Medicinal cannabis for chronic pain

How does it fit into my medical practitioner tool kit?

JACQUELYN NASH MB BS, FANZCA, FFPMANZCA
DIARMUID McCOY MB BCh BAO(NUI), FFARCSI, FFPMANZCA, FANZCA, FFPMCAI

Although there is a broadly held perception in the community that medicinal cannabis is effective for relief of chronic pain, clinical studies have yet to clearly show this. There is, however, some evidence supporting the use of cannabinoids in treating severe nausea from chemotherapy, in some forms of epilepsy and in patients with multiple sclerosis.

Key points

- **The Faculty of Pain Medicine of the Australian and New Zealand College of Anaesthetists does not currently endorse the use of cannabinoids for chronic noncancer pain.**
- **Active engagement in a multimodal management program may or may not include medication use.**
- **There are concerns regarding the risk profile of medicinal cannabis.**
- **High quality clinical trials of cannabinoids for chronic pain are necessary.**

PAIN MANAGEMENT TODAY 2017; 4(1): 26-28

Dr Nash is Specialist Pain Medicine Physician and Specialist Anaesthetist, and Dr McCoy is Specialist Pain Medicine Physician at University Hospital Geelong and Pain Matrix, Epworth Hospital, Geelong, Vic.

Recent media attention on medicinal cannabis has created much interest in the community. How should GPs best tackle requests from patients for 'medicinal cannabis' to treat chronic pain? The challenge will be to navigate this topic relying on evidence-based medicine while educating patients and supporting them towards a well-rounded treatment plan.

Cannabis and chronic pain

Although some evidence exists for the use of cannabinoids in treating patients with severe nausea from chemotherapy, those with some forms of epilepsy and those with multiple sclerosis, it is more likely that requests in general practice for medicinal cannabis will come from patients with persistent pain. There are two reasons why this may be the case: firstly, the high prevalence (20%) of chronic pain in the general practice population in Australia, and secondly the fact that most patients using medicinal cannabis in North America and Europe report doing so to treat chronic pain.[1,2]

A request for medicinal cannabis from a patient is not unreasonable. There is a broadly held perception in the community that cannabis is effective for pain relief. Chronic pain can be a difficult condition to manage, as patients often have multiple facets of their life affected and are highly motivated to seek improvement in their condition. Added to this is the recent media coverage of medicinal cannabis and that preclinical science is supportive of a role of the endocannabinoid system in the regulation of pain. To date, however, clinical studies on the use of cannabinoids for chronic pain have failed to translate into clear positive findings.

A respectful and nonjudgemental discussion of the topic with the patient should ensue. This gives an opportunity to explore their current condition and to appraise their motivation and quality of life. Additional appointments may be necessary to ensure the patient is fully educated on the topic, thereby meeting the GP's clinical responsibility. A key part of the consultation process therefore will be to convey the current limitations and uncertainty of the efficacy and safety of medicinal cannabis, particularly in relation to long-term use.

Obtaining medicinal cannabis

Currently in Australia many patients with chronic illness obtain cannabis from sources that purportedly specialise in the cultivation of the drug for therapeutic purposes.

The Australian Federal Government passed laws in 2016 to legalise medicinal cannabis use for patients with painful and chronic conditions with products imported from overseas. Only one cannabis-containing product is currently registered in Australia (i.e. listed on the Australian Register of Therapeutic Goods) but it is not marketed – nabiximols. This is a prescription-only product formulated as an oromucosal spray, that has the specific indication of treatment of moderate to severe spasticity due to multiple sclerosis. Unapproved medicinal cannabis products are accessed through the Special Access Scheme (SAS) or Authorised Prescriber Scheme.

Legislation came into effect in October 2016 to allow the legal cultivation, production and manufacturing of medicinal cannabis products in this country, to make medicinal cannabis products available to certain patients, subject to therapeutic goods legislation and state and territory legislation. In February 2017, the Federal Government announced it would facilitate faster access to medicinal cannabis for patients by authorising controlled importation by approved suppliers from international sources until domestic production meets local needs. More details are available on the TGA website, www.tga.gov.au/access-medicinal-cannabis-products (Box).

The recent Victorian Law Reform Commission on the legalisation of medicinal cannabis for exceptional circumstances recommended regulatory oversight of the growing, manufacturing and dispensing of medicinal cannabis.[3] This is essential to ensure that the therapeutic agent is chemically and toxicologically safe and has known concentrations of active constituents. Medicinal cannabis can be administered in various ways, for example orally or sublingually, which will alter the pharmacokinetic effect. Smoked preparations are not recommended, and would be contrary to public health policy.

Cannabinoid drugs

The known cellular targets for cannabinoid drugs are the two subtypes of G-protein-coupled cannabinoid receptors, CB1 and CB2; the existence of additional cannabinoid receptors and expanded actions of those which are known is likely. The CB1 receptors are widely distributed in the brain and contribute to the psychoactive effects of cannabinoids; the CB2 receptors are more often located in peripheral cells and are thought to play a role in immune function. In animal models, the cannabinoid system has been found to play a role in inhibiting synaptic transmission in the brain and thus in synaptic plasticity.[4]

Cannabinoids are substances, natural or synthetic, that bind to cannabinoid receptors and produce pharmacological effects. At least 100 botanical cannabinoids and about 300 noncannabinoid chemicals have been identified from cannabis plants (*Cannabis sativa*). The two most studied cannabinoids are delta-9-tetrahydrocannabinol (THC) and cannabidiol (CBD). It is important to recognise that the various extracts from the cannabis plant, and indeed the synthetic cannabinoids, contain different amounts of the pharmacologically active compounds. Studies in humans can be difficult to collate and compare because of the different compounds and different concentrations of chemicals being studied.

Medicinal cannabis: useful websites

- **Faculty of Pain Medicine, Australian and New Zealand College of Anaesthetists**
  - *Statement on 'Medicinal Cannabis', with particular reference to its use in the management of patients with chronic non-cancer pain (PM10 2015)* http://fpm.anzca.edu.au/documents/pm10-april-2015.pdf
- **International Association for the Study of Pain**
  - *Medical cannabis and pain.* Pain Clinical Update 2014; 22(3) www.iasp-pain.org/PublicationsNews/NewsletterIssue.aspx?ItemNumber=3878
- **Therapeutic Goods Administration (Australian Government Department of Health)**
  - *Access to medicinal cannabis products* www.tga.gov.au/access-medicinal-cannabis-products

Efficacy

Preclinical studies, mostly in rodents, have shown efficacy of cannabinoids in reducing inflammatory and neuropathic pain. Unfortunately, similar efficacy in human studies of chronic pain, including neuropathic pain, has not been shown. A review of the evidence for cannabinoids in treating chronic pain published in 2014 suggest the effectiveness is unclear and any benefit is likely to be modest.[5] A possible exception may be the treatment of pain and spasticity in multiple sclerosis; further high quality studies are needed in this area.

Risks

The risks of cannabis use must also be examined. As with the question of efficacy, future research will shed more light on this area. Notably, to date there are few long-term studies.

Of concern, epidemiological studies have shown cannabis use to be an independent risk factor for psychosis.[6] Contraindications include a personal or family history of schizophrenia or psychosis, unstable ischaemic heart disease, severe kidney or liver disease and pregnancy. Particular caution has been suggested in those under the age of 25 years. Other issues to consider in the realm of risk–benefit analysis include risk of polypharmacy, cannabis dependence syndrome, seizure risk and potential cognitive, affective and volitional changes with long-term use.

There is some concern that enthusiastically embracing medicinal cannabis may in due course result in significant problems as yet unquantified. The experience of the liberal use of opioids for the management of chronic noncancer pain resulting in what is now considered an 'opioid epidemic' should serve to temper this enthusiasm.

The complexity of patients with persistent pain

The complexity of the chronic noncancer pain phenotype cannot be underestimated, and a 'single bullet' drug, including medical cannabis, is unlikely to solve the multifaceted problem of chronic pain. A thought-provoking Australian study has shown that patients taking opioids long-term for chronic noncancer pain have a higher prevalence of certain demographic and clinical features (including low income, unemployment, depression, suicidal ideation, history of childhood abuse or neglect, lifetime alcohol use disorder and lifetime cannabis use disorder), and were more likely to be concurrently prescribed benzodiazepines, antidepressants and antipsychotics.[7] The younger age groups in this study had higher rates of complexity, and it is this age bracket in which it is said that medicinal cannabis is likely to be used for pain in the countries in which its use has been approved.

A broad approach to the patient presenting with chronic pain and requesting medicinal cannabis involves assessing their pain not only biologically but also psychologically and socially. The Faculty of Pain Medicine of the Australian and New Zealand College of Anaesthetists endorses a multimodal management plan for chronic pain, one in which the patient is actively involved and medication may or may not play a role. A priority on functional outcomes is vital, as is appropriate follow up. Many management plans involve cessation of medication, particularly those medications that may decrease volition or active engagement, such as opioids or, indeed, cannabinoids.

What the future holds

The scientific literature is yet to identify a clear indication for the use of cannabinoids in patients with chronic noncancer pain. Until there is further evidence available, the Faculty of Pain Medicine will not endorse medicinal cannabis use for this indication.[8] A systematic review and meta-analysis on the topic concludes that 'currently available evidence suggests … beneficial effects may be partially (or completely) offset by potentially serious harms.'[9]

Medicinal cannabis has been considered as part of a treatment plan in a bewildering number of symptoms and signs, conditions and pathologies. These include persistent pain, nausea, sleep disturbances associated with obstructive sleep apnoea, fibromyalgia, multiple sclerosis, dementia, glaucoma, cancer-related cachexia, epilepsy and HIV/AIDS. Studies range from poor to high quality, and the conclusions from the better quality studies may be contradictory. When positive effects are recorded, adverse side effects may make medicinal cannabis a less attractive option and the predictable conclusion that further research is required is all that can be said.[10,11]

Preparation of legislation to support the provision of medicinal cannabis is currently under way in several states and territories in Australia. Political enthusiasm and patient expectation is, as yet, not matched by the current state of the science. The resulting lack of clarity makes caring for and managing patients with persistent pain even more complex.

Study of the cannabinoid system is increasing and some potential may still emerge for safe and effective analgesics. Randomised controlled trials are needed, with adequate sample sizes and long-term monitoring of functional outcomes. Doctors must keep abreast of the literature on this topic and continue to review the evidence. It is vital to educate patients as to why, at the moment, medicinal cannabis is not the best treatment for chronic noncancer pain.

Conclusion

At the present time the use of cannabinoids for chronic noncancer pain is not endorsed in Australia by the Faculty of Pain Medicine of the Australian and New Zealand College of Anaesthetists. There are concerns regarding the risk profile of medicinal cannabis and high quality clinical trials of cannabinoids for chronic pain are necessary. Quality research is welcomed into all measures that promise an improvement in the management of a condition that affects 20% of the population and costs billions of dollars. **PMT**

References

1. Henderson J V, Harrison CM, Britt HC, Bayram CF, Miller GC. Prevalence, causes, severity, impact, and management of chronic pain in Australian general practice patients. Pain Med 2013; 14: 1346-1361.
2. Blyth FM, March LM, Brnabic AJM, Jorm LR, Williamson M, Cousins MJ. Chronic pain in Australia: a prevalence study. Pain 2001; 89: 127-134.
3. Victorian Law Reform Commission. Medicinal cannabis: report. Melbourne: Victorian Law Reform Commission. Available online at: http://lawreform.vic.gov.au/projects/medicinal-cannabis/medicinal-cannabis-report-pdf (accessed April 2017).
4. Hosking RD, Zajicek JP. Therapeutic potential of cannabis in pain medicine. Br J Anaesth 2008; 101: 59-68.
5. Farrell M, Buchbinder R, Hall W. Should doctors prescribe cannabinoids? BMJ 2014; 348: g2737.
6. Moore THM, Zammit S, Lingford-Hughes A, et al. Cannabis use and risk of psychotic or affective mental health outcomes: a systematic review. Lancet 2007; 370: 319-328.
7. Campbell G, Nielsen S, Bruno R, et al. The Pain and Opioids IN Treatment study: characteristics of a cohort using opioids to manage chronic non-cancer pain. Pain 2015; 156: 231-242.
8. Faculty of Pain Medicine. Professional documents. Available online at: http://fpm.anzca.edu.au/Resources/Professional-documents (accessed April 2017).
9. Martín-Sánchez E, Furukawa TA, Taylor J, Martin JLR. Systematic review and meta-analysis of cannabis treatment for chronic pain. Pain Med 2009; 10: 1353-1368.
10. Whiting PF, Wolff RF, Deshpande S, et al Cannabinoids for medical use: a systematic review and met-analysis. JAMA 2015; 313: 2456-2473.
11. The National Academies of Sciences Engineering Medicine. The health effects of cannabis and cannabinoids: the current state of evidence and recommendations for research (2017). Washington DC: National Academies Press; 2017. http://www.nap.edu/24625 (accessed April 2017).

COMPETING INTERESTS: None.

Don't miss

Read about nontraumatic shoulder pain in the Acute Pain Presentations section on page 33.