 8th day post admission.

3. Discussion

SARS-2 attaches to human cells through a variety of receptors including ACE-2. Respiratory and gastrointestinal cells are particularly vulnerable and evidence indicates that sufficient viral replication occurs within 96-hours to become clinically significant [3]. If patients are to be treated successfully in the outpatient setting, clinicians must begin treatment in those patients who are symptomatic soon enough to prevent the subsequent InflammoThrombotic sequelae responsible for the deaths of hundreds of thousands of people.

Efforts by clinicians to provide both outpatient and inpatient treatment for CoVid-19 patients have been hampered by the lack of scientific data comparing various treatments. In the absence of that scientific data clinicians are left with few options; they can either do nothing or they can apply treatment based upon anecdotal information.

HCQ proponents have argued for the initiation of HCQ as soon as the clinician thinks the patient has SARS-2. Arguably treatment in this patient may have been started too late for HCQ to provide clinical benefit or perhaps the patient might have benefitted from a combination of HCQ and interferon in the prehospital setting [4]. Once again, the failure to adequately investigate such drug combinations has resulted in clinicians having little scientific data from which to make clinical decisions. Given these current limitations it

is important that we use what anecdotal data we have while accumulating results from scientific research.

Viruses including SARS-2 are one of many factors involved in InflammoThrombotic reactions produced by the immune system [5] resulting in inflammation and blood clots [6] that have proven to be associated with deaths in SARS-2 patients. The original Theory [5] explaining this mandates that once admitted to hospital, SARS-2/CoVid patients be treated accordingly to address the resulting inflammation and thrombotic reactions. Options for treatment at these stages are shown in (Figure 2).

Measurement of the InflammoThrombotic response [1] to SARS-2 makes it possible to direct treatment as was done in this patient thereby tailoring the specific treatment based upon the actual clinical response. In this instance, the patient was evaluated and admitted for treatment following failure of HCQ and zinc. This treatment consisted of prone positioning, use of beta-2 bronchodilator nebulizer treatment, administration of low dose heparin to reduce the potential formation of thrombi, and the initiation of both interferon (IFN) and interleukin-6 inhibitor (IL6-I) treatments.

Anecdotal and now some research data demonstrates that treatment with IFN - common in Cuba - particularly when combined with an IL6-I appears to be promising. Currently only approximately 100 deaths from CoVid have been reported in Cuba and this may represent the benefit of combining IFN and IL6-I's. While this represents only one such case example, it emphasizes the importance of objectively evaluating CoVid-19 patients and initiating treatment intervention early.

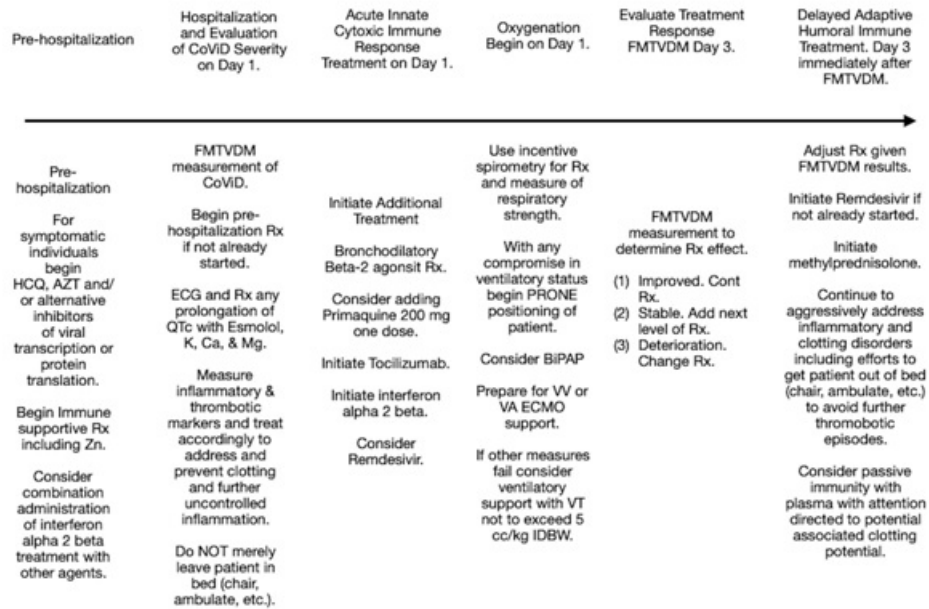


Figure 2: Inflammation and Cardiovascular Disease FMTVDM CoViD Proposed Treatment Protocol.

As we continue to collect scientific results from objective research studies, we encourage physicians to make decisions on behalf of their patients. When possible using the results of scientific research but in the absence of that information, using their best clinical decision making skills and the data – both anecdotal and otherwise – on behalf of their patients; recognizing that the alternative is to do nothing.

4. Acknowledgement

FMTVDM is IP patented to the first author and was made available following training to participating sites without cost. The figures are reproduced with the expressed consent of the first author. These patients are part of a larger NCT04349410 study to be published elsewhere in its entirety.

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