LETTER

Lack of Efficacy of SGLT2-i in Severe Pneumonia Related to Novel Coronavirus (nCoV) Infection: No Little Help from Our Friends

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Italy is facing a dramatic health emergency related to COVID-19 initially spreading from Wuhan, China, and subsequently worldwide. Lombardy is the Italian region with the highest prevalence of positive cases, hospitalized patients, and percentage of deaths, and this is of great concern. Thinking about a possible way to help our patients, we hypothesized that sodium–glucose cotransporter 2 inhibitors (SGLT2-i), used in subjects with type 2 diabetes, could be of a certain efficacy in non-diabetic patients with hypoxemia and interstitial lung edema due to SARS-CoV-2 infection. The main physiopathological reasons supporting the use of SGLT2-i are their ability to shift energy metabolism [1], to increase hematocrit [2], to determine glucose excretion with associated Na^+ loss, and increase in osmotic diuresis [3]. Moreover, SGLT2-i may block the Na^+/H^+ antiporter, consequently reducing cytoplasmic Na^+ and Ca^{2+} , thus offering cellular

protection. SGLT2-i may selectively reduce interstitial volume with minimal change in blood volume, thus limiting the aberrant reflex neuro-humoral stimulation that occurs in the setting of intravascular depletion [4]. Furthermore, SGLT2-i may exert anti-inflammatory properties in animal models [5]. Finally, non-diabetic subjects are also prescribed SGLT2-i to reduce the incidence of worsening heart failure or cardiovascular-related death.

On the basis of the aforementioned hypothetical activities, three non-diabetic hospitalized patients with severe bilateral interstitial COVID-19-related pneumonia were treated “off-label” with SGLT2-i immediately after hospital admission. Patient 1 suffered also from allergic asthmatic bronchitis; patient 2 underwent coronary angioplasty in 2016; patient 3, female did not previously take any medication. Patients were 50–60 years of age and a mix of both men and women. They presented with fever, a respiratory rate greater than 30 breaths/min, and severe respiratory distress with SpO_2 of 93% or less on room air at a resting state. At admission, lung CT scan showed multifocal patchy shadows or ground glass opacities located in the periphery, subpleural area, and bilateral lower lobes. Nasopharyngeal and oropharyngeal specimens tested positive for SARS-CoV-2; tests for other respiratory viruses and for bacterial pathogens tested negative. Patients were treated in accordance with international guidelines; moreover,

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after a complete explanation about possible risks and benefits, they signed an informed consent form for “off-label” adjunctive oral therapy with empagliflozin 10 mg for 5–7 days.

Hematology and biochemistry laboratory testing revealed a variable evolution in inflammatory markers. Control chest imaging did not show complete reduction in interstitial lung involvement during the patients’ hospital length of stay (LOS). The patients described here were selected and are younger than the patients we typically take care of in our ward. Nevertheless, they required attention because of their symptoms and hypoxia caused by the COVID-19-related pneumonia. Usually, between 12 and 16 days are required for symptoms to lessen and to see signs improvement (unless complications occur). Unfortunately, we did not observe any reduction in the LOS or any favorable action related to the SGLT2-i dose received by the patients. Expected potential benefits might have led to a reduction of interstitial lung imbibition, to a possible metabolic energy shift, and potentially to an inflammatory response improvement. Not knowing whether there could be an effect and a need to systematically study the clinical application of SGLT2-i treatment in non-diabetic patients suffering from COVID-19 severe pneumonia hospitalized in an internal medicine ward, our anecdotal experience did not show any of the pathophysiologic changes we postulated.

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Compliance with Ethics Guidelines. Ethical approval was waived by the ethics committee (Comitato Etico di Bergamo - ASST Papa Giovanni 23). Informed consent to take part in the study was obtained from the patients.

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