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Letter to Editor Open Access

Indomethacin As Acute and Rescue Treatment for Cytokine Storm in Clinically Severe COVID-19 Infection

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Letter to the Editor

Dear Sir/Madam,

The second pandemic wave caused by SARS-CoV-2 infection in the European and American countries led to stressed and overflowed health systems.

Fortunately, in contrast to spring this year, we are able to understand the disease in greater detail. The clinical manifestations present a spectrum from asymptomatic or mild symptoms to Acute Respiratory Distress Syndrome (ARDS) and pneumonia. Although age and co-morbidities are known to induce a progression of diseases severity, we saw very often also young and healthy people with dysregulated immune responses in our hospital. The reason for the sometimes unexpected-aggravation of COVID-19 infection during day 3-7 was identified in a hyper-inflammatory state, which is called 'cytokine storm' [1].

Il-6 should be the leading cytokine in this cytokine storm [2] and at the moment over 20 registered COVID-19 tocilizumab trials (humanized anti.IL-6R antibody) for to treat hospitalized patients are under WHO attention.

The aim should be to prevent the progression of mild/moderate disease to a critical stage with hospitalization by inhibition and down regulation of the hyper-inflammatory cytokine storm.

NSAIDS are widely used to treat COVID-19 symptoms like fever, pain and inflammation, but we would like to hallmark on indomethacin, which is at the moment prescribed by insiders, but is not commonly used or even recommended by the COVID guidelines. Indomethacin could aid more specifically than the others NSAIDS both, to prevent or reduce the cytokine storm formed by IL-6 and therefore to inhibit virus replication.

Indomethacin differs from the others NSAIDs with its own anti-inflammatory effect [3] and is known to block Il-6 in chronic inflammation effectively [4]. Indomethacin was shown to have a potent antiviral activity against SARS coronavirus independently by its anti-inflammatory effects [5,6].

We treated two patients, a 54 year old man and a 50 year old woman at day 3 and day 2, respectively. The both had at this time fever over 38.5 C and respiratory symptoms. Indomethacin was given with 50 mg every 8 hours. We saw a reduction in temperature within 10 hours to 37.2 and 36.9 respectively. Unfortunately, but due to the shortage of laboratory and inpatient analysis and work-up while hitting by the second wave of COVID, we did not have Chest x-ray, CT-scan or further laboratory testing's (WBC, CRP, IL-6, d-dimers, LDH). Pragmatic clinical surveillance was achieved in due course. After 10 days the virus PCR was negative, antibodies were detected at normal concentration.

We propose not to lower the doses at the beginning of infection [7], but to start the 2-4 day, depending on fever and coughing with 3 × 50 mg/daily with gastric protective agents to reduce hyper inflammation and to avoid disease severity induced by the cytokine storm.

According to the literature, the best performing dosing regimens are 50 mg three-times-a-day IR (Immediate Release) formulation, or 75 mg twice-a-day for the SR (Sustained Release) formulation. The treatment with the SR formulation at the dose of 75 mg twice-a-day is expected to achieve a complete response in three days for the treatment in patients infected by the SARS-CoV-2 coronavirus. Our experience and these results suggest that indomethacin could be considered as a promising candidate for the treatment of SARS-CoV-2 whose potential therapeutic effect needs to be further assessed in a prospective clinical trial. Moreover further studies are necessary to develop a clinical protocol and to define when indomethacin should be combined with other NSAIDS like aspirin or paracetamol.

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