Clinical Memorandum

Medical use of cannabinoids

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The Royal Australian & New Zealand College of Psychiatrists

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RANZCP clinical memoranda provide targeted information about emerging evidence relating to aspects of psychiatric practice.

Purpose

Despite promising results from clinical trials into the potential therapeutic benefits of medicines containing cannabinoids, there are still significant gaps in our knowledge about the efficacy, effectiveness and safety of these products. Further research is required to ascertain the potential risks and benefits of the targeted medical use of cannabinoids.

The Royal Australian and New Zealand College of Psychiatrists (RANZCP) supports legislation that facilitates the research and, where backed by sufficient evidence, appropriate regulation of medicines containing cannabinoids. The Therapeutic Goods Administration in Australia and the New Zealand Medicines and Medical Devices Safety Authority (Medsafe) run well-established regulatory regimes which ensure that consumers have timely access to therapeutic advances with acceptable standards of effectiveness and safety. Medicines containing cannabinoids should follow the same approval process as other new pharmaceuticals to ensure these standards are met before they are accessible.

Key messages

- Although there is increasing public and medical interest in medicinal cannabis, the evidence upon which to base an assessment of the efficacy, effectiveness and safety of medicinal cannabis products is limited.
- Medicines containing cannabinoids should follow the same approval process as other new pharmaceuticals to ensure acceptable standards of effectiveness and safety are met before they are publicly accessible.
- The RANZCP encourages further high-quality research regarding the use of cannabinoids for the treatment of psychiatric conditions under standard research trial conditions.

Scope

This clinical memorandum is concerned with medicinal products derived from elements of the cannabis plant prescribed to alleviate physical or mental suffering.

Cannabis contains a variety of chemical compounds including cannabinoids which can be extracted from the plant for medical use. In addition to these cannabis derivatives, cannabinoids can also be manufactured synthetically. Both cannabis derivatives and synthetic cannabinoids may be manufactured in the form of medicines. The use of herbal cannabis as a medication is difficult to evaluate due to the lack of standardisation of active cannabinoids and dose, as well as the conflation of medicinal use with recreational use, ingestion by smoking and risks of diversion (Martin and Bonomo, 2016).

Background

Cannabis extracts and/or synthetic formulations have been licensed for medical use in countries including New Zealand, Canada, Great Britain and Germany, as well as most jurisdictions in Australia and some states in the USA. Their use includes the treatment of severe spasticity in multiple sclerosis, nausea and vomiting due to cytotoxics, treatment-resistant epilepsy, and loss of appetite and cachexia.

Evidence

The use of cannabinoids for medical purposes is currently under scientific investigation. Although there is increasing public interest in medicinal cannabis, the evidence upon which to base an assessment of the efficacy, effectiveness and safety of medicinal cannabis products is limited. It is also important to note that any therapeutic potential which medicines containing cannabinoids may have will not necessarily extend to the cannabis plant itself.

Clinical trials have identified the therapeutic potential of cannabinoids including tetrahydrocannabinol (THC) and cannabidiol. Cannabinoids have shown promise relating to a range of medical presentations including conditions such as multiple sclerosis and glaucoma (Grotenhermen and Müller-Vahl, 2012) and certain forms of epilepsy (Devinsky et al., 2017), medical symptoms such as chronic pain, particularly peripheral and central neuropathic pain and inflammation-mediated chronic pain (Fine and Rosenfeld, 2013) as well as for use as an antiemetic drug for patients undergoing chemotherapy (Grotenhermen and Müller-Vahl, 2012).

Use in psychiatry

Some studies have suggested therapeutic potential in the treatment of cannabis dependence (Levin et al., 2011) as well as psychiatric conditions including anxiety, depression and psychosis (Crippa, Zuardi and Hallak, 2010). There is also some evidence that cannabinoids may be useful in the treatment of Tourette syndrome (Müller-Vahl, 2013). However, evidence of the efficacy of cannabinoids for treatment of these conditions is not well-established. Based on currently available evidence, the RANZCP supports further high-quality research in this area. Any research conducted into the potential use of cannabinoids for the treatment of psychiatric conditions should be conducted under research trial conditions that include oversight by an institutional research ethics committee and careful monitoring and reporting of outcomes.

Safety concerns

There are potential safety concerns surrounding the medical use of cannabinoids. Studies into the recreational use of cannabis have demonstrated a variety of effects including acute psychoactive effects, such as memory impairment, euphoria, and declines in psychomotor and cognitive performance, and physical side effects, such as tiredness, dizziness, tachycardia, orthostatic hypotension, muscle relaxation, and increased appetite (Grotenhermen and Müller-Vahl, 2012). Several studies have linked illicit cannabis use to increased risks for chronic psychosis (Hall and Degenhardt, 2008; Fergusson et al., 2006) and cardiovascular responses including arrhythmias and myocardial infarction (Grotenhermen and Müller-Vahl, 2012; Fisher et al., 2005). The risks of addiction associated with illicit cannabis use also suggest caution (Degenhardt et al., 2015). However, studies looking at the side-effect profile of medical cannabinoids suggest they are relatively well tolerated (Wang et al., 1998) and an initial review of cannabidiol by the World Health Organization's Expert Committee on Drug Dependence found no associated public health risks or abuse potential (WHO, 2017). As with any medication, the side effects of specific cannabinoid medications should be evaluated with the use of a risk–benefit analysis based on evidence of efficacy and safety.

Some population groups may be particularly vulnerable to adverse events resulting from the use of medicinal cannabis products. Risk factors may include age, pregnancy, mental health status and

cognitive capacity, and cardiovascular disease (TGA, 2017). Further research is needed into the effects of medicines containing cannabinoids among vulnerable population groups.

Recommendations

Based on currently available evidence, the use of medicines containing cannabinoids for the treatment of psychiatric conditions is considered an innovative treatment. The RANZCP therefore makes the following recommendations:

- The regulation of medicines containing cannabinoids should occur according to the same approval process as other new pharmaceuticals.
- The clinical use of medicines containing cannabinoids should occur under robust clinical trials and case studies to test the efficacy, effectiveness and safety of long-term use of medicinal cannabinoid products, conducted under research trial conditions that include oversight by institutional research or clinical ethics committees and careful monitoring and reporting of outcomes.
- Psychiatrists who are considering the clinical use of medicines containing cannabinoids outside of a research trial should:
    - ensure that the patient is able and willing to consent to the treatment
    - ensure that clear information is provided to the patient, documented in the clinical notes, including an explanation that the use of cannabinoids is a novel treatment with detailed explanation of the current evidence and potential risks
    - discuss the treatment with peers (preferably including a second opinion)
    - ensure that medicines are accessed via appropriate processes in accordance with local laws
    - give due consideration to the medico-legal risks involved
    - where possible, seek institutional review by the medicines advisory committee or its equivalent
    - where possible, seek institutional research or clinical ethics committee consideration.

Where medicines containing cannabinoids are being prescribed 'off-label', see the RANZCP's Professional Practice Guideline 4: 'Off-label' prescribing in psychiatry for further information.

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Disclaimer

This information is intended to provide general guidance to practitioners, and should not be relied on as a substitute for proper assessment with respect to the merits of each case and the needs of the patient. The RANZCP endeavours to ensure that information is accurate and current at the time of preparation, but takes no responsibility for matters arising from changed circumstances, information or material that may have become subsequently available.

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