

Renal Adverse Effects of Sunitinib

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Recently, agents that inhibit vascular endothelial growth factor (VEGF), including bevacizumab, sunitinib and sorafenib were introduced in clinical practice. Although renal adverse effects of bevacizumab were well known, those of sunitinib are still rarely described. We therefore investigated the adverse renal effect of sunitinib such as proteinuria and renal dysfunction.

We performed a retrospective medical record analysis of patients who had received sunitinib for more than 3 months from November 2005 to February 2011. Patients with renal parenchyme invasion or obstructive uropathy were excluded. Proteinuria was defined as $\geq 2+$ protein on urine dipstick test and aggravation of preexisting proteinuria was defined as an increase of 2 grade or more on dipstick test or more than 2 fold increase on urine protein creatinine ratio (uPCR). Renal insufficiency (RI) was defined as an increase 50% or 0.5 mg/dL in serum creatinine (sCr) level and eGFR < 60 ml/min /1.73m² or sCr > 1.4 mg/dL.

153 patients (mean age; 59 ± 1.02 year-old, male:female; 78:22) were enrolled and underlying diseases were renal cell carcinoma and transitional cell carcinoma (81%), gastrointestinal stromal tumor (12.4%), thyroid cancer (2.6%), lung cancer (1.3%), gliomatosis cerebri (1.3%), hepatocellular carcinoma (1.3%) and angiosarcoma (0.7%). The mean baseline creatinine of the patients was 1.24 mg/dL. Proteinuria was developed in 19/117 (16.2%) patients and preexisting proteinuria was aggravated in 10/117 (8.6%) patients after the start of sunitinib. Following discontinuation of sunitinib, proteinuria was improved or disappeared in 20/29 (68.9%) patients but persistent in 9/29 (31.0%) patients. Risk factors for proteinuria were dyslipidemia and renal insufficiency at the start of sunitinib ($p < 0.05$). RI was detected in 17 (11.1%) patients after the start of sunitinib and maximum Cr was 5.1mg/dl. Risk factors for RI were previous adjuvant chemotherapy and nephrectomy ($p < 0.05$). RI was improved in 3 patients (17.7%), but persisted in 14 patients (82.4%) after the cessation of sunitinib. Although clinical significance of renal adverse effects of sunitinib is still uncertain, proteinuria and renal dysfunction were more common than previously reported. Regular monitoring of proteinuria and renal dysfunction should be considered in patients who are on sunitinib.

Key Words: Sunitinib, Tyrosine kinase inhibitor, Nephrotoxicity