

## ***Cannabis Reduces Opioid Dose in the Treatment of Chronic Non-Cancer Pain***

To the Editor:

Cannabinoids block pain responses in virtually every laboratory pain model tested. In models of acute or physiological pain, cannabinoids are highly effective against thermal, mechanical, and chemical pain, and are comparable to opioids in potency and efficacy.<sup>1</sup> In models of chronic pain, cannabinoids exhibit efficacy in the modulation of both inflammatory<sup>2</sup> and neuropathic pain.<sup>3</sup> Recent reviews describe an endogenous cannabinoid system involved in pain modulation that produces analgesia through the same brainstem circuitry involved in opioid analgesia.<sup>1,4,5,6</sup> Although co-administration of  $\Delta$ -9-tetrahydrocannabinol (THC) with  $\mu$  opioid agonists can potentiate the antinociceptive effects of each agent, an opioid is not required for cannabinoid analgesia.<sup>5,6</sup> Co-administration of a cannabinoid may lead to a lower opioid requirement. In an N-of-1 trial, oral THC reduced the pain of familial Mediterranean fever such that the use of breakthrough opioid for pain relief decreased significantly.<sup>7</sup>

Recently, in Canada, the Medical Marijuana Access Program allows patients to apply to Health Canada for access to dried cannabis for medicinal purposes. Although smoked cannabis is not an ideal delivery system, it is efficient and results in plasma concentration curves parallel to those seen after intravenous administration.<sup>8</sup> We present three patients who used small doses of smoked marijuana in combination with an opioid.

### *Case 1*

A 47-year-old woman with a ten-year history of chronic progressive multiple sclerosis (MS) had headache, multisite joint pain, bladder spasm, and leg spasticity. Ambulation was significantly compromised by the joint pain and leg spasticity. She was wheelchair dependent, and also suffered from severe insomnia and fatigue, which she attributed to the combination of pain, bladder spasm, and leg spasticity. Physical examination revealed paraparesis, weakness

in the left upper extremity, tremor involving both hands, intranuclear ophthalmoplegia and L'Hermitte's sign. Previous treatment included steroids, physiotherapy, acupuncture, interdisciplinary pain management, intramuscular injections of botulinum toxin, amitriptyline, fluoxetine, amantadine, acetaminophen with codeine, oxycodone, nonsteroidal anti-inflammatory drugs (NSAIDs), and baclofen. The patient's medications prior to access to smoked marijuana consisted of long-acting morphine 75 mg per day, tizanidine 24 mg per day, and sertraline 150 mg at bedtime. In spite of these treatments, the patient did not obtain adequate control of her pain, spasticity, or sleep.

The patient received permission for access to smoked marijuana and began to use a dose of 2–4 puffs of smoked marijuana at bedtime on a regular basis. Over the next six months, the morphine was reduced to 45 mg per day, tizanidine to 6 mg once per day, and sertraline to between 100 mg and 150 mg at bedtime. The patient reported improvement in pain, spasticity, bladder spasm, and sleep. The patient denied any adverse side effects, other than she felt somewhat "high" if she smoked more than 4 puffs per dose. She was able to adjust the dose so that this did not occur. The patient received legal access in the autumn of 2000 and continues to use marijuana.

### *Case 2*

A 35-year-old HIV-positive man was initially assessed in 1992 for four-month history of HIV-related painful peripheral neuropathy involving the lower limbs and hands. His pain had initially involved the plantar aspect of his feet and had spread proximally to involve the lower leg and thighs, and later his hands. The pain was described as severe "stinging, numb, tingling, and throbbing" pain that was unpredictable and poorly controlled. On physical examination, positive findings included patches of hypesthesia and hyperalgesia to pinprick testing in a stocking-glove distribution. Electromyography studies were reported as normal. Prior treatments had included trials of physiotherapy, acupuncture, psychological therapies, NSAIDs, tricyclic antidepressants, anticonvulsants, intravenous and oral local anesthetics, and opioids. His medication regimen consisted of long-acting morphine 360 mg per day with morphine

sulfate 75 mg 4 times daily for breakthrough pain, and gabapentin 2,400 mg per day. The patient continued to report moderate to severe levels of pain.

After receiving approval to use marijuana in 2000, the patient began using smoked marijuana in a dose of 3–4 puffs 3–4 times per day. Over four months, the patient's dose of morphine decreased to 180 mg per day and by 9 months he had discontinued the morphine. By September 2001, he discontinued gabapentin. The patient was able to manage without the use of an opioid or gabapentin until February 2002, at which time he developed an episode of herpes zoster involving thoracic dermatomes T7 to T9 on the left side. Morphine was temporarily re-introduced for 8 weeks during the acute episode in a dose of 15 mg three times daily. The patient reported that the smoked marijuana was helpful for both the HIV neuropathy and the herpes zoster pain, but he required the additional analgesia provided by the opioid during the acute phase of the herpes zoster infection. He has since discontinued the morphine and remains opioid-free as of August 2002. The patient denied side effects related to the use of smoked marijuana.

### Case 3

A 44-year-old man presented with a 6-year history of low back and left leg pain, which had resulted from a work-related fall from a ten-foot high landing onto the edge of a metal tank, striking his lumbar spine. Physical examination revealed a decrease in lumbar lordosis, wasting of paravertebral musculature, decreased extension at the lumbar spine, decreased straight leg raising from the supine position to 60° on the right and to 45° on the left, tenderness to palpation over the L3-4 to L5-1 facet joints, normal deep tendon reflexes bilaterally and hypesthesia to pinprick testing over the lateral aspect of the left calf. Previous treatments had included physiotherapy, transcutaneous electrical nerve stimulation, acupuncture, lumbar facet joint injections, radiofrequency facet neurolysis, and trials of NSAIDs, tricyclic antidepressant analgesics, muscle relaxants, tramadol, and long-acting morphine. The patient's medications prior to the introduction of smoked marijuana consisted of long-acting morphine 150 mg per day and cyclobenzaprine 10 mg three times per day.

The patient reported poor pain control with this regimen and initiated a trial of smoked marijuana. He reported using several puffs to one joint 4–5 times per day. After using the smoked marijuana on a regular basis for 2 weeks, the patient was able to decrease his morphine to 90 mg per day; after two more weeks, he decreased the morphine to 60 mg per day and his cyclobenzaprine to 10 mg once daily. He reported good pain control and was able to continue in his wage earning work. The patient continues to report improved pain control using the cannabis along with the lower dose of morphine as of August 2002.

### Comment

These cases are consistent with preclinical work demonstrating that cannabinoids exhibit analgesic effects and may potentiate the antinociceptive effects of opioids. These patients were able to decrease the dose of opioid by 60–100% as compared to before the regular use of smoked marijuana. With the introduction of smoked marijuana, each patient reported better pain control. Unfortunately, the source of smoked marijuana used by patients, and the percentage of THC in it, is unknown. All patients reported previous exposure to cannabis at some time in their lives before the onset of their pain, and the relevance of this experience also is unknown. Standardized measures of pain were not used, and the information presented was based on the patients' verbal report when they presented for follow-up appointments at the Pain Management Unit. Nonetheless, these cases suggest that further research regarding the role of cannabinoids as analgesics and the combination of cannabinoids with opioids in the control of pain is needed.

Mary E. Lynch, MD, FRCPC  
Alexander J. Clark, MD, FRCPC  
Queen Elizabeth II Health Sciences Center  
Dalhousie University  
Halifax, Nova Scotia, Canada

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