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CASE REPORT – OPEN ACCESS

Management of Sacubitril/Valsartan Combination in an End-stage Heart Failure Patient Hospitalized for COVID-19 Pneumonia: Should we Withdraw Temporarily or Continue?

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ABSTRACT

Background: Many factors were blamed for the worse prognosis in COVID-19. Heart failure patients are thought to be under increased risk because of either immune-compromised basal status or possible interaction of viral infection with on-going medications, such as the Renin-Angiotensin-Aldosterone system (RAAS) blockers. Sacubitril is a neprilysin inhibitor and its' combination with valsartan is recommended as a novel medication for heart failure.

Case Report: A 71 years of age female with end-stage heart failure was hospitalized for COVID-19 pneumonia. She was under sacubitril/valsartan combination for the heart failure, and at the end of the first week of hospitalization, clinical and laboratory parameters recovered uneventfully. Sacubitril/valsartan therapy was continued without complications during the in-hospital course.

Conclusion: Specific therapies for heart failure should not be withdrawn in COVID-19. To our knowledge, this is the first case report documenting the clinical progress of a COVID-19 pneumonia patient who was already under sacubitril/valsartan treatment.

Keywords: COVID-19 pneumonia, heart failure, neprilysin inhibition, sacubitril, valsartan

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INTRODUCTION

The role of the Renin-Angiotensin-Aldosterone system (RAAS) blockers in COVID-19 patients is conflicting, and there have been no proven harmful or protective effects of RAAS blockers in this clinical context yet (1–3). On the other hand, the stoppage of specific medical therapies in heart failure patients can be harmful and may result in worsening of congestive symptoms. Sacubitril is a neprilysin inhibitor and is an effective medical therapy in the end-stage heart failure patients. The combination of sacubitril and valsartan was highly recommended in recent clinical guidelines which issued heart failure patients (4). Clinical data about the effects of sacubitril/valsartan combination in COVID-19 infected heart failure patients who are already on this specific therapy is limited (5). In this report, we aimed to present the clinical follow-up of a patient with COVID-19 with relevant laboratory parameters who was already under sacubitril/valsartan therapy for advanced heart failure.

CASE REPORT

A 71 years old female patient was admitted to emergency service with complaints of shortness of breath, fatigue and muscle weakness. Her fever was 38.0° C and her thoracic computed tomography depicted bilateral, patchy, ground-glass areas consistent with COVID-19 viral pneumonia (Fig. 1). C-reactive protein (CRP) was 175.8 mg/L and she had a low lymphocyte level of 710/mm^3 and 5.7% of total white blood cell (WBC) count (Table 1). She was under advanced heart failure treatment for non-ischemic cardiomyopathy as acetylsalicylic acid 1x100 mg, spironolactone 1x25 mg, carvedilol 2x6.25 mg, rosuvastatin 1x10 mg and sacubitril/valsartan 2x97/103 mg. Left ventricular ejection fraction was measured as 34% at admission. She was hospitalized in the intensive care unit, and on the day following the hospitalization, she was entubated because of severe respiratory insufficiency.

We started for COVID-19 viral pneumonia treatment as hydroxychloroquine 2x200 mg, favipiravir (2x1600 mg loading and 2x600 mg maintenance dose), and azithromycin (1x500 mg loading dose and 1x250 mg maintenance dose), and for possible thrombotic complications also enoxaparine 2x4000IU (adjusted dose for renal functions). We did not withdraw her specific treatment for advanced heart failure and sacubitril/valsartan, carvedilol and spironolactone were continued.

The patient was extubated at the 6th day following her index intubation. A marked increase in lymphocyte count was detected at the end of the first week of her hospitalization (Lymphocyte count increased from 710/

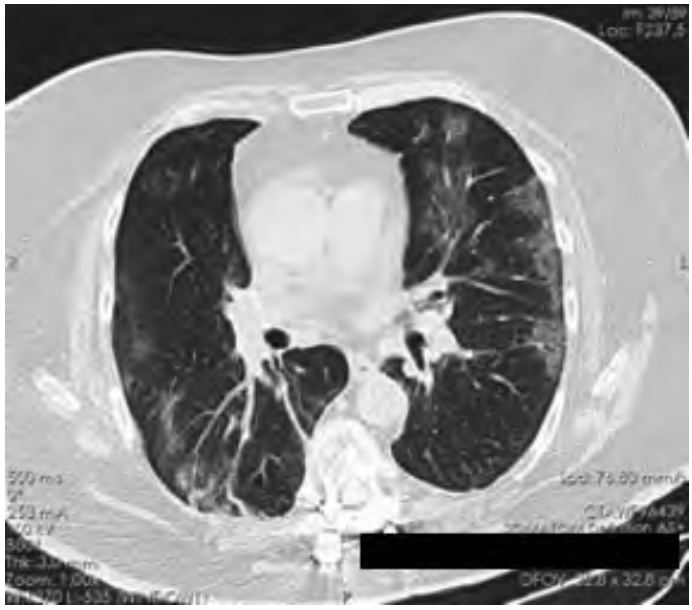

Figure 1. Computerized tomography revealed bilateral, ground-glass, patchy infiltrations compatible with COVID-19 pneumonia

mm^3 to 1530/mm^3 in the peripheral venous blood sample. The patient was discharged at the end of the 11th-day hospitalization without any complication. Patient's consent was obtained for this case study.

DISCUSSION

In preliminary reports, lymphocyte count was defined as an important predictor for worse prognosis in the course of COVID-19 infections and authors recommended the close monitoring of lymphocyte count for the prediction of clinical prognosis (6). Yang et al. (7) even offered the repletion of lymphocytes as an additional solution for the restriction of target-organ damage. Low lymphocyte count was also related to increased incidence for cytokine storm in another study (8). Higher neutrophil to lymphocyte ratios was also related to increased cytokine storm in this study (8). In the light of these evidences, low lymphocyte count should be prevented in the early phase of COVID-19 infection.

Previous studies demonstrated an increment in lymphocyte counts in heart failure patients treated by neprilysin inhibitor (9, 10). Anti-inflammatory effect mainly driven by the protection of lymphocyte count may be an important feature of sacubitril in patients with chronic heart failure. As an additional clinical effect, early administration of neprilysin inhibitor in decompensated heart failure may also result in a decrease in high sensitive C-reactive protein (hs-CRP) levels (9). In our case, we detected an increase in lymphocyte count and a relative decrease in hs-CRP level at the end of the first week after hospitalization. Sacubitril/valsartan may have a possible modulatory role on an anti-inflammatory response, which can result in a better clinical outcome in COVID-19 infection. We need further randomized clinical trials searching for changes in inflammatory markers in the patients with COVID-19 who are already taking sacubitril/valsartan therapy chronically.

Table 1. Clinical parameters of the patient at admission and follow-up

Parameter	At emergency admission	At the end of 1st week following hospitalization
White blood count (K/mm^3)	12.39	11.74
Lymphocyte count (K/mm^3)	0.71	1.53
C-reactive protein (mg/L)	175.8	13.9
QTc interval (ms)	442	437
Systolic blood pressure (mmHg)	89	115
Diastolic blood pressure (mmHg)	47	65
Serum potassium level (mEq/L)	3.6	4.3

CONCLUSION

Directed, specific treatments for chronic diseases, especially for heart failure, should not be withdrawn in COVID-19 infections. Depending on hemodynamic monitorization, sacubitril/valsartan should be continued in patients with heart failure admitted with COVID-19 pneumonia. Additionally, sacubitril/valsartan combination may have positive effects on the clinic with its' anti-inflammatory role mainly driven by an increase in lymphocyte counts and a decrease in the incidence of the cytokine storm.

Informed Consent: Written informed consent was obtained from the patient.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept – AÇ, CA; Design – AÇ; Supervision – CA; Resource – AÇ, CA; Materials – CA0; Data Collection and/or Processing – CA; Analysis and/or Interpretation – AÇ, CA; Literature Search – AÇ; Writing – AÇ; Critical Reviews – CA.

Conflict of Interest: The authors have no conflict of interest to declare.

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REFERENCES

1. Acanfora D, Ciccone MM, Scicchitano P, Acanfora C, Casucci G. Sacubitril/valsartan in COVID-19 patients: the need for trials. Eur Heart J Cardiovasc Pharmacother 2020; 6(4): 253–4. [CrossRef]
2. Iaccarino G, Borghi C, Cicero AFG, Ferri C, Minuz P, Muiesan ML, et al. Renin-angiotensin system inhibition in cardiovascular patients at the time of COVID19: much ado for nothing? A statement of activity from the Directors of the Board and the Scientific Directors of the Italian Society of Hypertension. High Blood Press Cardiovasc Prev 2020;27:105–8. [CrossRef]
3. Zhang P, Zhu L, Cai J, Lei F, Qin JJ, Xie J, et al. Association of inpatient use of angiotensin-converting enzyme inhibitors and angiotensin II receptor blockers with mortality among patients with hypertension hospitalized with COVID-19. Circ Res 2020; 126(12): 1671–81. [CrossRef]
4. Ponikowski P, Voors AA, Anker SD, Bueno H, Cleland JGF, Coats AJS, et al; ESC Scientific Document Group. 2016 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure: The Task Force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC)Developed with the special contribution of the Heart Failure Association (HFA) of the ESC. Eur Heart J 2016;3 7(27): 2129–200. [CrossRef]

5. Petramala L, Letizia C. Response to: Neprilysin inhibitor-angiotensin II receptor blocker combination (sacubitril/valsartan). Eur Heart J Cardiovasc Pharmacother 2020; 6(4): 252. [CrossRef]
6. Acanfora D, Ciccone MM, Scicchitano P, Acanfora C, Casucci G. Neprilysin inhibitor-angiotensin II receptor blocker combination (sacubitril/valsartan): rationale for adoption in SARS-CoV-2 patients. Eur Heart J Cardiovasc Pharmacother 2020; 6(3): 135–6. [CrossRef]
7. Yang X, Yu Y, Xu J, Shu H, Xia J, Liu H, et al. Clinical course and outcomes of critically ill patients with SARS-CoV-2 pneumonia in Wuhan, China: a single-centered, retrospective, observational study. Lancet Respir Med 2020; 8(5): 475–81. [CrossRef]
8. Liu J, Li S, Liu J, Liang B, Wang X, Wang H, et al. Longitudinal characteristics of lymphocyte responses and cytokine profiles in the peripheral blood of SARS-CoV-2 infected patients. EBioMedicine 2020; 55: 102763. [CrossRef]
9. Zhang H, Liu G, Zhou W, Zhang W, Wang K, Zhang J. Neprilysin inhibitor-angiotensin II receptor blocker combination therapy (sacubitril/valsartan) suppresses atherosclerotic plaque formation and inhibits inflammation in apolipoprotein E-deficient mice. Sci Rep 2019; 9(1): 6509–15. [CrossRef]
10. Acanfora D, Scicchitano P, Acanfora C, Maestri R, Goglia F, Incalzi RA, et al. Early initiation of sacubitril/valsartan in patients with chronic heart failure after acute decompensation: A Case Series Analysis. Clin Drug Investig 2020; 40(5): 493–501. [CrossRef]