Royal College of Physicians

RCR The Royal College of Radiologists

Recommendations on cannabis-based products for medicinal use

These recommendations have been jointly produced by the Royal College of Physicians (RCP), the Royal College of Radiologists (RCR) and in liaison with the Faculty of Pain Medicine of the Royal College of Anaesthetists.

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1. Background

Professor Dame Sally Davies, the chief medical adviser to the UK government, recently examined evidence of the medicinal benefit of cannabis-based products. She concluded that there is now sufficient evidence of medicinal benefit in some conditions and advised that the whole class of cannabis-based medicinal products should be moved out of Schedule 1 of the Misuse of Drugs Regulations 2001.[1]

The Advisory Council on the Misuse of Drugs agreed that there is now evidence of medicinal benefit for some cannabis-derived products in certain medical conditions for some patients, although they deferred any recommendations on the rescheduling of synthetic cannabinoids for further consideration as part of their longer term review, due in summer 2019. They also advised that clinicians in the UK should have the option to prescribe cannabis-derived medicinal products (hereafter referred to as 'cannabis-based products for medicinal use' (CBPM), which is the term used in legislation) that meet the requirements for medicinal standards to patients with certain medical conditions.[2]

The decisions to prescribe will be restricted to registered medical practitioners on the General Medical Council's specialist register. The National Institute of Health and Care Excellence (NICE) has been commissioned to produce formal guidelines by October 2019 but in view of the need for interim guidance on the use of CBPM the Royal College of Physicians (RCP) was asked to produce such guidance around the management of cancer, palliative and chronic pain, including in multiple sclerosis.

The following guidance has been produced by a collaboration of the RCP Joint Specialty Committee for Palliative Medicine, the Royal College of Radiologists (RCR) and the Faculty of Pain Medicine.

2. CBPM for chemotherapy-induced nausea and vomiting (CINV)

2.1 Summary

There is good evidence that cannabinoids are effective in preventing CINV but they have a high side effect profile and there are more efficacious agents available. Cannabinoids should remain an option for those who have failed standard therapies but not used as a first-line treatment.

2.2 Treatment of CINV

Cannabinoids, most particularly nabilone, a synthetic analogue of Δ9-tetrahydrocannabinol (Δ9-THC),[3] have randomised controlled trial (RCT) evidence of efficacy in prevention of CINV but have high side effect profiles in the form of neurological symptoms.[4] Discontinuation rates for cannabinoid therapy are high in published trials. Most of the data is relatively old and they have not been directly compared against neurokinin-1 receptor antagonists which have emerged as the most effective agents for highly emetogenic agents such as cisplatin.

2.3 Prevention of CINV

There is some potential emerging evidence of the efficacy of cannabinoids in anticipatory CINV.[5] Anticipatory CINV is less common as there are efficacious therapeutic agents managing CINV preventing its development. However, it can be a distressing symptom for which there are limited therapeutic options.

2.4 Adverse effects of CBPM

Anecdotally, cannabinoids are either extremely well liked or significantly disliked by patients (perhaps in both cases because of the euphoria they can sometimes produce).

CBPM have significant adverse effects including psychological, neurological and gastrointestinal. Psychosis is a particular concern.[6,7] Oromucosal preparations such as Sativex® can cause buccal irritation and ulceration.

3. CBPM for pain

3.1 Summary

There is limited research available from which to create guidance on the effect of CBPM on pain in palliative care patients, including those with cancer. Studies show mixed results or statistically significant results of uncertain clinical significance. In view of this and the adverse effects associated with CBPM, their place in the treatment of pain in palliative care patients is unclear and not recommended in routine clinical practice. There is no robust evidence for the use of CBPM in chronic pain and their use is not recommended.

3.2 Pain in palliative care context

A combined formulation of Δ9-THC with cannabidiol (nabiximols, sold under the brand name Sativex®) is the CBPM which has been studied in this population. In patients with multiple sclerosis and refractory spasticity, a meta-analysis found a statistically significant benefit with uncertain clinical significance for the use of Sativex®.[3] In the treatment of cancer pain, Sativex® shows mixed results from five RCTs, with two showing some benefit and three showing no benefit over placebo.[8,9,10,11]

3.3 Chronic neuropathic pain

The Cochrane review[12] in March 2018 concluded, 'There is a lack of good evidence that any cannabis-derived product works for any chronic neuropathic pain.' It also concluded that 'The potential benefits of cannabis-based medicine in chronic neuropathic pain might be outweighed by their potential harms.'

A comprehensive meta-analysis of pharmacotherapy for neuropathic pain was published in *The Lancet Neurology* in 2015.[13] It is important and robust because it accessed the unpublished trials and used the GRADE system to draw conclusions. It recommended against the use of cannabinoids in neuropathic pain, mainly because of negative results, potential misuse, diversion, and long-term mental health risks of cannabis particularly in susceptible individuals. Only two of nine trials of nabiximols in neuropathic pain were positive.

A review and accompanying editorial in *Pain*[14,15] concluded, 'It appears unlikely that cannabinoids are highly effective medicines for chronic non-cancer pain.'

National reports from the USA,[16] Australia[17] and Ireland[18] all comment on the lack of good quality evidence regarding short and long-term outcomes for both benefit and harm. The widespread use of high-dose opioids in the absence of good long-term evidence over the past 20 years is already the cause of considerable concern, and it is not difficult to see potential parallels.

Patients living with chronic pain often have complex comorbidities and a multidisciplinary approach to management that includes physical and psychological therapy rather than reliance on medicines alone is more likely to be effective.

4. Non-CBPM forms of 'cannabis'

The use of unrefined dried plants containing a variety of cannabinoids and other pharmaco-active chemicals of varying quantity cannot be supported due to the variability of preparations and lack of any trial evidence. The potential for exposure to unknown significantly harmful chemicals and potential diversion to non-medical use are also strong arguments against support for their use in patients. Therefore, only pharmaceutical grade products that are licensed by the Medicines and Healthcare products Regulatory Agency (MHRA) or supplied in accordance with MHRA guidance on the supply of unlicensed cannabis-based products for medicinal use should be considered.

5. Other comments

Cannabinoids do present a class of agents with potential benefit in the management of patients with chronic pain, given the limited pharmaceutical armoury. If there are specific patient populations that will benefit they should not be denied access when the evidence is available.

However, the medicinal use of cannabinoids needs to be carefully considered and researched in a comprehensive fashion, as would be the case for any new medicinal product reaching the therapeutic market. Anecdotal positive reporting is not a mechanism to protect public safety.

We recommend that a database is established for the analysis of data from all areas. Such a database would need to be independent, compulsory, fully funded and under the auspices of a suitable organisation (eg NICE) to assess the value of treatments of relative rarity.

6. References

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www.rcplondon.ac.uk/medicinal-use-cannabis-based-products