

The Association Between CYP2C19 Gene Distribution and Medical Cannabis Treatment

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Abstract : Introduction: As the legal use of cannabis is being widely accepted throughout the world, medical cannabis has been explored in order to become an alternative cure for patients. Tetrahydrocannabinol (THC) and Cannabidiol (CBD) are natural cannabinoids found in the Cannabis plant which is proved to have positive treatment for various diseases and symptoms such as chronic pain, neuropathic pain, spasticity resulting from multiple sclerosis, reduce cancer-associated pain, autism spectrum disorders (ASD), dementia, cannabis and opioid dependence, psychoses/schizophrenia, general social anxiety, posttraumatic stress disorder, anorexia nervosa, attention-deficit hyperactivity disorder, and Tourette's disorder. Regardless of all the medical benefits, THC, if not metabolized, can lead to mild up to severe adverse drug reactions (ADR). The enzyme CYP2C19 was found to be one of the metabolizers of THC. However, the suballele CYP2C19*2 manifests as a poor metabolizer which could lead to higher levels of THC than usual, possibly leading to various ADRs. Objective: The aim of this study was to investigate the distribution of CYP2C19, specifically CYP2C19*2, genes in Thai patients treated with medical cannabis along with adverse drug reactions. Materials and Methods: Clinical data and EDTA whole blood for DNA extraction and genotyping were collected from patients for this study. CYP2C19*2 (681G>A, rs4244285) genotyping was conducted using the Real-time PCR (ABI, Foster City, CA, USA). Results: There were 42 medical cannabis-induced ADRs cases and 18 medical cannabis tolerance controls who were included in this study. A total of 60 patients were observed where 38 (63.3%) patients were female and 22 (36.7%) were male, with a range of age approximately 19 - 87 years. The most apparent ADRs for medical cannabis treatment were dry mouth/dry throat (76.7%), followed by tachycardia (70%), nausea (30%) and a few arrhythmias (10%). In the total of 27 cases, we found a frequency of 18 CYP2C19*1/*1 alleles (normal metabolizers, 66.7%), 8 CYP2C19*1/*2 alleles (intermediate metabolizers, 29.6%) and 1 CYP2C19*2/*2 alleles (poor metabolizers, 3.7%). Meanwhile, 63.6% of CYP2C19*1/*1, 36.3% and 0% of CYP2C19*1/*2 and *2/*2 in the tolerance controls group, respectively. Conclusions: This is the first study to confirm the distribution of CYP2C19*2 allele and the prevalence of poor metabolizer genes in Thai patients who received medical cannabis for treatment. Thus, CYP2C19 allele might serve as a pharmacogenetics marker for screening before initiating treatment.

Keywords : medical cannabis, adverse drug reactions, CYP2C19, tetrahydrocannabinol, poor metabolizer

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