

Dietary Supplements – Harmless or Hazardous? An Unexpected Tango of Turmeric and Tacrolimus in Transplant Recipients

Mr Tristan Williams¹, Dr Joyce Popoola^{1,2}

¹Department of Nephrology and Renal Transplantation, St George's University Hospitals NHS Foundation Trust, London, United Kingdom, ²Centre for Clinical Education, St George's University, London, United Kingdom

Tacrolimus a calcineurin inhibitor is often used as an immunosuppressant post solid organ transplants (1). Therapy requires careful monitoring due to its narrow therapeutic index. It is largely metabolised by hepatic CYP3A4 enzymes leading to potential for interactions with other medication, herbal supplements and food. Concentrations are reduced by CYP3A4-inducers like rifampicin, phenytoin and herbal remedies (e.g. St John's Wort), risking sub-therapeutic blood concentrations and graft rejection. Conversely CYP3A4-inhibitors such as azole-antifungals, macrolide-antibiotics, calcium channel blockers, herbal remedies (e.g. Schisandra sphenanthera) and grapefruit juice increase concentrations risking toxicity. (2)

Several herbal remedies and supplements are being widely advocated as a part of a healthy life style or as non-medical remedies for ailments. Turmeric, an Asian spice/food colouring and traditional medicine is used for conditions including indigestion, arthritis, biliary disorders, peptic ulcers, ulcerative colitis, cancer, dementia, depression, diabetes and hypercholesterolemia.(3-5).

Here we report a case series of raised tacrolimus/creatinine concentrations associated with increased ingestion of turmeric. This was first noted in Patients 1 and 2 (husband and wife) in a routine renal transplant clinic. Both had sudden serum tacrolimus and creatinine rises around the same time. A subsequent consultation revealed they had started using turmeric in their home cooking weeks leading up to their clinic appointments. Following turmeric avoidance and temporal dose adjustments blood tacrolimus and creatinine concentrations returned to therapeutic range for both patients. A third and fourth patient who had abrupt tacrolimus concentration rises were found to be sprinkling turmeric on food and/or using it to make tea. Following tacrolimus dose reduction and advice to avoid using excessive amounts of turmeric blood tacrolimus concentrations also returned to therapeutic range.

It has been suggested that turmeric moderately inhibits the action of hepatic CYP3A4 enzyme. In an animal model study the AUC values of tacrolimus in rats pre-treated with grapefruit, ginger or turmeric juice were significantly larger than those pre-treated with water. A further study found that pretreatment with turmeric increases the plasma levels of tacrolimus in a murine model. In one published case a tacrolimus concentration of 29 ng/ml was recorded, leading to nephrotoxicity, following ingestion of '15 spoonfuls' of turmeric a day for ten days prior to testing. (5) The curcumin component of turmeric has been reported to alter function and expression of P-gp and CYP3A enzymes, however the clinical relevance of this remains unclear. (6,7)

The risk of drug-drug interactions with tacrolimus is well documented and common knowledge amongst healthcare professionals. However herbal medication and supplements are often overlooked or their use goes unreported by the patient. The risks are often not considered by the patients using them. Given that food supplements such as turmeric could have an effect on tacrolimus concentrations it is vital that patient's medications are reviewed regularly. This should include any over-the-counter, herbal remedies and supplements. Patients should receive regular education to ensure that they are vigilant and that they seek advice from a healthcare professional before taking any supplementary medications. Healthcare professionals also need to have awareness of seemingly harmless fads.