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LETTER TO THE EDITOR

Febuxostat for hyperuricemia: experience with patients on chronic hemodialysis treatment

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To the Editor

Febuxostat a non-purine xanthine oxidase inhibitor, which recently received marketing approval, has used as an option for the treatment of hyperuricemia because it undergoes hepatic metabolism and may require less dose adjustment in association with renal function [1]. However, information regarding the therapeutic benefit of such an agent among chronic kidney disease (CKD) patients is limited. We would like to present our experience with five cases of chronic hemodialysis (HD) patients whose hyperuricemia was successfully treated by oral febuxostat with no apparent adverse events. All patients were male with an average age of 66.6 ± 18.5 years. No urate lowering agents (ULTs) had been used in the three out of five patients and the other two patients were switched from oral allopurinol to febuxostat. No one reported previous gout attacks. Patients 1–3 were placed on 10 mg febuxostat daily, while patients 4 and 5 were administered 20 mg/day febuxostat. The average values of the serum uric acid (UA) levels just before and after the initiation of oral febuxostat were 10.1 ± 0.9 mg/dl (mean ± SD) and 6.2 ± 0.9 mg/dl ($p = 0.0014$), respectively (Fig. 1). No acute gout flares were reported during a four-month follow-up, and the serum UA level remained at most around 6.0 mg/dl without any significant changes in laboratory profiles and clinical signs. Patient 5 showed a marked reduction in serum UA level to 1.3 mg/dl, and febuxostat was discontinued, and his serum UA levels were finally maintained around 4.0–6.0 mg/dl by febuxostat with a post dialysis dose of 10 mg three times a week.

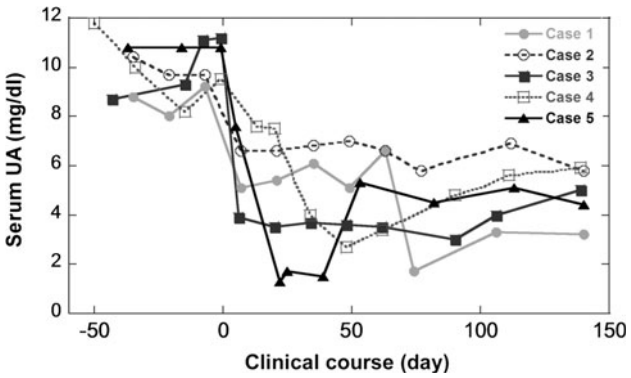

Fig. 1 The longitudinal changes in the serum UA level before and after the administration of oral febuxostat in each patient. Day 0 is designated as the point when the oral febuxostat was initiated. Before the initiation of oral febuxostat, patients 3 and 4 had been treated with oral allopurinol 100 and 50 mg/day, respectively. Note that there is a patient (Case 5) with a marked reduction in serum UA level of 1.3 mg/dl after the initiation of 20 mg/day oral febuxostat

The current observations suggest that even relatively low doses of febuxostat, which is approved at a dose of 40–60 mg/day as the standard dosages for the treatment of hyperuricemia with gouty arthritis in Japan, may work effectively among chronic HD patients for the prompt reduction of serum UA at a level that has been arbitrarily proposed as a therapeutic target for hyperuricemia [2, 3].

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Previous observations demonstrating the significant association between higher serum UA levels and lower mortality among HD patients, which may be dependent on the favorable nutritional status [4], do not preclude us from pursuing further investigations regarding the clinical significance of lowering the serum UA with febuxostat in terms of the concomitant reduction of oxidative stress by the blockade of xanthine oxidase [5]. Although the validity of the treatment with ULTs in asymptomatic patients with hyperuricemia (a serum UA level higher than 8 mg/dl), which has been recommended and applied in Japan, remains to be delineated, we should bear in mind that the prevalence of refractory gout and/or gouty tophi is much lower in Japan in comparison to that in the US and Europe, where negative opinions regarding pharmaceutical interventions predominate [2]. Apparently, the clinical impact of febuxostat on the overall management of asymptomatic hyperuricemia associated with CKD needs to be evaluated in greater detail, and the optimal serum UA levels and dosage of febuxostat for chronic HD patients should be determined.

Conflict of interest None declared

References

1. Hosoya T, Ono I. A repeated oral administration study of febuxostat (TMX-67), a non-purine-selective inhibitor of xanthine oxidase, in patients with impaired renal function in Japan: pharmacokinetic and pharmacodynamic study. J Clin Rheumatol. 2011;17(4 suppl 2):S27–34.
2. Yamanaka H; Japanese Society of Gout and Nucleic Acid Metabolism. Japanese guideline for the management of hyperuricemia and gout: second edition. Nucleosides Nucleotides Nucleic Acids. 2011;30:1018–29.
3. El-Zawawy H, Mandell BF. Managing gout: how is it different in patients with chronic kidney disease? Cleve Clin J Med. 2010;77:919–28.
4. Latif W, Karaboyas A, Tong L, Winchester JF, Arrington CJ, Pisoni RL, Marshall MR, Kleophas W, Levin NW, Sen A, Robinson BM, Saran R. Uric acid levels and all-cause and cardiovascular mortality in the hemodialysis population. Clin J Am Soc Nephrol. 2011;6:2470–7.
5. Tsuda H, Kawada N, Kaimori JY, Kitamura H, Moriyama T, Rakugi H, Takahara S, Isaka Y. Febuxostat suppressed renal ischemia-reperfusion injury via reduced oxidative stress. Biochem Biophys Res Commun. 2012;427:266–72.