PALLIATIVE CARE NETWORK OF WISCONSIN

FAST FACTS AND CONCEPTS #93
CANNABINOIDS IN THE TREATMENT OF SYMPTOMS IN CANCER AND AIDS

L Scott Wilner MD and Robert M Arnold MD

Introduction The healing properties of cannabis have been asserted for centuries. Popular claims notwithstanding, there are no data to support the use of marijuana in the treatment of asthma, anxiety, depression, epilepsy, glaucoma, alcohol withdrawal, or infection; and limited data to support using cannabinoids as analgesics. Recent scientific studies of cannabinoids for symptom management have focused on nausea/vomiting and appetite stimulation.

Terminology *Cannabis sativa* is the Indian hemp plant. *Marijuana* is a psychoactive substance derived from the plant. *Cannabinoids* are the biologically active compounds in the plant. *THC* is delta)-9 tetrahydrocannabinol, the major cannabinoid. *Dronabinol* is synthetic THC and the main ingredient in the Schedule 3 drug Marinol. *Nabilone* is an engineered THC analog that forms the basis of the Schedule 2 drug Cesamet.

Pharmacology Cannabinoids act on cannabinoid receptors: the CB_1 receptor in the CNS and on the CB_2 receptor localized primarily to immune cells. Dronabinol and nabilone are well absorbed orally, but first pass metabolism and protein binding limit bioavailability. Dronabinol has a faster onset of action (~30 minutes), while nabilone has a longer duration of action (typically 8 – 12 hours, but potentially as long as 24 hours in some patients). Alternative delivery systems – including inhalers, suppositories, and transdermal patches – are being evaluated.

Anti-emetic Use Dronabinol and nabilone are FDA approved for the treatment of nausea and vomiting associated with cancer chemotherapy in patients who have failed to respond to conventional antiemetics. Cannabinoids in this context have two limitations. First, studies show that these agents, while efficacious in – and preferred by – many patients, have potent side effects and a variably narrow therapeutic window. Second, newer types of antiemetic therapy, including the 5-HT3 receptor antagonists and a neurokinin-1 receptor antagonist, have since been developed that appear to be both extremely effective and generally well tolerated. There are no published studies comparing dronabinol and nabilone to these newer generation agents, or to each other.

Orexigenic Use (Appetite Stimulation) Dronabinol is FDA approved for the treatment of anorexia associated with weight loss in patients with HIV/AIDS. Early studies of dronabinol in this population showed promising increases in caloric intake and stabilization or gains in weight. However, later analysis showed that the effect sometimes represented accumulation of water or fat instead of the preferred lean body mass. Nabilone is not approved as an appetite stimulant. The evidence supporting the use of cannabinoids for cancer associated anorexia is limited and with mixed results. Cancer patients using cannabinoids may have improved enjoyment of food, increased protein intake, and improved premeal appetite. There are also reports improved quality of sleep while on cannabinoids.

Side Effects Side effects are both physiologic (hypotension with reflex tachycardia, gastroparesis, ataxia, somnolence, dry mouth) and psychologic (euphoria, poor concentration, and – at high doses – anxiety, delusions, and hallucinations). Symptoms are typically dose related, vary among patients, and are worse in the elderly. Tolerance to many of these effects develops over 1 to 2 weeks. Dronabinol contains sesame oil and poses a risk of anaphylaxis to those with a hypersensitivity to sesame seeds or nuts. Relative contraindications include a history of seizures, and concurrent use of alcohol, sedatives, hypnotics, or other psychoactive agents. Patients taking cannabinoids should be advised not to drive.

Prescribing Guidelines ANTIEMETIC: Dronabinol is dosed 5 mg/m^2 starting 2 hours before chemotherapy and every 4 hours thereafter, to a total of 4 to 6 doses daily. It can be titrated by 2.5 mg/m^2, to a per-dose maximum of 15 mg/m^2. Nabilone is dosed 1 mg twice daily, starting 3 hours before chemotherapy. It can be increased to 2 mg per dose, with a maximum of 6 mg/day in 3 divided doses. Nabilone is typically less expensive. OREXIGENIC: Dronabinol is started at 2.5 mg twice daily, one hour before lunch and dinner, or as a single 2.5 mg dose at night. It can be increased gradually to a maximum of 20 mg/day, in divided doses.

References

1. Walsh D, Nelson KA, Mahmoud FA. Established and potential therapeutic applications of cannabinoids in oncology. *Supp Care Cancer*. 2003; 11:137-143.
2. Otten EJ. Marijuana. In: LR Goldfrank, NE Flomenbaum, et al, eds. *Toxicologic Emergencies,* 7th Edition. New York, NY: McGraw-Hill; 2002.
3. Tramer MR, Carroll D, Campbell FA, et al. Cannabinoids for control of chemotherapy induced nausea and vomiting: quantitative systematic review. *BMJ.* 2001; 323:16-21.
4. Beal JE, Olson R, Laubenstein L, et al. Dronabinol as a Treatment for Anorexia with Weight Loss in Patients with AIDS. *J Pain Symptom Manage*. 1995; 10:89-97.
5. Jatoi A, Windschitl HE, et al. Dronabinol Versus Megestrol Acetate Versus Combination Therapy for Cancer-Associated Anorexia: A North Central Cancer Treatment Group Study. *J Clin Oncol.* 2002; 20:567-573.
6. Slatkin NE. Cannabinoids in the treatment of chemotherapy-induced nausea and vomiting: beyond prevention of acute emesis. *J Support Oncol.* 2007; 5(Suppl 3):1-9.
7. Davis M, Maida V, et al. The emerging role of cannabinoid neuromodulators in symptom management. *Supp Care Cancer.* 2007; 15(1):63-71.
8. Ben Amar M. Cannabinoids in medicine: A review of their therapeutic potential. *J Ethnopharmacology.* 2006; 105:1-25.
9. Anonymous. Nabilone (Cesamet) for chemotherapy-induced nausea and vomiting. *Medical Letter on Drugs & Therapeutics*. 2006; 48(1249/1250):103-4.
10. Nemechek PM, Polsky B, Gottlieb MS. Treatment Guidelines for HIV-associated wasting. *Mayo Clinic Proc.* 2000; 75(4):386-94.
11. Brisbois TD, Kock IH, Watanabe SM. Delta-9-tetrahydrocannabinol may palliate alterted chemosensory perception in cancer patients: results of a randomized, double-blind, placebo-controlled pilot trial. *Ann Oncol.* 2011;22: 2986-93.

Version History: This *Fast Fact* was originally edited by David E Weissman MD. 2nd Edition was edited by Drew A Rosielle and published December 2007; 3rd Edition June 2015. Current version re-copy-edited April 2009; then again June 2015 by Dr. Sam Maiser in which reference #11 was added and incorporated into the text.