

## Cannabidiol & calcineurin inhibitors- A not so benign interaction

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Cannabidiol (CBD) oil is increasingly available as an herbal or over-the-counter supplement with widespread use. Like many non-regulated supplements many patients and healthcare professionals may perceive it to be a benign adjunct to pain control.

A patient with established renal failure due to focal segmental glomerulosclerosis underwent a renal transplant in the 1990s. He attended his routine transplant clinic appointment complaining of chronic joint pain arising from his gouty tophi along with a tremor and difficulty sleeping. Further discussion revealed that in addition to his regular medications, which included tacrolimus, mycophenolate mofetil and prednisolone, he had recently started taking CBD oil. He was unaware of the exact dose and had not sought medical advice before commencing CBD oil but felt that it had vastly improved his quality of life with amelioration of his tremor, pain and poor sleep.

Routine blood tests performed at the time of clinic demonstrated an acute kidney injury with his creatinine rising to 242  $\mu\text{mol/L}$  from a baseline of 190, there was a concomitant rise in his tacrolimus levels (13.8  $\mu\text{g/L}$ ). Tacrolimus levels and renal function returned to a prior baseline with cessation of CBD oil.

Cannabidiol (CBD) oil is available widely in the UK including in health food shops; it is different from medical cannabis. Studies have shown that CBD inhibits cytochrome P450 3A4 (CYP3A4), the same system that metabolizes tacrolimus.<sup>1</sup> Therefore, theoretically, use of cannabidiol alongside a CYP3A4 substrate like tacrolimus, will increase blood levels of tacrolimus and may increase the risk of adverse effects. The interaction between CBD oil and calcineurin inhibitors is not predictable as the concentration of CBD oil varies widely.

The use of herbal supplements is not recommended in transplant recipients due to the lack of data on their safety, efficacy and inter-batch variability. Supplements may be either directly nephrotoxic or interfere with the metabolism of immunosuppressants. There is minimal formal pharmacokinetic data on interactions between calcineurin inhibitors and CBD oil but patients using tacrolimus, ciclosporin or sirolimus should be advised against using CBD oil.

### References

1. Yamaori S, Ebisawa J, Okushima Y, Yamamoto I, Watanabe K. Potent inhibition of human cytochrome P450 3A isoforms by cannabidiol: Role of phenolic hydroxyl groups in the resorcinol moiety. *Life Sci.* 2011;88(15-16):730-736. doi:10.1016/j.lfs.2011.02.017