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CASE REPORT
Heart failure

Evolution of B-type natriuretic peptide and N-terminal pro-brain natriuretic peptide during acute decompensated heart failure in a chronic heart failure patient with reduced ejection fraction treated with Sacubitril/Valsartan: a case report

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Background B-type natriuretic peptide (BNP) and the N-terminal proBNP (NT-proBNP) exhibit different evolution in chronic heart failure patients with reduced ejection fraction treated with Sacubitril/Valsartan; BNP increasing or remaining stable, while NT-proBNP decreases. However, how this difference translates upon acute decompensation is unknown.

Case summary Herein, we described in a 78-year-old woman with chronic heart failure with reduced ejection fraction treated with Sacubitril/Valsartan who had acute decompensated heart failure (ADHF). BNP and NT-proBNP were markedly high during ADHF and showed parallel return to baseline level after clinical improvement.

Discussion BNP and NT-proBNP retained similar value for the diagnosis of ADHF in patient treated with Sacubitril/Valsartan. These findings strongly suggest that either BNP or NT-proBNP can be used indifferently in this context, while their relative use is debated in chronic heart failure.

Keywords BNP • NT-proBNP • Acute decompensated heart failure • Sacubitril/Valsartan • Case report

Learning points

- In acute decompensated heart failure (ADHF), B-type natriuretic peptide (BNP) and the N-terminal proBNP appeared to retain similar increase and evolution in a heart failure with reduced ejection fraction patient treated with Sacubitril/Valsartan, suggesting that either peptide could be used to screen for ADHF with similar diagnostic performance.

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Introduction

Sacubitril/Valsartan is a first-in-class combination of angiotensin receptor blocker and neprilysin inhibitor. Sacubitril/Valsartan is now recommended for the treatment of chronic heart failure with reduced ejection fraction (HFrEF) that remains symptomatic despite optimal treatment as per international guidelines.[1] In chronic HFrEF treated with Sacubitril/Valsartan, immunoreactive B-type natriuretic peptide (BNP) remained stable in the following months despite improved risk of death, while N-terminal proBNP (NT-proBNP) decreased by ∼20%.[2,3] While the discrepant response of BNP and NT-proBNP was attributed to different sensitivity of the two peptides to neprilysin degradation, the increase in BNP most likely results from an increase in proBNP glycosylation[2,4] rather than the protection of BNP from neprilysin degradation,[5] although further studies are warranted to clarify this aspect. However, the progression of BNP and NT-proBNP in patients receiving Sacubitril/Valsartan during acute decompensated heart failure (ADHF) is not known.

Timeline

Timeline	Events
A year before admission	Progression of heart failure with reduced ejection fraction Multiple acute hypertensive events requiring unplanned visit to cardiologist
Three months before admission	Introduction of Sacubitril/Valsartan
Clinical presentation at admission	Stroke leading to an hypertensive non-ischaemic decompensation of heart failure • Systolic blood pressure: 180 mmHg, diastolic blood pressure: 110 mmHg • Pulmonary oedema • Normal electrocardiogram • Left ventricular ejection function: 25%, left ventricular end-diastolic diameter: 63 mm, *E*/*A*: 2.4, and *E*/*E*′: 17
Cardiac biomarkers	B-type natriuretic peptide (BNP): 4208 pg/mL (<100 pg/mL) N-terminal proBNP (NT-proBNP): 8240 pg/mL (<300 pg/mL) High-sensitivity troponin T: 9 ng/L (<14 ng/L)
Six days after effective treatment	Clinical improvement of acute decompensated heart failure Parallel decrease in biomarkers, including BNP and NT-proBNP

Case presentation

A 78-year-old Afro-Caribbean woman was hospitalized for ADHF as a consequence of a stroke. She had a history of hypertension, chronic HFrEF, aortic and mitral insufficiency, and chronic kidney disease (glomerular filtration rate: 45 mL/min/1.73 m^2). Her last echocardiography, 2 years prior to presentation, found a left ventricular end-diastolic diameter (LVEDD) at 65 mm, left ventricular ejection function (LVEF) at 35%, restrictive diastolic dysfunction, pulmonary blood pressure (BP) at 55 mmHg, and an aortic and mitral insufficiency grade 2. BNP before Sacubitril/Valsartan—i.e. 3 month before her current admission—was ∼200 pg/mL. During the last year, she had three episodes of acute dyspnoea due to hypertension that required unplanned visits to her cardiologist without hospitalization. At the last visit, her cardiologist introduced Sacubitril/Valsartan. The introduction of Sacubitril/Valsartan occurred 3 months before her hospitalization for stroke, with an improvement in symptoms and without alteration of renal function. At the time of hospitalization, treatment was: Sacubitril/Valsartan 24/26 mg in the morning, Furosemide 40 mg per day, Bisoprolol 5 mg b.i.d., Allopurinol 100 mg b.i.d.

The patient was admitted for a right hemiplegia caused by a stroke, which provoked an abrupt rise in BP (systolic BP: 180 mmHg, diastolic BP: 110 mmHg) leading to a concomitant acute pulmonary oedema (APE).[6–8] She had hypoxaemic respiratory distress (dyspnoea, polypnoea, and crackles), and electrocardiogram showed a regular sinus rhythm without ischaemic sign confirmed by normal plasma level of high-sensitivity troponin T [9 ng/L (normal <14 ng/L)]. Chest X-ray showed bilateral alveolo-interstitial syndrome. Echocardiography showed a 25% LVEF, increased filling pressures (*E*/*A* 2.4 and *E*/*E*′ 17), known aortic and mitral insufficiency, and a LVEDD of 63 mm. At admission, measurements of immunoreactive BNP and NT-proBNP were 4208 pg/mL (normal <100 pg/mL) and 8240 pg/mL (normal <300 pg/mL), respectively. Other biological results at admission showed limited cholestasis [alkaline phosphatase: 189 UI/L (normal: 35–104 UI/L), γ-glutamyltransferase: 124 UI/L (normal 5–36 UI/L)] and worsened renal function [creatinine: 135 µmol/L (normal: 44–80 µmol/L)], reflecting moderate right heart congestion. Clinical, biological, and echocardiographic parameters led to a diagnostic of non-ischaemic ADHF, secondary to the sympathetic surge provoked by the stroke. Faced with respiratory distress, the patient received urgent APE treatment[1]: intravenous (IV) bolus of Furosemide (80 mg) and Urapidil continuous infusion (30 mg/h) for 2 days, followed by oral intake afterwards (40 mg Furosemide once a day and 60 mg Urapidil three times a day). Dyspnoea was relieved within 2 h, allowing cerebral magnetic resonance imaging (MRI) to be performed. Cerebral MRI showed a left middle cerebral artery stroke with thrombus in this artery which was successfully treated by thrombectomy followed by treatment with acetylsalicylic acid (75 mg o.d.). Cardiac clinical symptoms improved and biology returned to baseline values, allowing discharge from intensive care unit at 6 days. Importantly, Sacubitril/Valsartan treatment was continued during hospitalization, the patient receiving 24/26 mg Sacubitril/Valsartan every morning after blood work. BNP, NT-proBNP, and circulating neprilysin (cNEP) activity were measured from samples collected every morning prior the intake of Sacubitril/Valsartan during hospitalization (*Figure 1*). Both BNP and NT-proBNP were high at admission and showed paralleled decrease up to discharge. Circulating neprilysin activity remained constant and low throughout the hospitalization.

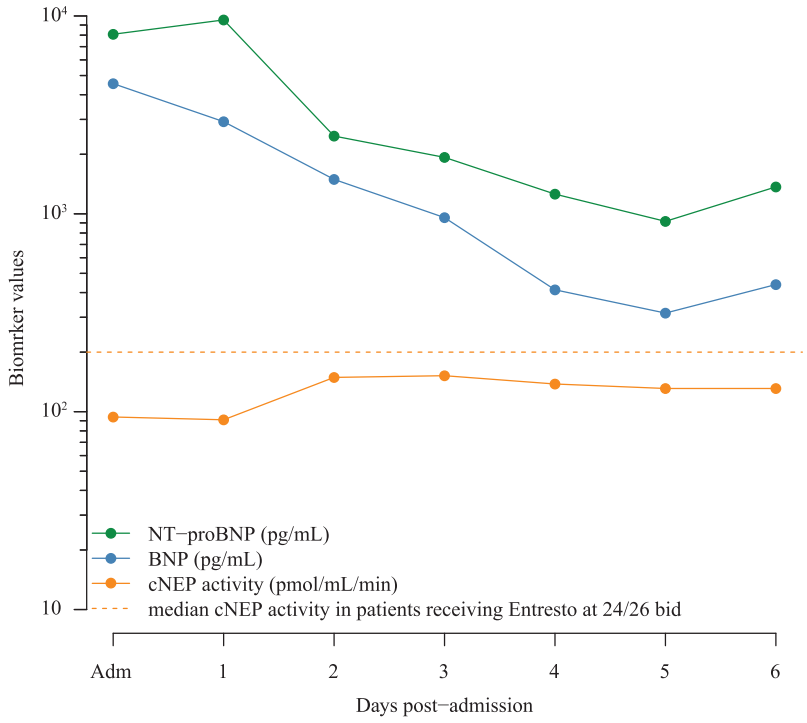


Figure 1 Temporal evolution of BNP, NT-proBNP and cNEP activity from admission (Adm) to discharge (Day 6). Dotted orange line represents the median value of cNEP activity in patients receiving 24/26 mg Sacubitril/Valsartan bid.[2]

The patient was then transferred to the neurology and rehabilitation department where she stayed 2 months. She was not specifically subjected to a cardiology follow-up but did not suffer from any cardiovascular event. As her neurological condition improved, she was released and follow-up stopped at this time.

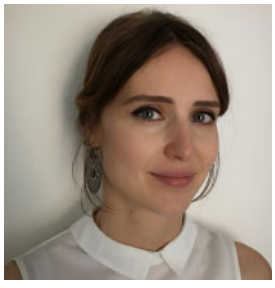
Discussion

Here, we present the first case showing the evolution of BNP and NT-proBNP in ADHF in a patient receiving Sacubitril/Valsartan as her treatment for HFrEF. Both BNP and NT-proBNP retained similar values for the diagnostic of hypertensive ADHF—and probably ADHF in general—in patients treated with Sacubitril/Valsartan. Even though the patient was taking a low dose of Sacubitril/Valsartan (half the minimum dose), cNEP activity was low and below the median threshold found in patients receiving Sacubitril/Valsartan 24/26 mg b.i.d.,[2] strongly suggesting the pharmacological efficacy of her treatment over a 24 h period. Of note, the pharmacological efficacy of such a low dose of Sacubitril/Valsartan could be explained by her chronic renal failure since ~50% of sacubitrilate—the active metabolite of Sacubitril—is eliminated in the urine.[9]

Conclusion

In conclusion, BNP and NT-proBNP can most likely be used equivalently for the diagnostic of ADHF in patients receiving Sacubitril/Valsartan even though studies are warranted to establish whether BNP and NT-proBNP retain similar diagnostic performance in this context.

Lead author biography



Ambre Tiepolo completed her medical studies at the University of Paris Sorbonne and holds a diploma in cardiovascular ultrasound. She is currently a hospital practitioner in the intensive care unit at the Lariboisière university Hospital in Paris. She is also a research fellow in the cardiovascular endocrinology group in Inserm research unit UMR-S 942.

Supplementary material

Supplementary material is available at *European Heart Journal - Case Reports* online.

Slide sets: A fully edited slide set detailing this case and suitable for local presentation is available online as Supplementary data.

Consent: The author/s confirm that written consent for submission and publication of this case report including image(s) and associated text has been obtained from the patient in line with COPE guidance.

Conflict of interest: none declared.

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