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Medication sparing after medical cannabis initiation: A case study of a chronic pain patient in Project Twenty21

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Abstract

Prescribed cannabinoids are legal in the UK and are increasingly being used for a variety of conditions, with one of the most frequent conditions being chronic pain. Within this cohort, there is developing evidence that cannabis-based medicinal products are associated with opioid and other medication sparing. However, at present, the National Institute for Health and Care Excellence (NICE) does not recommend the prescription of cannabis-based medicinal products to treat chronic pain due to the lack of randomised controlled trial evidence for this condition. Here we present a case study of a 61-year-old woman with idiopathic small fibre neuropathy, who was prescribed the gabapentinoid pregabalin, in combination at different times with various other agents including amitriptyline, duloxetine, lamotrigine, meloxicam and topical capsaicin, over a 17-year period for the associated neuropathic pain. Although her pain was relatively well controlled, the patient reported hearing loss, sleepiness, tinnitus, confusion and worsening anxiety possibly as a result of prolonged pregabalin use. Efforts were made to reduce the pregabalin dose but any attempts to reduce below a total daily dose of 350 mg resulted in unacceptable pain for the patient. In 2021, the patient was enrolled in Project Twenty21, the UK's first medical cannabis registry, and prescribed full plant extract delta-9-tetrahydrocannabinol 10 mg: cannabidiol 15 mg/mL of oil, prescribed at a dose range of 0.1–0.5 mL twice daily. As a result, the patient managed to reduce her pregabalin down to 37.5 mg total daily dose. The patient now feels she has 'been given a second chance at life' and her husband describes her as 'a new woman'. This patient feels that she is in a position to finally stop treatment with pregabalin, as a result of medical cannabis controlling her pain. Highlighting the potential benefits of cannabis-based medicinal products to treat chronic pain, our case study indicates the value of including real-world evidence when assessing the benefits and safety of cannabis-based medicinal products.

Keywords

chronic pain, medical cannabis, cannabis-based medicinal products, Project Twenty21 (T21), real-world evidence

Introduction

Chronic neuropathic pain is a pervasive and often disabling condition (Nutt et al., 2021). Chronic pain is estimated to affect between one-third and one-half of the adult population in the UK, contributing to major social and economic costs (Fayaz et al., 2016), and likely to be associated with broad limitations on functions and a marked reduction in perceived quality of life (Hadi et al., 2019).

Despite considerable advances in our understanding of this condition, there remains a lack of effective pharmacological treatments for chronic pain symptoms. Cannabis-based medicinal products (CBMPs), legal in the UK since 1 November 2018, are a potential treatment option for this often hard-to-treat cohort (Schlag et al., 2022). However, prescribing in the UK remains severely limited, due in part, to restrictive guidelines by the National Institute for Health and Care Excellence (NICE).

At present, NICE does not recommend the prescription of CBMPs for chronic pain. Reasons for this are complex, including considerable medicolegal and bureaucratic hurdles (Nutt et al., 2020), as well as a concern by the medical profession that the randomized control trial

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(RCT) evidence base for medical cannabis in relation to pain is too limited: ranging from weakly positive to inconclusive or negative (e.g. Boychuck et al., 2015; Finnerup et al., 2015; Whiting et al., 2015).

Despite current limitations in RCT evidence for the use of CBMPs to treat chronic pain, large numbers of patients globally are using CBMPs to treat chronic pain. Real-world evidence (RWE) consistently shows that various pain conditions are by far the most common conditions for which cannabis is prescribed (Schlag et al., 2021). Currently, up to 90% of US patients in state-level medical cannabis registries list chronic pain as their qualifying condition for the medical program (Wiese and Wilson-Poe, 2018). Emerging observational data from UK-based registries corroborate these findings (Erridge et al., 2021; Sakal et al., 2021). Additionally, an increasing number of observational studies highlight that CBMPs may be used as an alternative treatment by intermittent or chronic opioid users to mitigate their pain hence potentially contributing to opioid and other medication sparing (Takakuwa et al., 2020).

$N = 1$ trials such as this case study are an important facet of medical practice, as each time a medicine is prescribed, an $n = 1$ trial is conducted (Schlag et al., 2022). In certain patients the trial is a success, the patient responds well without the burden of side effects, in other patients, the adverse effects outweigh the therapeutic benefits.

Panel 1: Project Twenty 21 (T21)

Launched in August 2020, Project Twenty 21 (T21) is a multicentre, observational patient registry for patients seeking treatment with prescribed cannabinoids (please see: https://www.drugscience.org.uk/twenty21/). A previous paper offers a detailed description of the methodology of this approach (Sakal et al., 2021). The over-arching goal of T21 is to collect prospective data from substantial numbers of people who receive CBMPs for a variety of conditions, in order to contribute to both the scientific literature and regulatory aspects on the safety and effectiveness of these products in real-world settings. The benefits of widening the scientific evidence base on CBMPs to also include observational data, in addition to RCTs, are potentially substantial: cannabis is a complex medicine, and its broad variety of compounds in different ratios, makes assessing the evidence through RCTs alone particularly challenging.

Case presentation

A 61-year-old woman, who developed idiopathic small fibre neuropathy, following tendonitis surgery in 2002, was prescribed the gabapentinoid pregabalin, at a dose of 300 mg twice daily, in combination at different times with various other agents including amitriptyline, duloxetine, lamotrigine, meloxicam, and topical capsaicin, over a 17-year period for the associated neuropathic pain. Although her pain was relatively well controlled, the patient reported hearing loss, sleepiness, tinnitus, confusion, and worsening anxiety possibly as a result of prolonged pregabalin use.

The patient presented at her GP practice in Jan 2021, stable on pregabalin 300 mg twice daily as monotherapy, in addition to over-the-counter cannabidiol (CBD) tincture (Puresport CBD Pure CBD Oil Tincture 150 mg/mL CBD, 0 mg/mL delta-9-tetrahydrocannabinol (THC)) at varying doses of 30–60 mg CBD per day in divided doses. The CBD tincture had been recommended to the patient by friends as an effective analgesic, she had been using it for approximately 6 months and reported that it did help to reduce her pain in combination with the pregabalin. It was her desire to gradually reduce her daily pregabalin dose down to zero, mainly over concerns about ototoxicity. She was supported in the process by regular telephone consultations with a pharmacist prescriber. After several months of incremental decreases in pregabalin dosing, the patient reached a stage where no further reductions were possible, and any attempt to reduce below 200 mg pregabalin twice daily, resulted in a return of symptoms. Duloxetine 30 mg daily was added back into her drug regimen in April 2021 and further attempts were made to reduce the pregabalin dose but any attempts to reduce below a total daily dose of 350 mg resulted in unacceptable pain for the patient.

Treatment

In June 2021, the patient was referred to the chronic pain arm of the Project Twenty21 medical cannabis clinical treatment initiative [https://www.drugscience.org.uk/twenty21/] and by early August 2021 the patient was enrolled on the registry and prescribed full plant extract THC 10 mg: CBD 15 mg/mL of oil. She was initiated on a dose of 0.1–0.5 mL twice daily as required with a slow up-titration of 0.1 mL every 2 days advised.

Outcome and follow-up

She experienced initial drowsiness as a side effect of the cannabis oil and had to titrate more slowly than originally advised settling on 0.1 mL every 3–5 days. It is possible that sedative effects from the cannabis oil were accentuated via a pharmacodynamic interaction between the oil and the pregabalin (Gilmarten et al., 2021). By the end of August, the patient had managed to reduce to a total daily dose of 175 mg pregabalin and was using between 0.2 and 0.4 mL of cannabis oil BD. In the period between September 2021 to January 2022, the patient up-titrated her cannabis oil to a stabilised dose of 0.3 mL BD, and she was also able to reduce her pregabalin down to 37.5 mg total daily dose, aided by the prescription of

pregabalin tablets which can be split in two to allow 12.5 mg denominations. She currently feels empowered to reduce the pregabalin down further, and also wishes to stop duloxetine eventually. Other than drowsiness, the patient has experienced vivid dreams as a side effect of the medical cannabis, and as a result, does not take the cannabis oil later than 4 pm.

The patient feels she has 'been given a second chance of life' and her husband describes her as 'a new woman', after ca. 4 months of treatment as part of Project T21. It is a possibility that this patient will be able to finally stop treatment with pregabalin, after over 17 years, as a result of medical cannabis controlling her pain. This case supports the growing RWE for the clinical utility of medical cannabis in pain syndromes (Aviram et al., 2021; Nutt et al., 2020; Takakuwa et al., 2020), and also contributes to the developing literature indicating that CBMPs may function as a substitute for other prescription drugs (e.g. Kvamme et al., 2021).

Discussion

NICE recommends that patients suffering from neuropathic pain (other than trigeminal neuralgia) are offered amitriptyline, duloxetine, gabapentin or pregabalin which should be titrated according to response and tolerability [https://cks.nice.org.uk/topics/neuropathic-pain-drug-treatment/]. This patient group is challenging to manage and often ends up taking combinations of drugs at the maximum doses leading to increased frequency of side effects, and drug interactions (Haanpää et al., 2010; Fornasari, 2017). Problems of tolerance and addiction can also often manifest (Point and Hein, 2022; Voon et al., 2017).

Additionally, many patients do not sufficiently benefit from the recommended treatments. Approximately 40%–60% of patients only partially relieve their pain on recommended regimens (Dworkin et al., 2007). The pain associated with small fibre neuropathy is particularly difficult to manage and even drugs considered efficacious only reduce the magnitude of pain by 20% to 40% (Lacomis, 2002). In our case study, some of the recommended treatments were efficacious, but prolonged courses at high doses led to unacceptable side effects for the patient. The prescription of CBMPs provided a better solution for this patient than previously prescribed medications, relieving her pain symptoms, and contributing to other medication sparing, hence reducing the associated intolerable side effects. In turn, the patient could be afforded a better quality of life.

In light of recent findings reporting that nearly a quarter (24.9%) of chronic pain patients are prescribed six or more medications (Schlag et al., 2022) the value of medication reduction for this cohort needs to be acknowledged. A growing body of academic research suggests that individuals are using cannabis as a substitute for prescription drugs, particularly, narcotics/opioids (e.g., Corroon et al., 2017; Lucas et al., 2019).

Medical cannabis offers clinicians another treatment option and should be considered especially once all recommended treatments have failed or are only achieving partial pain management. As with other drugs, CBMPs need to be embedded in a multimodal treatment plan, with appropriate safeguarding support, and ongoing pharmacovigilance such as provided by T21.

Limitations and future research

Our case study supports the utility of RWE, in addition to clinical trial approaches, in studying the potential benefits and safety of prescribed cannabinoids in treating chronic pain. However, as we present a single case study, we cannot draw wider conclusions from current findings. More research is needed especially in relation to opioid and other medication sparing, as well as the longer-term efficacy and safety of CBMPs on chronic pain.

The value of CBMPs for pain management remains controversial. In the UK, the relative lack of expert-based recommendations, clinical experience, education, and patient support for these medicines still presents a major challenge for both patients and clinicians. It is vital to continue building up the evidence base, both through RCTs as well as RWE, as presented here.

Panel 2: Patient's perspective

I have had peripheral neuropathy for over 17 years and I have tried all sorts of medications and treatments, (traditional and alternative), too many to mention but include ketamine infusions and I even twice trialed a spinal cord stimulator. Nothing has come anywhere close to the pain relief I gain from the prescription cannabis that I have been taking whilst on the Twenty21 Trial.

I have struggled with side effects from medication and also bouts of depression in the early days of my diagnosis. My mood has always, understandably, been affected due to the constant pain but now I get very little break-through pain. I am able to do twice as much as was able to do – I am now much more active!

I am so very grateful that Peter Sunderland, the pharmacist at my GP's surgery, persuaded me to go on the trial. My family and friends have all remarked on how well and happy I am now.

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References

Aviram J, Lewitus GM, Vysotski Y, et al. (2021) Prolonged medical cannabis treatment is associated with quality of life improvement and reduction of analgesic medication consumption in chronic pain patients. *Frontiers in Pharmacology* 19(12): 613805.

Boychuk DG, Goddard G, Mauro G, et al. (2015) The effectiveness of cannabinoids in the management of chronic nonmalignant neuropathic pain: A systematic review. *Journal of Oral Facial Pain Headache* 29: 7–14.

Corroon JMJr, Mischley LK and Sexton M (2017) Cannabis as a substitute for prescription drugs – a cross-sectional study. *Journal of Pain Research* 10: 989–998.

Dworkin RH, O'Connor AB, Backonja M, et al. (2007) Pharmacologic management of neuropathic pain: evidence-based recommendations. *Pain* 132(3): 237–251.

Erridge S, Salazar O, Kawka M, et al. (2021) An initial analysis of the UK medical cannabis registry: Outcome analysis of first 129 patients. *Neuropsychopharmacology Reports* 4193(3): 362–370.

Fayaz A, Croft P, Langford RM, et al. (2016) Prevalence of chronic pain in the UK: A systematic review and meta-analysis of population studies. *BMJ Open* 6(6): e010364.

Finnerup NB, Attal N, Haroutounian S, et al. (2015) Pharmacotherapy for neuropathic pain in adults: A systematic review and meta-analysis. *Lancet Neurology* 14(2): 162–173.

Fornasari D (2017) Pharmacotherapy for neuropathic pain: A review. *Pain and Therapy* 6: 25–33.

Gilmarten CGS, Dowd Z, Parker APJ, et al. (2021) Interaction of cannabidiol with other antiseizure medications: A narrative review. *Seizure* 86: 189–196.

Haanpää ML, Gourlay GK, Kent JL, et al. (2010) Treatment considerations for patients with neuropathic pain and other medical comorbidities. *Mayo Clinic Proceedings* 85(3 Suppl): S15–S25.

Hadi MA, McHugh GA and Closs SJ (2019) Impact of chronic pain on patients' quality of life: A comparative mixed-methods study. *Journal of Patient Experience* 6: 133–141.

Kvamme S, Pedersen M, Thomsen K, et al. (2021) Exploring the use of cannabis as a substitute for prescription drugs in a convenience sample. *Harm Reduction Journal* 18(1): 72–90.

Lacomis D (2002) Small-fiber neuropathy. *Muscle & Nerve* 26(2): 173–188.

Lucas P, Baron EP and Jikomes N (2019) Medical cannabis patterns of use and substitution for opioids & other pharmaceutical drugs, alcohol, tobacco, and illicit substances; results from a cross-sectional survey of authorized patients. *Harm Reduction Journal* 16(1): 9.

Nutt DJ, Bazire S, Phillips LD, et al. (2020) So near yet so far: Why won't the UK prescribe medical cannabis? *BMJ Open* 10(9): e038687.

Nutt DJ, Philipps L, Barnes M, et al. (2021) A multicriteria decision analysis comparing pharmacotherapy for chronic neuropathic pain, including cannabinoids and cannabis-based medical products. *Cannabis and Cannabinoid Research* 7(3): 482–500.

Point C and Hein M (2022) Pregabalin misuse: An emerging public health problem. *Revue Medicale de Bruxelles* 43: 165–168.

Sakal C, Lynskey M, Schlag AK, et al. (2021) Developing a real-world evidence base for prescribed cannabis in the United Kingdom: Preliminary findings from Project Twenty 21. *Psychopharmacology* 239: 1147–1155.

Schlag AK, O'Sullivan S, Zafar R, et al. (2021) Current controversies in medical cannabis: Recent developments in human clinical applications and potential therapeutics. *Neuropharmacology* 191: 108586.

Schlag AK, Lynskey M, Fayaz A, et al. (2022a) Characteristics of people seeking prescribed cannabinoids for the treatment of chronic pain: Evidence from Project Twenty 21. *Frontiers in Pain Research* 3: 891498. https://www.frontiersin.org/article/10.3389/fpain.2022.891498

Schlag AK, Zafar RR, Lynskey MT, et al. (2022b) The value of real world evidence: The case of medical cannabis. *Frontiers in Psychiatry* 13: 1027159. https://www.frontiersin.org/articles/10.3389/fpsyt.2022.1027159

Takakuwa KM, Hergenrather JY, Shofer FS, et al. (2020) The impact of medical cannabis on intermittent and chronic opioid users with back pain: How cannabis diminished prescription opioid usage. *Cannabis and Cannabinoid Research* 5(3): 263–270.

Voon P, Karamouzian M and Kerr T (2017) Chronic pain and opioid misuse: A review of reviews. *Substance Abuse: Treatment, Prevention, and Policy* 12: 36–45.

Whiting PF, Wolff RF, Deshpande S, et al. (2015) Cannabinoids for medical use: A systematic review and meta-analysis. *JAMA* 313: 2456–2473.

Wiese B and Wilson-Poe AR (2018) Emerging evidence for cannabis' role in opioid use disorder. *Cannabis and Cannabinoid Research* 3: 179–189.