Annals of Orthopaedics, Trauma and Rehabilitation

Case Report

Drug-Induced Gout with Neprilysin Inhibitors

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ARTICLE INFO

Received Date: May 17, 2018
Accepted Date: May 31, 2019
Published Date: June 03, 2019

KEYWORDS

Gout
Side-Effects
Neprilysin Inhibitor
Heart Failure

Citation for this article: Vantard M, Ramon A, Dautriche A, Laroche D and Ornetti P. Drug-Induced Gout With Neprilysin Inhibitors. Annals of Orthopaedics, Trauma and Rehabilitation. 2019; 2(1):129

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INTRODUCTION

A number of pharmacological drugs can induce hyperuricemia, and sometimes gout, usually by interfering with the renal tubular excretion of urate but also by increasing the formation of uric acid. We report the case of a 74-year-old patient hospitalized for refractory gout-related polyarthritis despite treatment by allopurinol at maximum dose concomitant with the introduction of Entresto®, which is an association of the neprilysin inhibitor Sacubitril [1] and the angiotens in receptor blocker (ARB, not known to influence hyperuricemia)[2].

This neprilysin inhibitor is part of a new class of therapies used in the third line of chronic heart failure with compromised left ventricular ejection fraction (<35%) [3,4]. The patient was being monitored for arrhythmic cardiomyopathy which led to severe heart failure and was taking Furosemide and spironolactone for five years, without history of hyperuricemia or gout. The patient reported that the gout flare-ups were concomitant with the initiation of Entresto®, associated with a progressive increase in serum uric acid level until 470 micromole/l despite initiation of urate-lowering therapy by allopurinol up to the maximum dose, in association with colchicine. Corticosteroid treatment (per os + injections) was used to control the flare-up during hospitalization, and the patient was then given febuxostat knowing that treatment with the neprilysin inhibitor could not be stopped. A partial response to febuxostat was observed, with decrease of uric acid level and frequency of acute gout attacks.

Entresto® was retained as the source of hyperuricemia in this patient in view of the sequence of events, and the case was documented in the French national pharmacovigilance bank. The risk of gout is not mentioned in the product characteristics for the combination of Neprilysin inhibitor and fixed-dose ARB, nor are there any published cases [4,5]. However, 6 other cases involving neprilysin inhibitors have already been reported in the French national pharmacovigilance bank since these drugs arrived on the market in 2016. The most detailed case was that of an 80-year-old patient, with no gout, who was under long term treatment with bisoprolol, amiodarone, spironolactone and furosemide. Three days after the introduction of Entresto®, the patient had a gout flare-up that persisted despite the discontinuation of furosemide and the introduction of colchicine. The gout did not respond to treatment with febuxostat.

Though the exact mechanism has not yet been established, this hyperuricemic effect of Sacubitril may potentially be a result of its diuretic effects, similar to the effects of thiazide or furosemide, by reducing urate excretion by both directly and indirectly increasing urate reabsorption and decreasing urate secretion. Moreover, caution should be exercised when these drugs are used in combination with NSAIDs and colchicine in the elderly and/or patients with impaired renal function, since there is a risk of further deterioration in renal function [3,6]. The potential risk of drug interaction between urate-lowering therapy (allopurinol, febuxostat) and sacubitril via cytochrome CYP450 appears limited [1,7] but cannot be excluded. Going forward, physicians should be familiar with this new heart failure drug given its potential side-effect on hyperuricemia and gout.

DISCLOSURE

The authors report no financial disclosure or potential conflicts of interest or funding source.

REFERENCES

1. Havakuk O, Elkayam U. (2017). Angiotensin Receptor-Neprilysin Inhibition. J Cardiovasc Pharmacol Ther. 22: 356-364.
2. Wolff ML, Cruz JL, Vanderman AJ, Brown JN. (2015). The effect of angiotensin II receptor blockers on hyperuricemia. Ther Adv Chronic Dis. 6: 339-346.
3. McCarthy CP, McEvoy JW. (2017). Let Us Not Forget the Long-term Safety Concerns of Sacubitril/Valsartan. JAMA Cardiol. 2: 818-819.
4. Tyler JM, Teerlink JR. (2017). The safety of sacubitril-valsartan for the treatment of chronic heart failure. Expert Opin Drug Saf. 16: 257-263.
5. Joly JM, Desai AS. (2018). Sacubitril/Valsartan: From Clinical Trials to Real-world Experience.Curr Treat Options Cardiovasc Med. 20: 45.
6. Hua Y, Wang I, Liu B, Kelly DJ, Reid C, et al. (2017). Angiotensin receptor neprilysin inhibitor LCZ696: pharmacology, pharmacokinetics and clinical development.Future Cardiol. 13:103-115.
7. Cayot A, Laroche D, Disson-Dautriche A, Arbault A, Maillefert JF, et al. (2014). Cytochrome P450 interactions and clinical implication in rheumatology. Clin Rheumatol. 33: 1231-1238.