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Case Report

Role of Prostaglandin E1 in the Treatment of Severe Cardio-Pulmonary Dysfunction in COVID-19 Infections: A Review Article Including a Case Report

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Abstract

Background: One of the most challenging characteristics of the novel pandemic of COVID-19, is that there are various degrees of severity of symptoms, from asymptomatic to life-threatening forms. COVID-19 infection results in an increase in serum levels of cytokines such as interleukin-6 (IL-6) and interleukin-8 (IL-8) and their relationship with acute lung injury has been shown previously. Prostaglandin E1 is one of a family of naturally occurring acidic lipids with pulmonary and systemic vasodilator effects and anti-inflammatory properties. Starting from these considerations, we can postulate a possible role for the PGE 1 in increasing the levels of NO and might be effective in reducing mortality and morbidity in patients with COVID-19 infection. **Clinical Case:** A 54-old man, was admitted to Emergency Room (ER) complaining of dyspnoea and fever. Phisical examination was characterized by tachypnoea, tachycardia and hypotension and hypoxemia at transcutaneous saturation. High Resolution Computed Tomography (HRCT) showed bilateral interstitial pneumonia with ground glass opacities (visual involvement of 80% of pulmonary parenchimal). Later we decide to use prostanoid drugs in infusion. We observed a progressive clinical and echocardiography improvement, evidenced by partial recovery of EF (45%).The Patient underwent Cardiac Magnetic Resonance (CMR) that showed typical Takotsubo cardiomyopathy. **Conclusion:** Considering the biochemical mechanisms involved in COVID19 infection and previous experiences justifying the off-label use of PGE1 as a possible synergic drug in the treatment of COVID19 infection should be considered.

Keywords: Covid-19 infection; Prostaglandin; Takotsubo cardiomyopathy

Introduction

One of the most challenging characteristics of the novel pandemic of COVID-19, is that there are various degrees of severity of symptoms, from asymptomatic to life-threatening forms. As recently reported by Zhang et al., considering the biochemical parameters, elevated levels of infection-related biomarkers and inflammatory cytokines, neutrophilia and lymphocytopenia seem to be correlated to the most severe cases of the infection [1]. There are clinical factors significantly correlated with higher risks of acute respiratory distress syndrome (ARDS) and death, such as being in an older age group, high fever, and comorbidities as obesity. COVID-19 causes the typical ARDS pathological changes of diffuse alveolar damage in the lung [2]. Several studies

demonstrated a strong correlation between pulmonary hypertension and Nitric Oxide (NO): a high level of pulmonary pressure is a pathological condition characterized by endothelial dysfunction, in which NO availability is impaired with concomitant increased release of IL-6 by the dysfunctional endothelium [3,4]. COVID-19 infection results in an increase in serum levels of cytokines such as interleukin-6 (IL-6) and interleukin-8 (IL-8) [5] and their relationship with acute lung injury has been shown previously [6]. Prostaglandin E1 (PGE1) is one of a family of naturally occurring acidic lipids with pulmonary and systemic vasodilator effects and anti-inflammatory properties, these drugs represents the standard medical treatment for the management of arterial pulmonary hypertension [7]. Administration of a low dose of PGE1 (20 ng.kg-1. min-1) has previously been shown to reduce IL-6 production and improve oxygenation and has been shown to attenuate the duration of systemic inflammatory response syndrome. Starting from these considerations and focusing attention on the role of IL-6 and NO, we can postulate a possible role for the PGE 1 in increasing the levels of NO and might be effective in reducing mortality and morbidity in patients with COVID-19 infection, especially in terms of pulmonary complications. Particular and beneficial effect of PGE1 in heart failure with pulmonary hypertension, were described with dual mechanism of action: one acute, predominantly vasodilator effect on the pulmonary arterial system and another, on the alveolar arterioles which depends on local mediators (endothelin, nitric oxide and angiotensin II) [8,9]. Our tertiary care hospital in Parma, Italy, has largely been repurposed to care for patients with COVID-19, reaching more than 800 hospital beds dedicated to patients with COVID-19 at the peak of the pandemic. Within 1 week, we provided care for four patients with COVID-19 with cardiorespiratory failure. One of these patients with confirmed COVID-19 pneumonia was young and active patients with no comorbidity.

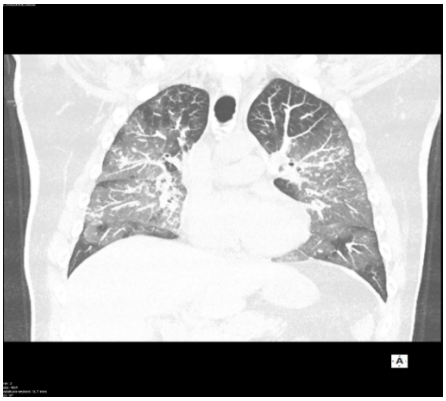

Figure 1: High Resolution Computed Tomography (HRCT) showed bilateral interstitial pneumonia with ground glass opacities.

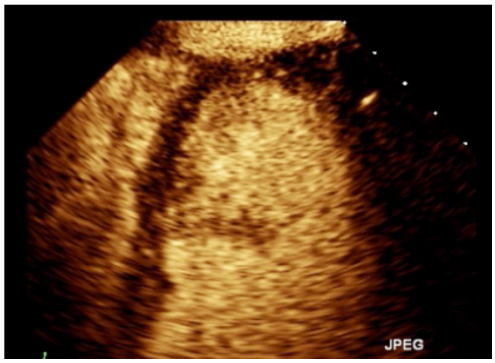

Figure 2: Echocardiogram showed severe ventricular dysfunction.

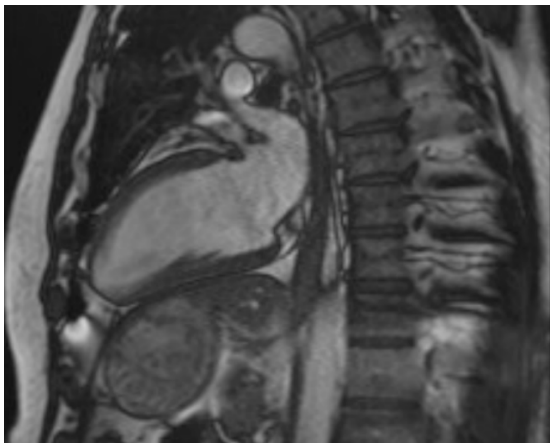

Figure 3: No oedema in T2 weighted images.

Case Presentation

A 54-old man, was admitted to Emergency Room (ER) complaining of dyspnea, deep asthenia and fever (41°C), from four days initially treated with ceftriaxone. Phisical examination was characterized by tachypnoea (respiratory rate 30 acts/ minute), tachycardia and hypotension (arterial pressure 90/60 mmHg) and hypoxemia at transcutaneous saturation (Sat o2 85%). High Resolution Computed Tomography (HRCT) showed bilateral interstitial pneumonia with ground glass opacities (visual involvement of 80% of pulmonary parenchimal) Figure 1. No comorbidities were declared. The patient have no history of arrhythmia before being admitted for COVID. Nasofaringeal swab was positive for SARS-CoV 2 and ECG revealed Atrio-Ventricular Nodal Reentrant Tachycardia (AVRNT) with heart rate of 140 bpm, partially responsive to Valsalva maneuver. Echocardiogram showed severe ventricular disfunction (Ejection Fraction, EF, 30-35%) with hypokinesia of apical region associated with hyperkinesis of medio-basal segments, mild mitral regurgitation, and slight pericardial effusion Figure 2. Laboratory

tests were TnI hs 10 ng/L first detection - 26 ng/L second detection (normal range 2.3-17.8 ng/L), PCR > 250 mg/L (normal range 0.5-5 mg/L), D-dimer 1893 ng/ml (normal range <500 ng/ml), PCT 3.10 ng/ml (normal range 0-0.5 ng/ml). The worsening of clinical condition needed an orotracheal intubation and a transfer to Intensive Care Unit (ICU), after five days from the hospital admission. The Patient was treated with many antiviral drugs: Tocilizumab 8 mg / kg i.v. in single dose and Remdesivir 200 mg i.v. the first day then 100 mg / day i.v. in the following 4 days and steroid therapy, with little benefit on cardio respiratory function Later, one week after admission to the hospital, we decided to use prostanoid drugs in infusion; PGE1 was infused from at a mean dose of 10 ng/kg/min for a total of 24 h over seven consecutive days. Positive end-expiratory pressure (PEEP) were progressively reduced at the mechanical ventilation. We observed a progressive clinical and echocardiography improvement, evidenced by partial recovery of EF (45%). The Patient underwent Cardiac Magnetic Resonance (CMR) that showed typical Takotsubo cardiomyopathy characterized by thinning and hypo-akinesis of apical wall of left ventricle ("apical ballooning") and normokinesis of basal/medium segments; no Late Gadolinium Enhancements (LGE); no oedema in T2 weighted images Figure 3. Follow-up echocardiogram confirmed recovery of EF (50%) associated with mild hypokinesia of apical segments.

Conclusion

Changes in blood coagulation during severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection have been described by Han and colleagues [10] Systemic proinflammatory cytokine response is a mediator of atherosclerosis by inducing the expression of procoagulant factors, local inflammation, and haemodynamic alterations. Considering the biochemical mechanisms involved in COVID19 infection and previous experiences justifying the off-label use of PGE1 (or similar),theese can will be a possible synergic drug in the treatment of COVID19 infection. In view of the young and seemingly healthy patients who develop severe pulmonary vascular disease complications during SARS-CoV-2 infection, a prospective registry should be established to aid an understanding of the prevalence of pulmonary vasculitis and heart dysfunction in patients with COVID-19, with the aim of defining therapeutic protocols.

Declaration

Ethical Approval: Not applicable.

Ethics statement: This study was conducted in accordance with Good Clinical Practice and the current version of the revised Declaration of Helsinki. Written informed consent was obtained from each patient prior to enrolment.

Consent to publication: yes, I have no funding in this research. There is any conflict of interest.

Availability of data and materials: Yes.

Authors' Contributions: WS wrote, conceived and produced the photographic material of the manuscript; CC undertook the literature search.

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