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Febuxostat Use and the Risk of the Adverse Clinical Outcomes in Patients with Diabetic Nephropathy

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Background: Although several studies demonstrated that reducing uric acid level by allopurinol could be beneficial clinical effects in patients with chronic kidney disease, the long-term safety of febuxostat, which is a drug that inhibits xanthine oxidase, in patients with progressive kidney disease is not fully investigated. Thus, this study was proposed to investigate the clinical impact of the febuxostat in patients with diabetic nephropathy.

Methods: From 2004 to 2015, 972 patients who diagnosed with diabetic nephropathy were identified from the Yonsei University Health System. The patients were divided into two groups based on the use of febuxostat. The use of febuxostat was defined as the patients being taken more than 90 days of febuxostat during follow up period. The primary outcome is all-cause mortality, incident major adverse cardiac and cererovascular events (MACCEs), and end-stage renal disease (ESRD). MACCEs included cardiovascular events, cerebrovascular events and peripheral vascular disease.

Results: The mean age was 60.1±13.3 years, and 582 patients (59.9%) were male. Among 972 patients who diagnosed with diabetic nephropathy, 152 (15.6%) patients were classified as the febuxostat user. The febuxostat users were significantly older (65.9±13.2 vs 59.0±13.1 years, P<0.001) and higher uric acid (7.1±2.1 vs 5.3±1.7 mg/dl, P<0.001), while estimated glomerular filtration rate (eGFR) was significantly lower (52.3±24.8 vs 75.1±23.0 ml/min/1.73m^2, P<0.001) in febuxostat user group. During a mean follow-up duration of 45.4±29.3 months, all-cause mortality, MACCEs, and ESRD were observed in 62 (6.4%), 221 (22.7%), and 128 (13.2%) patients, respectively. In multiple Cox regression analysis, febuxostat user did not showed the differences with all-cause mortality (hazard ratio [HR], 0.901; 95% confidence interval [CI], 0.331-2.454, P=0.838) and MACCEs (HR, 1.151; 95% CI, 0.655-2.023, P=0.624), while the incidence of ESRD was significantly higher in febuxostat user group compared to the non-user (HR, 1.950; 95% CI, 1.062-3.581, P=0.031) after adjustment for age, sex, history of hypertension, uric acid, hemoglobin, phosphate, serum albumin, tCO2, total cholesterol, eGFR, urine albumin-to-creatinine ratio, and the use of allopurinol.

Conclusion: In present analysis, febuxostat user showed significantly higher incidence of ESRD in patients with diabetic nephropathy. These findings suggest that the use of febuxostat can be a hazard effect in progression of diabetic nephropathy.

Keywords: Diabetic Nephropathy, End-stage renal disease, Febuxostat