CASE REPORT

The use of cannabinoids in chronic pain

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reynoldstd@doctors.org.uk**SUMMARY**

We present the case of a 56-year-old man who developed chronic pain following the excision of a facial cancer that was poorly controlled despite multiple analgesic medications. Following the starting of nabilone (a synthetic cannabinoid) his pain control was greatly improved and this had a huge impact on his quality of life. We also managed to significantly reduce his doses of opioid analgesia and ketamine. We review the current literature regarding the medicinal use of cannabinoids, with an emphasis on chronic pain, in an attempt to clarify their role and how to select patients who may benefit from this treatment.

BACKGROUND

Chronic pain is notoriously difficult to treat, is a major contributor to time away from the workplace each year and places a significant strain on the resources of the National Health Service.

Once the conventional medications that are incorporated in the WHO pain ladder have been tried but there is still significant pain and disability, we often find it difficult to know where to go next.

CASE PRESENTATION

We highlight the case of a 56-year-old man who was diagnosed with squamous cell carcinoma of the right side of his lower lip in 2008 with spread to his right submandibular gland. He underwent a local resection and neck dissection with adjuvant chemoradiotherapy.

Although there was no sign of local regional recurrence, in the aftermath of his surgery he went on to develop neuropathic pain affecting the right side of his face that he compared to severe sunburn or pouring boiling water over his skin. These symptoms were made worse by exposure to cold/wet weather and proved severely disabling, leading to increasing social isolation to the point that he had contemplated suicide.

He was subsequently referred to one of the palliative care consultants with a special interest in chronic pain management, and was also placed on the waiting list for insertion of a spinal cord stimulator in an attempt to control his pain.

Pain control became increasingly difficult with minimal benefit perceived from initial treatment with paracetamol and non-steroidal anti-inflammatory drugs and subsequent rotation through several different opioid analgesics (including oral morphine and oxycodone preparations). He was therefore admitted to his local hospice in October 2012 in an attempt to improve his pain management.

On admission he was taking regular oxycontin 280 mg twice daily (with oxynorm 50 mg hourly as

breakthrough analgesia), ketamine 100 mg four times a day, pregabalin 200 mg three times a day, diazepam 2 mg twice daily, mirtazapine 15 mg daily and citalopram 20 mg daily.

He explained that oxynorm and ketamine provided some benefit for up to 2 h but he felt that he had developed a tolerance to these effects.

INVESTIGATIONS

Routine blood tests were unremarkable and cross-sectional imaging prior to admission showed no evidence of recurrence.

TREATMENT

We initially increased the doses of oxycontin and ketamine with minimal benefit. He started hypnotherapy with some improvement of symptoms (pain levels fell from 10/10 to 7–8/10 severity).

On further discussion with the patient, he informed us that he had once tried cannabis used by a friend and felt some benefit to his pain levels.

Owing to his limited pain control we decided to start a trial of nabilone (a synthetic cannabinoid) to see whether this could improve his symptoms.

OUTCOME AND FOLLOW-UP

Within days of starting nabilone (at a dose of 1 mg twice daily), the pain control was greatly improved. He described only a residual itching sensation and was able to touch the right side of his face and ear comfortably for the first time in 4 years.

This clearly had a massive effect on his quality of life. It allowed him to shave and go out in cold/wet weather without pain for the first time since his surgery. Even things as simple as hugging loved ones had been impossible prior to this.

He went several days without requiring any breakthrough analgesia and we were subsequently able to reduce his oxycodone and ketamine doses without adversely impacting on his symptom control.

The only adverse effect encountered on starting of nabilone was initial light-headedness that disappeared within 48 h of starting the medication.

He was reviewed in the clinic after 1 month and he remained well and pain free. We have managed to reduce his ketamine further with the hope of stopping this in due course.

DISCUSSION

The use of cannabinoids as a medical therapy remains controversial. An ethical debate persists regarding whether we should produce medical therapies derived from a drug that is illegal in many parts of the world and that has also been linked with serious adverse effects on the health of the user.

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For example, research carried out by the British Lung Foundation suggested that smoking cannabis on a regular basis might be more harmful than smoking tobacco in terms of the development of lung cancer and suppression of the immune system (leading to opportunistic infections). Furthermore, there has been some research that suggests that smoking cannabis with tobacco may lead to greater rates of chronic obstructive airways disease than smoking tobacco alone. There is also some dispute as to the long-term psychiatric and cognitive effects of regular cannabis use.

Nonetheless cannabis has been used for centuries for medicinal purposes and it has been demonstrated that the use of cannabis (and medical therapies derived from it) can have a number of beneficial effects on the user.

Cannabinoids work by acting upon a variety of receptors leading to a complex interaction with neurotransmission within the peripheral and central nervous systems.¹

The receptor that has been most extensively studied is the cannabinoid type 1 (CB1) receptor.

This receptor is distributed throughout the nervous system (with particularly high levels in the brain). It is found at three principal levels:

1. Brain—primarily thalamus, amygdala and periaqueductal grey matter (all areas known to be associated with nociception).
2. Spinal cord—primarily dorsolateral funiculus and superficial dorsal horn.
3. Peripheral sensory nerve endings.

The cannabinoid type 2 (CB2) receptor has also been described and appears to have a greater role within the immune system, where it may have a role in dampening down chronic inflammatory processes.¹

The main evidence-based clinical uses of cannabinoids at present are in the treatment of refractory chemotherapy-related nausea, neuropathic pain and spasticity in multiple sclerosis and AIDS-related anorexia.

At present there is no strong evidence base for the use of cannabinoids in chronic non-cancer pain. However, evidence to support the use of cannabinoids in this area appears to be emerging.

In addition to the case that we highlight earlier, there is other anecdotal evidence in the literature to support the use of cannabinoids in this context. For example, Berlach *et al*² describe 20 patients from Canada who used nabilone as an adjunctive treatment for the management of non-cancer pain for a median period of 18 months. Of these 20 patients, 9 described an improvement in pain levels and 15 described an overall improvement in their quality of life.

Furthermore, Abrams *et al*³ researched HIV-related sensory neuropathy and found that smoking three cannabis cigarettes daily for 5 days improved neuropathic pain in 34% of those who used them (compared to 17% of placebo-matched controls — $p=0.03$). Interestingly, the first cigarette (at the start of the 5-day period) reduced pain ratings by 72% among the cannabis group compared with 15% of the placebo cigarettes ($p<0.001$).

Furthermore, Pinsger *et al*⁴ found that among 30 patients with spinal pain taking conventional treatments, the pain intensity ratings and quality of life scores both improved during cannabinoid use (compared with crossover to placebo) and when allowed to blindly switch to their preferred drug at the end of the crossover, more than 85% favoured nabilone.

Frank *et al*⁵ compared the use of nabilone with dihydrocodeine in chronic neuropathic pain and found that dihydrocodeine resulted in lower pain scores after 6 weeks of treatment (scored on visual analogue scale) and fewer side effects.

Most of the 96 patients involved in this study had peripheral neuropathic pain (which appears less susceptible to cannabinoids in the current literature), rather than conditions that are characterised by central pain and spasticity. The reduced efficacy may relate to lower concentrations of cannabinoid receptors peripherally.

The main side effects that are associated with cannabinoids appear to be dysphoria and altered perception. There is often some tiredness, light-headedness and dry mouth on commencement (or increasing dosage). This tends to settle within the first few days.⁶

It is advisable, therefore, to avoid driving/operating machinery during this period.

It would appear that most adverse effects that have been encountered in clinical trials are fairly minor in severity. Lynch *et al*⁶ performed a systematic review of cannabinoid use in chronic non-cancer pain and found that they are both safe and (moderately) effective among the 18 randomised trials considered. There were no serious adverse effects related to cannabinoid use in these trials.

There is, however, on-going concern about the long-term effects on cognitive function, especially if used in younger patients (most trials conducted to date have consisted of small numbers of patients, followed over shorter periods).⁶

Clearly the use of cannabinoids in chronic pain is still in its infancy. The jury remains out regarding the optimum selection criteria for the use of cannabinoids in chronic pain; however, there appears to be an emerging role for them as an adjunct to traditional therapies.

Although much of the supportive evidence related to cannabinoid use seems to be geared around the central effects (concerning use in central pain syndromes and spasticity), this case suggests that there may well be beneficial effects in peripheral chronic pain as well.

Whether these effects in our patient are due to direct actions upon peripheral nerve endings or whether he had undergone central remodelling as a result of his peripheral lesions that was dampened down by cannabinoids is not yet clear.

This case also emphasises the importance of taking a thorough pain history to include a full drug history including recreational drug use (and their effects).

The next step will be to carry out larger studies conducted over longer time periods in a variety of conditions associated with pain to isolate which groups are likely to respond to cannabinoids, together with possible adverse effects that may arise and need to be actively monitored for with long-term cannabinoid use.

Learning points

- ▶ Chronic pain is often difficult to treat and can be extremely disabling.
- ▶ A thorough pain history is essential in the management of chronic pain.
- ▶ Novel therapies are available that can produce encouraging results once more conventional avenues have been exhausted. Cannabinoids offer one such option.
- ▶ The use of cannabinoids as an adjunctive medical therapy is still controversial but appears to be gathering an evidence basis.
- ▶ Further research is needed to find which patients are likely to respond best to cannabinoid therapies.

Contributors This patient was admitted under the care of HLO. TDR was one of the junior doctors caring for this patient during his admission. TDR wrote the case report regarding this patient that was reviewed by HLO and amendments were made.

Competing interests None.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

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