Case Report

Intravenous lidocaine infusion in a case of severe COVID-19 infection

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Abstract

A subset of patients with COVID-19 develops a severe inflammatory response that may lead to respiratory and multiorgan failure. Effective treatment strategies to mitigate or interrupt this self-destructive inflammatory process are limited. The local anesthetic lidocaine has anti-inflammatory properties in addition to its analgesic, antiarrhythmic, and sedating effects that may be beneficial in critically ill COVID-19 patients. We report the case of a patient with COVID-19 induced severe respiratory distress who was intubated and received supportive treatment including proning and neuromuscular blockade. He developed a strong inflammatory response that we treated with an intermittent lidocaine infusion resulting in subsequent resolution. This case occurred prior to emerging data from a large dexamethasone use trial that demonstrated a survival benefit from its use in hospitalized COVID-19 patients. At the time, lidocaine was the only anti-inflammatory medication our patient received.

Keywords: COVID-19, lidocaine, respiratory distress syndrome, systemic inflammatory response syndrome

Introduction

A subset of patients with COVID-19 develops a severe inflammatory response that ultimately leads to respiratory and multiorgan failure. Effective strategies and drugs to mitigate or interrupt this self-destructive inflammatory process are limited. The local anesthetic lidocaine has anti-inflammatory properties in addition to its analgesic, antiarrhythmic, and sedating effects that may be beneficial in critically ill COVID-19 patients. We report our experience with an intermittent lidocaine infusion in a patient with a COVID-19 and subsequent resolution of the inflammatory response. We took care of this patient prior to "Recovery Trial," which was a large study using dexamethasone in COVID hospitalized patients.[1] The patients written informed consent for this report, and institutional review board authorization regarding information related to the health insurance portability and accountability act were obtained.

Case Report

A 71-year-old man (weight 77 kg, BMI 25.9 kg/m^2) with a past medical history notable for previous deep venous thrombosis as well as diffuse large B-cell lymphoma recently treated with rituximab, cyclophosphamide, hydroxydaunorubicin hydrochloride, oncovin and prednisone, and minimal residual disease was hospitalized early during the first surge of the pandemic with shortness of breath, diarrhea, and presyncope. He was initially treated with oseltamivir and ceftriaxone to treat a suspected superimposed bacterial and influenza infection with adjustment to piperacillin and tazobactam when aspiration pneumonia was included in the differential diagnosis. Two days following admission, the patient's peripheral oxygen saturation

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declined to 82% despite increasing oxygen supplementation and care was escalated to an intensive care unit (ICU), where he was treated with high flow nasal cannula. Flows were gradually increased to 40 l/min with FiO_2 of 0.75. The chest X-ray showed scattered bilateral airspace and interstitial opacities with predominant peripheral distribution. His acute hypoxemic respiratory failure rapidly declined and necessitated urgent endotracheal intubation and mechanical ventilation. In parallel to the worsening respiratory function, upon admission to the ICU, we observed an acute increase in C-reactive protein (CRP) and ferritin levels from 65 to 104 μg/mL and from 747 ng/ml to 1307 ng/ml, respectively. Over the next 2 days these inflammatory markers continued to rise up to 224 μg/mL and 1755 ng/ml, respectively [Figure 1]. During this time, his oxygenation remained poor despite proning and intermittent neuromuscular blockade to maintain the P/F ratio above 100. A treatment trial with hydroxychloroquine was not tolerated as the patient developed a persistent increase in QTc of >500 ms. Additional treatment options discussed at the time in the medical community including Remdesivir and convalescent plasma were unavailable, and the family declined participation in an IL-6 inhibitor (sarilumab) trial. His hospitalization occurred 2 months before publication of data from the RECOVERY trial[1] that reported a survival benefit from dexamethasone in these patients, and we did not use any steroids in his treatment. Remdesivir and convalescent plasma trials were in preliminary stages, respectively, and only became available later at our hospital.

His hemodynamic status was labile with unpredictable episodes of hypertension and tachycardia. We treated these episodes with labetalol and more sedatives as needed to achieve a normal blood pressure.

Being mindful of the patient's critical condition, we elected to use a low-dose lidocaine infusion for analgesic as well as anti-inflammatory treatment. We initiated a lidocaine infusion at a rate of 45 mg/h, which amounted to a dose of 0.6 mg/kg/h in intervals of 12 h over a period of 5 days with a 1-day pause early in the course, for a total infusion time of 48 h. The QTc was measured frequently and no increase was noticed upon initiation of lidocaine. The patient's inflammatory markers initially continued to rise and peaked on day 4 after lidocaine initiation with CRP as high as 350 μg/mL and ferritin as high as 2069 ng/ml. However, we noted that the patient's hemodynamic status stabilized within a day of starting the lidocaine infusion. On day 5, we noted a decline of the CRP and ferritin levels to 192 μg/mL and to 590 ng/ml, respectively, and discontinued further lidocaine administration [Figure 1].

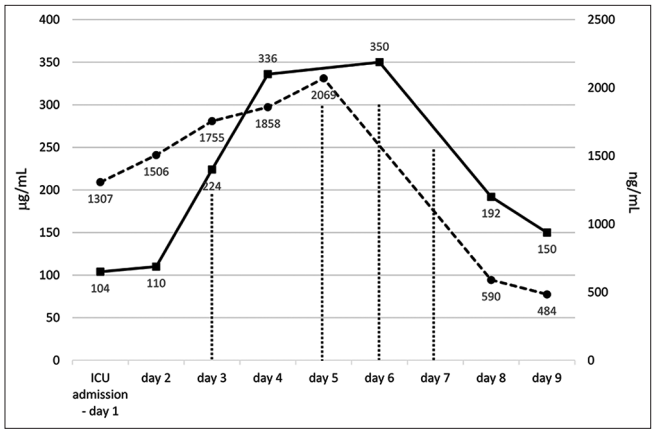

Figure 1: Dynamics of inflammatory markers and lidocaine treatment. CRP - C-reactive protein. ——■—— CRP (μg/ml), - - -●- - - Ferritin (ng/ml), ... Lidocaine infusion

Discussion

The pathophysiology of severe COVID-19 infection includes hyperinflammatory response to the virus. Serum ferritin and CRP levels can be used to track the inflammatory response and have been identified as predictors of a clinically severe COVID-19 course associated with a high mortality rate.[2] Timely control of extrapulmonary systemic hyperinflammation may reduce lung tissue injury and is thought to mitigate disease progression.[3]

Lidocaine potentiates GABA-ergic transmission and has known analgesic, antiarrhythmic, and antithrombotic properties, all of which may benefit the critically ill COVID-19 patients. Several studies report lidocaine's ability to decrease inflammation and cytokine levels although the exact mechanism is not fully understood.[4,5] Of particular interest for COVID-19 treatment could be demonstrated lidocaine-associated reduction in hyperoxic lung injury and preservation of pulmonary microvascular permeability.[6] Finnerty hypothesized that lidocaine infusion in COVID-19 patients may decrease the formation of neutrophil extracellular traps and modulate the severity of disease, and recommended it as a potential therapy.[7] Anti-inflammatory properties of nebulized lidocaine[8] have also been suggested for COVID-19, however, many hospitals including ours do not favor aerosolized medications in COVID patients, and we chose the intravenous route.

The effective dosing, timing, and duration of intravenous lidocaine for maximal anti-inflammatory benefit is unknown. We used lidocaine dosing information for pain management as guidance

for our approach whereby the optimum effect of lidocaine on pain occurs with 24–48 h of an infusion.[9] With concerns about potential lidocaine toxicity in this critically ill patient, and as we were not able to readily follow serum lidocaine levels at our institution, we chose an intermittent instead of a continuous infusion. We did not observe any clinical signs of lidocaine toxicity.

We noted an abrupt decline in the inflammatory markers between day 6 and day 8 after admission to the ICU, and we discontinued the infusion after a combined 48 h of lidocaine treatment. Han *et al*. did not describe such an acute decline in CRP levels following cytokine profiles in 14 critically ill patients with COVID-19 disease during their hospitalization.[10] It is conceivable that an association between recovery of inflammatory markers and lidocaine treatment may exist. While the reasons for our observation are likely multifactorial, it merits further exploration.

Auto-destructive inflammation is a key feature during severe COVID-19 infection. Lidocaine with its anti-inflammatory properties may mitigate the inflammatory response and possibly have additional antiarrhythmic, analgesic, antithrombotic, and sedative benefits. We describe a case with intermittent intravenous lidocaine administration for severe COVID-19 disease with successful patient outcome.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and othe r clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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