RACGP
Royal Australian College *of* General Practitioners

Medicinal use of cannabis products

Position statement – October 2016

Position

Further research is warranted and desirable to clarify the uncertainties of the relative efficacy and safety of medical cannabis products.

As is the case with all medications, cannabis products must be approved or registered through the Therapeutic Goods Administration (TGA) before they can be prescribed.

Cannabis and its medical use

General practitioners are faced with the pressing need to help patients manage chronic and debilitating conditions, with chronic pain affecting approximately one in five people[1]. Many patients do not respond well to main-stream treatments for serious symptoms of illness. With recent changes to legislation around medical cannabis and media coverage creating a perception of easy access, general practitioners may experience greater patient demand to prescribe cannabis-based medications. Prescribing always presents challenges in balancing patient-centred care, evidence-based practice, and the legislative requirements, particularly where there is potential for misuse of medicines[2].

Sources of cannabis

Cannabis is a complex plant comprised of more than 400 constituents, including approximately 70 cannabinoids[3]. The main active ingredients that are used for medical purposes are tetrahydrocannabinoid (THC) and cannabidol (CBD). THC is the psychoactive part of cannabis that produces a 'high', and it has been used to treat symptoms such as nausea, pain and muscle spasticity. CBD has no psychoactive properties, and has been used to treat several inflammatory disorders and epilepsy.

There are three main sources of cannabis used medicinally:

- Pharmaceutical: medical grade products with standardised content
- Medicinal-grade herbal cannabis: produced and processed in controlled standard conditions to a medical grade, free of adulterants, higher levels of CBD and other cannabinoids and lower levels of THC. This is provided to patients in herbal form, or processed as an oil, balm, capsule or pill.
- Herbal cannabis on the illegal market (potentially unstable THC and CBD and may contain adulterants).

Natural and synthetic cannabinoid products have been developed pharmaceutically and approved for medical use overseas[4]. There are three main products:

- dronabinol, a synthetic form of tetrahydrocannabinoid (THC)
- nabilone, a synthetic form of THC
- nabiximols, a chemically pure 50:50 mixture of TCH and cannabidiol (CBD)

In a number of countries, cannabinoid products such as those above are prescribed for nausea and vomiting associated with cancer chemotherapy, improving appetite for wasting illnesses, and improving muscle spasticity associated with multiple sclerosis[5-7].

The legal framework

In February 2016, the Australian Federal Government passed legislation that amended the Narcotic Drugs Act, allowing the supply of suitable medicinal cannabis products for the management of painful and chronic conditions[8]. This legislation does not relate to the decriminalisation of cannabis for general cultivation or recreational use and it does not include the provision of medicinal grade herbal cannabis, only processed, non-smokeable medicinal grade products[7].

Much of the detail remains unclear. For example, the legislation does not specify which products will be covered under the amendment, and it does not specify which particular conditions or symptoms will be eligible for treatment with cannabis-based products.

Before products can be prescribed, they must be registered with the Therapeutic Goods Administration (TGA) or, in rare circumstances, receive special approval from the TGA. The registration process requires evidence of testing and efficacy and it is therefore unlikely Australia will see a TGA registered medicinal cannabis product that GPs can prescribe any time soon.

Whilst there are currently no cannabis-based products that are lawfully produced in Australia, the medicinal use of pharmaceutical products containing cannabinoids is not prohibited, as long as authorisation for prescribing is granted from the Commonwealth Therapeutic Goods Administration and at this point in time, NSW Health[9].

Criteria for prescribing

Some unregistered pharmaceutical cannabinoids can be obtained by particular patients through the Special Access Scheme (SAS). The SAS is a program which allows therapeutic goods that are not registered in Australia to be supplied with TGA approval under specific circumstances by a physician with a schedule 8 permit[7]. Furthermore, as of August 1, 2016, the Poisons and Therapeutic Goods Amendment Regulation will allow doctors in NSW to apply to the NSW Health Board to prescribe cannabis-based products that are not currently on the Australian Register of Therapeutic Goods. Doctors will need approval from both the TGA and NSW Health before they can prescribe an unregistered cannabis-based product.

A national regulatory framework for prescribing medicinal cannabis products is currently being developed. Whilst there will be state variation, as every state differs in its legislature on medicines, the intention is to produce a cohesive, national framework that supports and compliments state legislation[9].

The evidence base for medicinal cannabis

The evidence base for the medical use of cannabis is currently incomplete. There remains much to be learned, particularly relating to treatment efficacy and the longer term side-effects of cannabis-based drugs. Recent systematic reviews and meta-analyses indicate that there is some therapeutic potential and that further research is warranted[10, 11] with a call for better designed clinical trials and longer duration of follow-up[3].

The emerging evidence suggests the use of cannabis medications for some patients with certain conditions that do not respond to mainstream treatments[3, 4]. Cannabis-based medications are associated with a significantly increased risk of short-term adverse events (AE)[10, 11].

The potential therapeutic effects of the full complement of all of the compounds in the cannabis plant have not been tested and is an area identified for future research. In particular, the synergistic or entourage effects from the full spectrum of constituents are thought to be important in treatment efficacy[7]. Similarly, how the constituent compounds may interact with other medications is not understood[3].

Whilst smoking of dried marijuana is the most common mode of use for medicinal purposes, its therapeutic efficacy is limited, with exposure to harmful carcinogens and variation of dosage of both THC and CBD[5]. Smoking also predisposes patients to respiratory infections, such as pneumonia, which is problematic for immune suppressed patients.

There is very little high quality evidence for the medical use of cannabis

The current evidence base for the medical use of cannabis is highly heterogeneous, comprising a relatively small number of randomised clinical trials when stratified by condition, symptom, or intervention type. The studies are also of variable quality i.e. high risk of bias such as incomplete outcome data, low statistical power, and short follow-up time[3, 10-12].

Longer duration clinical trials are needed in order to establish long term efficacy, tolerance, dependency and side effects of cannabis medications as well as the reliable dosing of delivery modes[13].

Moderate quality evidence from clinical trials supports the cautious use of cannabinoids for treating symptoms of illness for a narrow range of conditions[1, 5, 7, 11]. A snapshot of the quality of evidence for treating conditions with cannabis-based medications is provided in Table 1.

Table 1 **Indications for treatment with medical cannabis products**[10, 11]

Treatment	Conditions	GRADE# of evidence
Pain reduction	AIDS / HIV	Very low
	Cancer	Very low
	Diabetic peripheral neuropathy	Very low
	Arthritis	Moderate
	Chronic non-cancer pain	Moderate
Nausea and vomiting	Due to chemotherapy	Very low
Spasticity	Multiple sclerosis	Moderate
Appetite stimulation & weight gain	AIDS / HIV	Low
Mood	Depression	Very low
	Anxiety & depression	Low
Sleep	Insomnia	Very low
Tic severity	Tourette syndrome	Low

#Grading of Recommendations Assessment, Development and Evaluation (GRADE) is an approach to systematically compiling and assessing evidence that includes assessment of study bias and side-effects. GRADE ratings of the evidence:
High – further research is very unlikely to change our confidence in the estimate of effect;
Moderate – further research is likely to have an impact on our confidence in the estimate of effect and may change the estimate;
Low – further research is very likely to have an important impact on our confidence in the estimate of effect and it likely to change the estimate;
Very low – any estimate of effect is very uncertain.

Adverse events with cannabis-based medications

There is increased risk of short-term adverse events (AE) with cannabinoid use[11]. Table 2 summarises the findings of a pooled analysis examining AEs[11]. Compared with placebo or alternative medication, the risk of any AE was approximately three-fold, with serious AEs being less common but still significant (Table 2). Common AEs include asthenia, balance problems, confusion, dizziness, disorientation, diarrhoea, drowsiness, dry mouth, fatigue, hallucinations, nausea, somnolence and vomiting. Studies reported serious AEs as infections, head injury, lung disease, however, it was not always clear if these were attributed to treatment or disease progression. Likewise, reported study withdrawals included a range of reasons including being unable to tolerate medication effects.

Table 2 **Short-term adverse events reported in medicinal cannabis trials**[10, 11]

Drug	Active constituent	Odds of any short-term AE compared with placebo	(95% CI)
Pooled studies (all cannabinoids)			
Any AE		3.03	(2.42-3.80)
Serious AE		1.41	(1.04-1.92)
Withdrawal from use		2.94	(2.18-3.96)
Cannabinoid type			
Dronabinol	**THC**	3.01	(0.87-10.43)
Nabiximols	**THC:CBD**	2.41	(1.91-3.05)
Nabilone	**THC**	3.63	(1.31-10.02)
Levonantradol (a potent synthetic analogue of Dronabinol)	**THC**	4.84	(2.23-10.52)
THC capsules	**THC**	3.16	(2.03-4.93)
THC oromucosal spray	**THC**	2.00	(0.19-20.61)
THC / CBD capsules	**THC:CBD**	3.03	(2.42-3.82)

Education

In response to the publicity and changing legislation relating to medical cannabis, there is a need for public and medical education. This education should reflect the current state of knowledge and contextualise the use of medical cannabis as a last-resort medication for specific categories of illness that can only be prescribed in rare circumstances after stringent legislative criteria are satisfied.

Further information on the medical use of cannabis can be accessed from Cancer Council Australia website.

References

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