Therapeutic Drug Monitoring on the Safety of Sirolimus in Transplant Patients

Transplant Hastalarında Sirolimusun Güvenliğine Yönelik Terapötik İlaç İzlemi

Edibe Minareci

I read a case report on new-onset diabetes mellitus in five renal transplant recipients [1]. The authors highlighted sirolimus treatment as a reason for new-onset diabetes after transplantation (NODAT). They reported discrepancies regarding the mechanism of sirolimus-induced diabetes mellitus in the literature.

Sirolimus is an immunosuppressive agent that blocks the molecular target of rapamycin (mTOR inhibitor) [2]. This blockade leads to the inhibition of T- and B-cell proliferation and immunoglobulin production. The pharmacokinetics of sirolimus differs from that of other immunosuppressive drugs. This agent has a low bioavailability (14%) and high protein-binding ratio (92%) and undergoes extensive hepatic and intestinal metabolism via CYP3A4 and CYP3A5 [3]. Further, it has an excretion by p-glycoprotein. Hence, significant drug interactions can occur [4].

Therapeutic drug monitoring (TDM) is a useful tool required in these situations. Yılmaz et al. [1] reported that renal transplant patients were taking multi-drug treatment including antithymocytes, mycophenolate mofetil, prednisolone, and oral antidiabetics (the detailed drug regimen for cases 2, 3, 4, and 5 is not given). In this condition, prednisolone treatment is another important risk factor for diabetes mellitus development and especially for the drug–drug interaction with sirolimus. Steroids are well-known CYP3A4 and 3A5 inducer drugs [5]. In this case, TDM for serum concentrations of sirolimus were strongly recommended because it is incongruous to mention that sirolimus reached therapeutic concentrations in the combination treatment with steroid without using TDM.

The high variability in the pharmacokinetics of sirolimus makes TDM essential for individualizing the dose and thereby preventing toxicity and adverse events in transplant patients. Then, it will be justified to say that sirolimus treatment is the only reason for NODAT.

Peer-review: Externally peer-reviewed.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this case has received no financial support.

References