New Zealand doctors should be allowed to prescribe cannabis for pain

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NO

The answer is no. It is clear that the analgesic effect of medicinal cannabis is not superior when compared to conventional pain relief drugs and, furthermore, the side effect profile does not justify their widespread use. It is important to highlight that many of the studies that have been conducted on this topic are flawed and not of sufficient duration to show long-term adverse effects.

In New Zealand, the use of cannabis is illegal. There have been calls to allow the medicinal use of cannabis in New Zealand. A Bill was presented and defeated in the New Zealand Parliament in 2009. Currently, nabiximols (Sativex) is the only cannabinoid available and is for use for patients with multiple sclerosis with spasticity, under strict medical supervision.

Cannabis contains several chemical compounds, some of which have been used to relieve pain. It contains at least 60 pharmacologically active compounds. Delta-9-tetrahydrocannabinol (THC), the principal active ingredient, was first isolated in 1964. In the early 1990s, an endogenous cannabinoid system was discovered which is mediated by specific cannabinoid receptors. CB1 receptors are widely distributed in the brain,[1] in the cortex, basal ganglia, hippocampus, cerebellum and brain stem. They are also expressed in periaqueductal grey matter (PAG) and in substantia gelatinosa in the spinal cord. CB2 receptors are expressed in low amounts in the brain, and distributed in cutaneous nerve fibres and on blood and immune cells throughout the body. More recently, other types of cannabinoid receptors have been discovered. The first endogenous cannabinoid discovered was designated anandamide. The proposed analgesic efficacy of cannabinoids is mostly modulated through CB1 receptors in the nervous system.

Apart from naturally sourced cannabis, synthetic agonists have been developed. Nabilone (Cesamet) was licensed in 1981 to reduce nausea and vomiting associated with cancer chemotherapy. In 1985, dronabinol (Marinol) was introduced as an anti-emetic for use in similar situations. In 2005, Sativex, an equal mixture of delta-9-THC and a plant-derived compound cannabidiol, was approved for management of spasticity associated with multiple sclerosis.

In 2001, Campbell et al.[2] concluded that cannabinoids were superior to placebo, but no more effective than codeine in the treatment of post-operative pain. Their findings were based on a qualitative systematic review, including nine randomised controlled trials (RCTs). They calculated that the number needed to treat (NNT) was about 16 for 50% pain relief, and deemed cannabinoids unsuitable for use for acute pain treatment. The efficacy reported was no different to codeine in chronic non-cancer and cancer pain. Adverse effects were common and sometimes severe. The major side effect was sedation.

Rice et al.,[3] in a systematic review, examined 39 RCTs. Their findings showed low efficacy of cannabinoids together with side effects such as dizziness, drowsiness, light-headedness, dry mouth and gastrointestinal symptoms. They could not perform a meta-analysis as the trials were heterogeneous. Only one RCT reported a treatment period for up to 12 months. The remainder of the trial durations ranged from seven days to 14 weeks. Two studies reported the NNT for 50% reduction in pain was 4, and one study reported the NNT for 50% reduction in pain as 10. The numbers needed to harm (NNH) reported varied between 3 to 19 for major harm (defined as withdrawal from the trial) and 2 to 14 for minor harm (defined as the patient reporting any side effect).

Martin-Sánchez et al.[4] in another systematic review and meta-analysis concluded that there is moderate evidence of efficacy in the short term.

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However, they noted a high number of serious adverse events in the short term, principally affecting the central nervous system and an NNH close to 3. They also noted that most studies had flaws in terms of selection bias. Furthermore, blinding of the studies was not adequately tested. Only five studies analysed intention to treat bias. Lynch and Campbell,[5] in a systematic review of RCTs since 2003, concluded that use of cannabinoids demonstrated a modest analgesic effect. They did not find any major side effects. However, the major limitations of their review were that most of the trials were of short duration of between one and six weeks.

In 2014 Koppel et al.[6] reported findings of a systematic review of medical cannabis use in the treatment of central pain in multiple sclerosis. Thirty-three studies met the inclusion criteria. They concluded that patients with multiple sclerosis with central pain received some benefit, but highlighted that the placebo effect in these trials could be high and blinding could be compromised due to the cannabis users' recognition of their assigned group (treatment vs control).

In fact, the adverse effects of cannabinoids may be far reaching and can range from nausea to negative outcomes on mental health. Behavioural and mood changes, suicidal ideation, hallucinations, dizziness, fatigue, and feelings of intoxication have been reported. Cannabis has been associated with the risk of developing psychosis.[7] Several studies have shown a relationship between cannabis use and onset of psychosis. Acute use of cannabis has also been shown to impact on cognitive function and memory. A recent study[8] reported on the potential effect of cannabis on the heart. Cardiovascular complications induced by cannabis have risen, up to 3.6% in mostly men between the ages of 30 and 35 years in France during the 2006 to 2010 period reported to the French Addictovigilance Network.

To summarise, the current strength of evidence for use of cannabinoids to treat chronic pain is limited. Its efficacy is modest and this is clearly evident when we compare its analgesic effect to the drugs already available. It has potentially serious adverse effects. Most systematic reviews highlight the lack of good quality RCTs. The trials are of short duration, which is not sufficient to evaluate long-term side effects. If we seriously want to consider cannabinoids for potential analgesic use, robust long-term trials are needed, which is the expected industry norm prior to the introduction of new drugs.

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