Pharmacy Department

Medicinal Cannabis – the breakthrough learnings

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Objective:

To highlight a potential pharmacological interaction between plant-derived Cannabidiol (CBD) and the combined oral contraceptive pill (COCP)

Clinical Features:

A 16 year old female with background of severe refractory seizures was commenced on CBD as adjunct therapy to her current anti-epileptic medications.

CBD was introduced slowly with up titration over several weeks.

Two weeks later the patient experienced breakthrough menstrual bleeding as reported by her mother to the pharmacist. A COCP had previously provided good menstrual control over the past two years with no unplanned breakthrough bleeding.

Pharmacist Interventions:

Investigate possible interaction:

The timing of the breakthrough bleeding coinciding with CBD commencement and previous history of well controlled menstruation with the COCP raised suspicion of a drug-drug interaction between CBD and the COCP.

Information on pharmacological interactions between CBD and other medications is extremely limited. Literature searches and investigational brochures from manufacturers of CBD products were required to investigate this issue.

CBD appears to be metabolised primarily through the CYP450 pathway. Information available suggests:

- Possible inhibition of CYP1A2, CYP2B6, CYP2C19 and CYP3A4 substrates demonstrated in animals, humans and in vitro studies
- Possible induction of CYP1A2, CYP2B6 and CYP3A4 substrates demonstrated predominantly from in vitro studies

The COCP used is a CYP3A4 substrate therefore the assumption was made that CBD could have potentially induced metabolism of the COCP reducing its effectiveness on menstrual control.

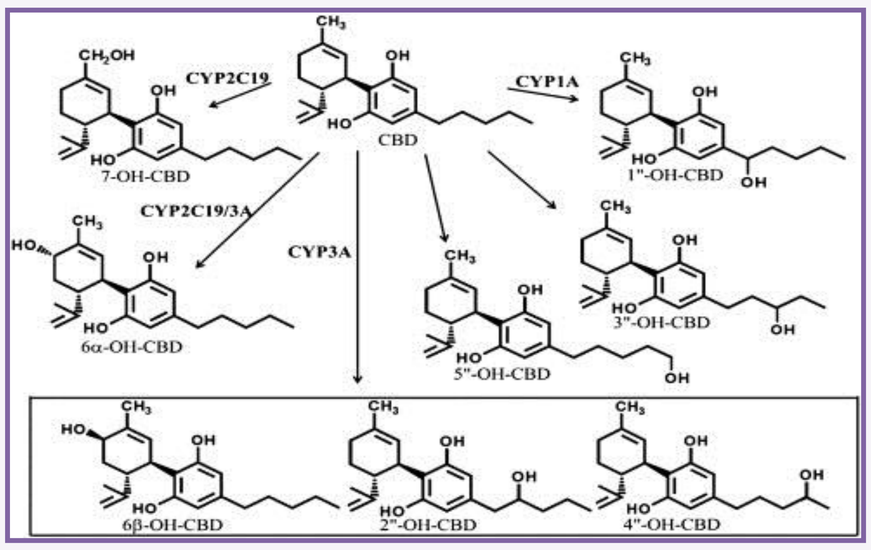
Report potential interaction:

The suspected interaction was reported to the TGA, the state health department and product manufacturer for further consideration.

Recommendations for interaction management:

The potential interaction was discussed with the CBD prescriber, the patient's GP and patient's parents. The pharmacist recommended switching the COCP to a progesterone only product (POP) such as the progesterone only pill or a progesterone depot injection for ongoing menstrual control as it would not be expected to have the same interaction potential.

Using a patient centred approach the pharmacist advised the GP and family to discuss the options and decide what suited the family best.



Case outcome:

Two weeks after changing from the COCP to a POP the mother reported breakthrough bleeding had slowed and at that time the patient had experienced two full breakthrough free days. Ongoing follow up has shown continuous control over patients menstruation with no unplanned breakthrough bleeding reported by the parents.

"The involvement of CYP in (CBD's) metabolism is clear and undisputable, whereas the clinical significance of their drug-drug interactions has yet to be evaluated in detail"[1]

Conclusions:

This case demonstrates that although medicinal cannabis is portrayed publically as a safe treatment option for patients with severe refractory epilepsy, there is still much to be learnt about CBD interactions with other medications.

A Pharmacist can play a critical role in identification and management of potential interactions by reviewing mechanisms of metabolism and making recommendations for treatment changes.

References:

1. Zendulka et al. Cannabinoids and Cytochrome P450 Interactions. Current Drug Metabolism. 2016. [Viewed 2017 Oct 3]. 17(3):206-226