

Medical Cannabis in the Palliation of Malignant Wounds—A Case Report

To the Editor:

Malignant wounds affect approximately 15% of cancer patients and represent a significant source of multidimensional suffering by patients and their caregivers.^{1,2} Although pain is the most common symptom associated with malignant wounds, other associated symptoms include mass effect, aesthetic (cosmetic) distress, exudation, odor, pruritus, and bleeding.² In the setting of advanced cancer, malignant wounds are nonhealable making the goals of care focused on wound palliation (wound-related pain and symptom management or palliative wound care).³

Anecdotal accounts of the use of topical extracts from the cannabis plant being used on open wounds date back to antiquity.⁴ In modern times, cannabinoid therapies have demonstrated efficacy as analgesic agents in both pharmaceutical and botanical formats.^{4–6} Since 2001, Canada is among a growing number of countries that has legalized botanical cannabis for medical purposes.⁴ Medical cannabis (MC), also known as medical marijuana, must be distinguished from recreational cannabis as it intends to relieve symptoms and potentially modulate diseases, as opposed to intending to deliver a psychomimetic state of high.⁴ MC in Canada is cultivated under quality-controlled conditions and is mandated by Health Canada to have reproducible levels of the main cannabinoid and noncannabinoid substances.⁴ Moreover, the composition of MC may be tailored to meet the particular needs of the patient.⁴ Its most clinically relevant components include the cannabinoid agents, delta-9-tetrahydrocannabinol (THC) and cannabidiol (CBD), and the noncannabinoid elements, terpenoids and flavonoids.⁴ Dubbed the entourage effect, it has been postulated that synergistic clinical effects occur among the main cannabinoid and noncannabinoid agents within MC.⁴ MC may be dispensed in dried botanical format that may be smoked, vaporized, or consumed as edibles. MC

extracts compounded in organic oils also may be administered orally.

The endogenous cannabinoid system, consisting of cannabinoid receptors and their endogenous ligands, is ubiquitous throughout the human body.⁴ Available research shows that cancer cells express higher levels of the cannabinoid receptors, CB1 and CB2, relative to their noncancer counterparts, while also demonstrating an overall state of upregulation.⁴ Human *in vitro* studies, using nonmelanoma skin lines, have demonstrated direct induction of tumor cell apoptosis and inhibition of tumor-related angiogenesis, both by way of activation of cannabinoid receptors.⁶

Case Report

A 44-year-old man was referred to our consultative palliative medicine clinic with an exophytic (fungating) wound involving his right cheek area. His clinical course over five months of follow-up are summarized in Table 1. Three years earlier, he was diagnosed with a squamous cell cancer of his right buccal cavity. He had the tumor surgically resected, followed by external beam radiotherapy and chemotherapy. Despite this appropriate cancer treatment, he developed a buccal recurrence that eventually eroded through his cheek, creating an oral cutaneous fistula and associated exophytic lesion. Over the two-year period before his referral to our clinic, he had elected to forego further conventional oncologic therapies in favor of mostly naturopathic treatments. Despite using high-dose hydromorphone, pregabalin, and dexamethasone, he continued to experience continuous (background) generalized right hemifacial pain along with volitional incident pain (wound-related procedural pain) occurring with wound dressing changes. He rated his average daily pain score as 9 of 10. In addition, he also reported having side effects from his analgesics, such as constipation and drowsiness. He also reported suffering severe aesthetic distress from his facial disfigurement along with right-sided trismus, depression, insomnia, nausea, and anorexia. In the course of his initial visit, the patient expressed

Table 1
Clinical Data

Date	Tumor Size (cm ²)	Average Daily Pain Score (0–10)	Analgesics	MC Therapy	PPSv2 (%)
November 12, 2015	8.75	9	Hydromorphone 30 mg/day Pregabalin 150 mg/day Decadron 4 mg/day	Vaporized	90
December 10, 2015	12.33	3	Hydromorphone 8 mg/day	Vaporized	90
January 21, 2016	26.44	3	Hydromorphone 8 mg/day	Vaporized	80
March 17, 2016	44.16	4	Hydromorphone 10 mg/day	Topical Oil	70
April 21, 2016	41.90	4	Hydromorphone 20 mg/day	Topical Oil	60

MC = medical cannabis; PPSv2 = Palliative Performance Scale, version 2.

dissatisfaction with his current analgesic regimen and inquired about obtaining MC. After fully evaluating his overall medical status, it was concluded that he had neither contraindications nor likelihood of drug-drug interactions. He also was counseled about potential side effects. Thus, he was offered a trial of vaporized MC (ARGYLE™; THC 7.25% + CBD 8.21%) from TWEED, Inc. delivered through a certified Volcano™ vaporizer unit. The particular strain was strategically chosen to maximize the analgesic potential of both THC and CBD while mitigating against the sedation and psychotomimetic side effects commonly experienced with high-dose THC strains.

On his second clinic visit, he reported significant reductions in both baseline and volitional incident pain. He indicated that he used 0.5–1.0 g of dried cannabis per day and vaporized every two to four hours and 15 minutes before his daily wound dressing change. His pain relief was so significant that he was able to discontinue pregabalin and dexamethasone while reducing hydromorphone to approximately 25% of his pre-MC dosage. He also reported experiencing less trismus and nausea, along with improved appetite, sleep, and effect. Importantly, he reported no negative effects from the MC. Furthermore, his overall performance status and symptom control was good enough to allow him to be working modified hours as a health care professional.

During his third and fourth clinic visits, his malignant wound was observed to have increased in size, yet his performance status only marginally declined, and his average daily pain scores remained within tolerable limits, while needing only small increases in daily opioid utilization. Unfortunately, his trismus and oral cutaneous fistula rendered the continued use of vaporized MC technically difficult. Because the patient had experienced such positive outcomes with MC therapy, he was eager to continue it through an alternate delivery system. Thus, we offered him a trial of topical MC compounded in nongenetically modified organic sunflower oil (ARGYLE THC 5.24% + CBD 8.02% from TWEED, Inc.). The patient was informed that this empiric trial was being offered in the complete absence of published human experience with it being applied topically to malignant wounds. The patient provided informed consent for the use of the MC oil topically. He was instructed to apply, and digitally spread, 1–2 cc of the MC oil to the entire malignant wound, both externally and intra-buccal. He also was advised to swish any residual oil throughout his oral cavity and swallow any residual.

On his fifth clinic visit, he reported having consistently used the topical MC four times daily. He stated that pain relief commenced with 10–15 minutes after application and lasted for up to two hours after

application. He did not report any negative experiences from the use of topical MC. Between his fourth and fifth clinic visits, his condition began to globally deteriorate, and he required a doubling in his daily opioid utilization. Interestingly, the size of his malignant wound decreased by about 5% over the four-week interval.

Four weeks after his last clinic visit, he was admitted to an acute general hospital with hypovolemia. As a result, he was lost to follow-up and ceased to use MC on his admission. He expired three weeks later.

Comment

The analgesic outcomes observed in this case are supported by the results of a recent systematic review and meta-analysis of cannabinoids for medical use.⁶ Unlike intact skin, which is polar and hydrophilic, wounds lack epithelial coverage and are nonpolar and lipophilic. Therefore, lipophilic compounds such as the THC and CBD cannabinoids may be readily absorbed through cutaneous wounds.

Before the use of topical MC oil, the patient's wound was growing rapidly. Yet, after a few weeks, a modest regression of his malignant wound was observed while the patient used topical MC. This secondary outcome suggests that topical MC may promote antineoplastic activity as per the findings of Casanova et al.⁷

In summary, this is the first case report to demonstrate the potential for MC to provide effective pain and symptom management in the setting of malignant wounds. The rapid onset of analgesia after topical placement suggests that the effects were mediated through absorption of the THC and CBD cannabinoids that subsequently interacted with peripheral nociceptors, immune cells, and cancer cells. The postapplication analgesia may be because of the gastrointestinal absorption of ingested residual MC oil. This case suggests that MC delivered in vaporized and topical oil formats warrants further investigation in human malignancy, including randomized controlled trials capable of establishing long-term efficacy, optimal dosage, schedules of administration, mixture composition, and safety.

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