See page 352 for suggested questions to begin discussion in your journal club.

# Efficacy of Crude Marijuana and Synthetic Delta-9-Tetrahydrocannabinol as Treatment for Chemotherapy-Induced Nausea and Vomiting: A Systematic Literature Review

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**Purpose/Objectives:** To synthesize the research to determine whether oral delta-9-tetrahydrocannabinol (THC) and smoked marijuana are effective treatments for chemotherapy-induced nausea and vomiting (CINV) and to evaluate side effects and patient preference of these treatments.

**Data Sources:** Original research, review articles, and other published articles in CINAHL®, MEDLINE®, and Cochrane Library databases.

**Data Synthesis:** Cannabinoids are effective in controlling CINV, and oral THC and smoked marijuana have similar efficacy. However, smoked marijuana may not be accessible or safe for all patients with cancer. Also, these drugs have a unique side-effect profile that may include alterations in motor control, dizziness, dysphoria, and decreased concentration.

**Conclusions:** This synthesis shows that cannabinoids are more effective than placebo and comparable to antiemetics such as prochlorperazine and ondansetron for CINV.

**Implications for Nursing:** Nurses should feel supported by the literature to recommend oral synthetic THC as a treatment for CINV to their patients and physician colleagues. Nurses should be cognizant of the side-effect profile for this medication and provide appropriate patient education.

Using marijuana as medicine is a controversial topic. One of the potential uses of marijuana is to decrease the incidence of chemotherapy-induced nausea and vomiting (CINV). Research on the topic spans decades and may provide useful insight for attenuation of these symptoms. The purpose of this article is to synthesize the literature on the efficacy of crude, or "smoked," marijuana and synthetic oral delta-9-tetrahydrocannabinol (THC) as treatments for CINV.

## Background

CINV is a significant, well-documented problem. The chemoreceptor trigger zone in the brain activates the emetic center secondary to chemical stimuli in the blood and cerebrospinal fluid. Chemotherapy stimulates the release of neurotransmitters such as dopamine, histamine, acetylcholine, and serotonin that are involved in the emetogenic pathways. The chemoreceptor trigger zone and the emetic center are rich in receptors for these neurotransmitters, resulting in CINV (Carrieri-Kohlman, Lindsey, & West, 2003). The risk for CINV is dependent on the drugs used for treatment. Chemotherapy drugs have varying levels of emetic, or vomit-inducing, potential. The emetogenicity of a chemotherapeutic agent is ranked on a scale of very low to very high and is associated with incidence of vomiting described as a percentage. Very low emetic potential has a less than 10% vomiting incidence, low emetic potential is 10%–30%, and moderately emetogenic is 30%–60%. High emetogenicity is associated with a 60%–90% incidence of vomiting, and very high emetic potential is 90% (Itano & Taoka, 2005). Regimens with multiple drugs can lead to increased CINV because their emetic potentials are combined. Higher doses of the medications increase the emetic potential, resulting in more severe symptoms (Gullatte, 2001).

CINV is an undesirable side effect; it is distressing physically and may result in decreased quality of life (QOL). Patients may experience nausea, vomiting, or a combination. Nausea may precede vomiting or may occur separately. The sensation of nausea may compromise patients physically by decreasing appetite, leading to poor nutrition or diminished movement that results in muscle decompensation. Nausea may restrict patients' QOL by

limiting social activities, personal enjoyment, or feelings of well-being. Vomiting can lead to malnutrition, poor dentition, and weight loss (Carrieri-Kohlman et al., 2003). Healthcare providers understand the potential effects of CINV and make every effort to attenuate the symptoms. However, conventional antiemetic regimens are not always successful, and alternatives should be sought.

*Cannabis sativa*, or marijuana, has been used since the first century AD in China and Assyria to treat pain, inflammation, epilepsy, and various other neuralgic disorders (Mechoulam & Hanu, 2001). People have used the drug recreationally and to reduce or eradicate unwanted side effects of medications or disease processes, such as nausea, vomiting, and appetite suppression. *C. sativa* contains more than 60 cannabinoids, including THC, which causes many of the psychoactive effects. THC is found in the resin-covered flowers and upper leaves of the female plant. Marijuana typically is smoked in a hand-rolled cigarette; its smoke is inhaled deeply and held in the lungs to ensure maximum absorption of THC (Hall, Christie, & Currow, 2005).

In the 1980s, researchers confirmed that THC binds to receptors in the human body that are highly selective and specific. The primary cannabinoid receptor (CB1) is found mainly in the brain, and the peripheral cannabinoid receptor (CB2) is found in the immune system. CB1 is mediated by guanosine triphosphate–binding proteins and accounts for the brain-mediated effects because of its location in the central nervous system. The effects include, but are not limited to, mood control, appetite, nausea control, motor function, and pain. CB2 is present in macrophages and the spleen and has immunomodulatory effects (Hall et al., 2005; Mechoulam & Hanu, 2001). The absence of cannabinoid receptors in the lower brainstem makes the potential for lethal overdoses practically impossible (Hall et al.). However, adverse effects of the drug such as impaired memory, decreased coordination, distorted perception, anxiety, and paranoia can be unpleasant.

Although researchers identified cannabinoid receptors and demonstrated that THC aided in decreasing CINV, the inhalation route resulted in limited acceptability of the treatment. In 1964, scientists were able to isolate THC and produce synthetic THC (dronabinol) in capsule form (Robson, 2001). The goal was to retain the usefulness of THC, bypassing the legalities and inhalation route of administration and making the medication more acceptable to patients. Dronabinol has been available for restricted use in the United States since 1985 (Robson). Nabilone, an analog of dronabinol, is used mainly in the United Kingdom and Canada but is seldom used in the United States because of its increased potency (Mechoulam & Hanu, 2001). In this article, dronabinol will be the medication specified in discussion of oral synthetic THC.

Research has been conducted sporadically during the past four decades regarding the efficacy of THC in controlling CINV. This review will synthesize the collective literature to assess the effectiveness of THC versus many different antiemetics. This synthesis will allow healthcare professionals to determine the usefulness of THC and give them the ability to make recommendations for its use in the cancer population.

The primary outcome of interest is to ascertain whether oral synthetic THC and smoked marijuana are effective in the treatment of CINV. Secondary outcomes are to evaluate the potential side effects of both treatments and patients' preferences for treatment.

## Methods

A systematic review was conducted to evaluate literature on the medical application of smoked marijuana and synthetic THC for the attenuation of CINV. Literature was identified from MEDLINE® (1966–present), CINAHL® (1982–present), and Cochrane Library (1970–present) databases through the following search terms: *nausea, vomiting, cancer, chemotherapy, cannabis, marijuana,* and *dronabinol*. Reference lists of articles also were searched for citations that may not have been found with the restrictive search terms. To be included in this review, studies had to be adult human clinical trials, including patients treated with smoked marijuana or oral synthetic THC for CINV, and published in English. The search yielded 18 citations that were relevant to the topic; 10 were clinical trials. A summary of all 10 studies can be found in Table 1.

The articles reviewed were evaluated based on the strength of evidence, study design, sample size, and purpose. All studies included in the synthesis evaluated THC for treatment of CINV, and most were randomized or placebo-controlled trials. Studies from the past four decades were included for a comprehensive synthesis of the literature.

## Results

### Delta-9-Tetrahydrocannabinol and Marijuana Versus Placebo

Two of the reviewed studies tested the efficacy of oral synthetic THC versus placebo for CINV. Sallan, Zinberg, and Frei (1975) tested oral THC and placebo in 22 patients with a range of neoplasms receiving chemotherapies of high to very high emetogenicities in a double-blind, randomized, placebo-controlled crossover study. Patients received a single dose of THC or placebo two hours prior to chemotherapy treatment and two and six hours after. Patients assessed whether the medication they received had antiemetic properties. Fourteen of 20 patients who received the THC capsule reported an antiemetic effect, whereas 0 of 22 patients receiving the placebo capsule reported an antiemetic

**Table 1. Articles Reviewed**

| Source | Purpose | Sample | Design | Treatment | Instrument | Results |
|---|---|---|---|---|---|---|
| Sallan et al., 1975 | Compared the effects of THC capsule versus placebo for CINV | 22 patients with various neoplasms on high or very high emetogenic chemotherapy | Controlled, randomized, crossover, double-blind | THC or placebo two hours prior to chemotherapy and two and six hours after | Patient evaluation of antiemetic properties | THC significantly better than placebo at controlling CINV |
| Chang et al., 1979 | THC capsule versus placebo capsule and placebo versus marijuana cigarette for treatment of CINV | 15 patients with osteogenic sarcoma on high-dose methotrexate | Double-blind, randomized, placebo-controlled | Phase I: placebo three times and THC three times in three-paired trials<br>Placebo or THC six hours before chemotherapy and every three hours for a total of five doses<br>If vomiting occurred, patients were switched to marijuana or placebo cigarette for remainder of trial. | THC blood levels were tested and, if patients vomited, frequency was noted. | THC blood levels less than 5 ng/ml: 44% vomited; between 5–10 ng/ml: 21% vomited; and more than 10 ng/ml: 6% vomited<br>Placebo capsules: 72% vomited<br>THC significantly better than placebo |
| Frytak et al., 1979 | Compared prochlorperazine, THC, and placebo to treat CINV; compared toxicities of each drug | 116 patients with GI cancer receiving 5-FU and semustine; 18 patients dropped from the study on day 1 secondary to CNS toxicity or excessive vomiting. | Randomized, double-blind, placebo-controlled | Prochlorperazine, THC, or placebo<br>On day 1: treatment given two hours before and two and eight hours after chemotherapy<br>On days 2–4: doses given three times daily before each regular mealtime | Patient interviews<br>Day 1: volunteered information<br>Day 2: Specific questions were asked regarding nausea and vomitting, appetite, mood, etc.<br>Number of times patient vomited was recorded. | THC and prochlorperazine better than placebo but equally effective<br>More side effects noted with THC |
| Orr et al., 1980 | Compared THC, prochlorperazine, and placebo for severe CINV | 55 patients with various malignancies receiving chemotherapy with moderate to high emetic potential | Double-blind, randomized, placebo-controlled, crossover | THC, compazine, or placebo prior to chemotherapy | Patient evaluations of nausea presence | No nausea in 73% receiving THC, 15% receiving prochlorperazine, and 9% receiving placebo<br>THC more effective than prochlorperazine for moderate to high emetogenic chemotherapy |
| Michigan Cancer Foundation, 1982 as cited in Musty & Rossi, 2001 | Smoked marijuana versus thiethylperazine for CINV | 165 patients | Randomized, crossover | Marijuana cigarette or thiethylperazine<br>If the treatment failed in 24 hours, patients were crossed over to the other treatment group. | Self-report and physician and nurse observations of nausea severity | No significant difference between drugs |
| Ungerleider et al., 1982 | THC versus prochlorperazine for CINV | 214 patients with a variety of malignancies receiving different chemotherapies | Double-blind, crossover | THC or prochlorperazine one hour before chemotherapy and then four hours thereafter for a total of four doses | Patient report of nausea, vomiting, and food intake | Both drugs equally effective in reducing CINV |

*(Continued on next page)*

5-FU—5-fluorouracil; CINV—chemotherapy-induced nausea and vomiting; CNS—central nervous system; ECOG—Eastern Cooperative Oncology Group; GI—gastrointestinal; THC—delta-9-tetrahydrocannabinol

**Table 1. Articles Reviewed (*Continued*)**

| Source | Purpose | Sample | Design | Treatment | Instrument | Results |
|---|---|---|---|---|---|---|
| New Mexico Health and Environment Department, 1983 as cited in Musty & Rossi, 2001 | THC capsule versus marijuana cigarette for treatment of CINV in patients refractory to traditional antiemetics | 142 total patients | Randomized | THC capsule or marijuana cigarette before chemotherapy and for five days after chemotherapy | Self-report using the Target Problem Rating Scale | Both effective at decreasing CINV, but no significant difference between the two treatments |
| Vinciguerra et al., 1988 | Smoked marijuana for CINV in patients refractory to standard antiemetics; patients' acceptance of inhalation route | 74 patients participated; 56 were evaluated. | Nonrandomized, no placebo | Marijuana starting six to eight hours prior to chemotherapy and every four to six hours thereafter for a total of four doses | Patient evaluations using scales 1–5 to evaluate nausea, vomiting, appetite, and mood | Marijuana found to be effective for CINV; 24% of patients dropped out of the study because they did not accept the inhalation route. |
| Lane et al., 1991 | Compared dronabinol and prochlorperazine alone and in combination for prevention and reduction of CINV | 62 patients with breast, colon, lung, lymphoma, or miscellaneous malignancies receiving both low and high emetogenic chemotherapy | Randomized, double-blind, parallel group, multicenter | 10 mg dronabinol plus placebo, 10 mg compazine plus placebo, or 10 mg compazine plus 10 mg dronabinol every six hours; treatment was started 24 hours prior to chemotherapy and continued 24 hours after chemotherapy completion. | Patient evaluation of feelings of nausea and number of times emesis occurred | The combination of dronabinol and compazine was found to be significantly more effective in controlling chemotherapy-induced nausea and vomiting than either drug alone. |
| Meiri et al., 2007 | Compared dronabinol, ondansetron, and combination for delayed CINV | 64 patients with various neoplasms not involving bone marrow receiving moderate to highly emetogenic chemotherapy | Randomized, double-blind, parallel group, placebo-controlled | Dexamethasone and ondansetron prior to chemotherapy<br>Four groups: dronabinol only, ondansetron only, dronabinol plus ondansetron, and placebo were dosed on a fixed schedule day 2 and flexible on days 3–5. | Patient report using a visual analog scale, number of vomiting episodes, and ECOG | No significant difference among three active treatment groups; all were significantly better than placebo for CINV. |

5-FU—5-fluorouracil; CINV—chemotherapy-induced nausea and vomiting; CNS—central nervous system; ECOG—Eastern Cooperative Oncology Group; GI—gastrointestinal; THC—delta-9-tetrahydrocannabinol

effect. The investigators determined that THC had antiemetic properties and was significantly better at reducing CINV than placebo ($p < 0.001$).

Chang et al. (1979) also published a study that compared oral THC and smoked marijuana to placebo. Fifteen patients with osteogenic sarcoma who were treated with high-dose methotrexate (high emetogenic potential) for 18 months after removal of their primary tumors participated in this double-blind, randomized, placebo-controlled study. Patients randomly received placebo three times and THC three times in three paired trials during six hospitalizations, which took approximately five to six months. Each patient received a dose of either placebo or THC capsule starting six hours prior to chemotherapy treatment and continuing every three hours for a total of five doses. If vomiting occurred, patients were switched to a random assignment of a placebo or marijuana cigarette for the remainder of that trial. Outcomes of treatment included blood levels of THC and number of vomiting episodes. The results showed that with THC blood levels less than 5 ng/ml, 44% of patients vomited; between 5–10 ng/ml, 21%; and with greater than 10 ng/ml, 6%. Seventy-two percent of patients who received the placebo vomited. The investigators concluded that THC was more effective than placebo even with blood levels lower than 5 ng/ml; as THC blood levels rose, the efficacy of the drug increased. The investigators found that THC was

significantly better than placebo in terms of number of vomiting episodes and their volume, degree, and duration of nausea ($p < 0.001$).

Another study tested crude marijuana as a treatment for CINV. Vincinguerra, Moore, and Brennan (1988) conducted a nonrandomized, one-group study that tested the efficacy and acceptability of inhaled, or smoked, marijuana for CINV in patients with histologically confirmed malignancies currently receiving chemotherapy who were refractory to standard antiemetics. Seventy-four patients initially agreed to participate in the study, but only 56 were evaluated. Eighteen patients dropped out of the study because they did not accept the administration route for various reasons. Patients were given multiple doses of marijuana, beginning six to eight hours prior to receiving chemotherapy treatment and every four to six hours thereafter for a total of four doses. Outcomes included patients' perceptions of nausea, vomiting, appetite, and mood. Thirty-four percent of patients rated marijuana as very effective (n = 18), 44% rated it as moderately effective (n = 26), and 22% reported no benefit (n = 12). The investigators found smoked marijuana to be effective for CINV based on the evaluations. However, the differences between responders and nonresponders were not statistically significant.

## Delta-9-Tetrahydrocannabinol Versus Phenothiazides

Prochlorperazine and other phenothiazides are traditional antiemetic medications that work by depressing the chemoreceptor trigger zone in the brain (Deglin & Vallerand, 2001). Four studies were reviewed that tested the efficacy of oral synthetic THC versus traditional oral antiemetics. Orr, McKernan, and Bloome (1980) compared oral THC, prochlorperazine, and placebo in patients with severe CINV. The 55 patients with various malignancies who participated in the double-blind, randomized crossover study were receiving chemotherapies of moderate to very high emetic potentials. Patients were given oral THC, compazine, or placebo prior to their chemotherapy treatments and were asked to evaluate their nausea within 24 hours of drug intake. Nausea was denied by 73% of patients receiving oral THC, 15% receiving prochlorperazine, and 9% receiving a placebo. The investigators concluded that oral THC was significantly more effective in controlling CINV with moderately to highly emetogenic chemotherapies ($p < 0.05$) than prochlorperazine or placebo, but not for very high emetogenic drugs.

Frytak et al. (1979) compared oral THC, prochlorperazine, and placebo for treating CINV in patients with gastrointestinal cancer receiving chemotherapies that elicited a strong emetic stimulus on day 1 and a weaker emetic stimulus on days 2–4. Patients were studied during the first cycle of chemotherapy only. A secondary purpose of the study was to compare the toxicities of each test drug. One hundred seventeen patients participated in the randomized, double-blind study; 116 were evaluated. Eighteen patients withdrew from the study on day 1 because of central nervous system (CNS) toxicity or excessive vomiting (10 were receiving THC, five prochlorperazine, and three placebo). On day 1, the medications initially were given two hours prior to chemotherapy treatments, with subsequent doses two and eight hours after chemotherapy initiation. On days 2–4, doses were given three times daily before each regular mealtime. Treatment effects, including nausea and vomiting, sedation, coordination, and feelings of being "high" were evaluated by participant interviews. The number of times each patient vomited was recorded. On day 1, significantly more patients receiving placebo reported nausea and vomiting compared to patients in the other two groups ($p < 0.05$). No statistically significant difference was observed between THC and prochlorperazine in regard to their antiemetic properties. Also, patients who received THC reported significantly more toxicities than patients receiving compazine or placebo. In addition, significant differences were noted in distribution for maximum sedation scores ($p < 0.007$), incoordination scores ($p < 0.0001$), and feelings of being "high" ($p < 0.0001$), with the group receiving THC reporting significantly more sedation, incoordination, and feelings of being "high."

Ungerleider et al. (1982) tested the efficacy of prochlorperazine versus oral THC on CINV in a randomized, double-blind, crossover study. Two hundred fourteen patients with a variety of malignancies being treated with different chemotherapies were involved, 73% of whom had received prochlorperazine before prior chemotherapy treatments with varying results. Eligibility requirements included prior chemotherapy with documented nausea and vomiting, or beginning the first cycle of a highly emetogenic drug or drug combination. The effectiveness was evaluated by patient report of nausea, vomiting, appetite, food intake, mood, interaction, and concentration. Patients' attitudes also were studied. Most (60%) patients had positive attitudes toward THC before the study began. Patients received prochlorperazine or THC one hour prior to chemotherapy treatment and every four hours thereafter for a total of four doses. No significant differences were observed in the ability of THC and prochlorperazine to treat nausea and vomiting, and both drugs were equally effective against chemotherapies of low, moderate, and high emetic potential. No significance was found between prior attitudes toward THC and how effective the drug was in terms of antiemetic potential.

## Delta-9-Tetrahydrocannabinol Plus Phenothiazides

Lane et al. (1991) found the combination of THC with another antiemetic to be most effective. The investigators conducted a randomized, double-blind, parallel-group study of 62 participants with breast, colon, lung,

lymphoma, or miscellaneous malignancies receiving low and high emetogenic chemotherapies to test dronabinol and prochlorperazine alone and in combination for the prevention and reduction of CINV. Patients evaluated their feelings of nausea and recorded the number of times emesis occurred. Patients received dronabinol plus placebo, compazine plus placebo, or dronabinol plus compazine every six hours. Treatment began 24 hours prior to chemotherapy and continued 24 hours after the chemotherapy infusion was complete for up to a total of six days. Outcomes measured included presence, duration, and severity of nausea and vomiting. Although the difference between drugs for presence of nausea was not statistically significant, the combination of dronabinol and prochlorperazine was significantly better at mitigating the duration and severity of CINV ($p < 0.001$) than either agent alone.

### Marijuana Versus Phenothiazides

In 1982, the Michigan Cancer Foundation (Musty & Rossi, 2001) conducted a randomized crossover study with 165 patients to test smoked marijuana and thiethyl perazine, a phenothiazide derivative, for control of CINV. Patients either smoked a marijuana cigarette or took thiethylperazine prior to chemotherapy. If either treatment failed in 24 hours, patients were crossed over to the alternate treatment group. Severity of nausea and time elapsed between chemotherapy and vomiting were measured. Results were determined by patients' self-report and observations made by doctors and nurses. Neither nausea severity nor time to vomiting differed significantly between the two test drugs.

### Oral Delta-9-Tetrahydrocannabinol Versus Marijuana

In 1983, the New Mexico Health and Environment Department (Musty & Rossi, 2001) conducted a randomized study comparing the THC capsule with a marijuana cigarette for the treatment of CINV in patients who were refractory to traditional antiemetics. A total of 142 patients participated; 67 participants took the THC capsule, and 75 participants smoked a marijuana cigarette. Patients used the treatments before chemotherapy as well as five days after chemotherapy treatments. The investigators found that both treatments were effective in decreasing CINV; no significant differences were observed between the two treatments.

### Oral Delta-9-Tetrahydrocannabinol Versus Serotonin Receptor Antagonists

Meiri et al. (2007) compared the efficacy of dronabinol (oral THC), ondansetron, and the combination of the two drugs for delayed CINV in a randomized, double-blind, placebo-controlled, parallel-group study involving 64 patients with various neoplasms not involving the bone marrow receiving moderately to highly emetogenic chemotherapy. Patients were randomized into four groups: dronabinol (group D), ondansetron (group O), dronabinol plus ondansetron (group DO), or placebo (group P). All patients received the standard antiemetic treatment of dexamethasone and ondansetron prior to chemotherapy. All patients, except for those in group P, also received dronabinol before and after chemotherapy on day 1. On day 2, group D received dronabinol four times per day, group O received ondansetron and placebo twice daily, group DO received dronabinol and ondansetron twice daily, and group P received placebo four times per day. On days 3–5, patients used a flexible dosing schedule of 2–4 capsules four times per day. The primary outcome measure was the prevalence of total response, defined as no vomiting, intensity of nausea less than 5 mm on a 0–100 mm visual analog scale, and no rescue medication use. Secondary outcomes measured included presence of nausea, vomiting episodes, duration and intensity of nausea, performance status, and QOL. Total response was achieved in 54% of patients in group D, 58% of patients in group O, 47% of patients in group DO, and 20% of patients in group P. None of the differences in the treatment arms were significant, but all of the active drugs were significantly more effective than a placebo in alleviating CINV. No statistically significant difference was observed among groups D, O, and DO in measurement of secondary outcomes.

## Discussion and Nursing Implications

The primary aim of this literature review was to determine whether oral synthetic THC or marijuana was effective against CINV. The studies suggest that marijuana and synthetic oral THC are more effective than placebo in treating CINV from drugs of high emetic potential. Another conclusion is that smoked marijuana and oral THC are equally efficacious in controlling symptoms of nausea and vomiting caused by drugs of moderate to high emetogenicities. When compared to traditional oral antiemetics, smoked marijuana and oral THC were found to be equally effective.

Secondary aims were to assess potential side effects of oral THC and marijuana and determine patients' preference for the treatments. Studies demonstrated that the side effects of smoked marijuana and oral THC are greater when compared to placebo and phenothiazide- and serotonin receptor antagonist antiemetics. In Frytak et al.'s 1979 study, 18 patients (from a sample size of 116) recused themselves from the study on day 1 secondary to increased CNS toxicity or excessive vomiting (10 from the THC group, 5 from the prochlorperazine group, and 3 from the placebo group). Patients taking the THC or prochlorperazine may have had more CNS toxicity than those receiving a placebo, but the investigators did not

state how many patients had CNS toxicity versus excessive vomiting or which drug category coincided with which complaint. As for the remaining participants, a portion found greater toxicities with oral THC capsules as opposed to traditional antiemetics. Patients did not appear to have a significant preference for oral THC versus other antiemetics, but studies suggest that the inhalation route of smoked marijuana was unacceptable to many patients. In a study by Vinciguerra et al. (1988), 18 patients (24% of the original sample size) removed themselves from the study after deeming the inhalation route unacceptable.

Limitations of the studies include small samples sizes and weak study designs. The studies by Chang et al. (1979) and Sallan et al. (1975) had sample sizes of fewer than 25 patients. However, Orr et al. (1980) and Frytak et al. (1979) had larger sample sizes to verify and validate their findings. Vinciguerra et al.'s (1988) study design was weak because it lacked a placebo control but was included in the analysis for its information regarding acceptability of the inhalation route of smoked marijuana. Although Sallan et al.'s (1975) results also were questionable because the THC dosing was changed midstudy, subsequent studies verified their findings.

Although oral THC and smoked marijuana were found to be equally effective, many reasons suggest that oral THC is the better treatment for CINV. Many people are unable to tolerate the harshness of marijuana smoke, making the marijuana cigarette a poor option (Voth, 2003). Infection also can be a concern when an immunocompromised patient is smoking crude marijuana that contains many bacteria and fungi because it is a natural substance (Voth). In addition, any smoked substance potentially can cause lung damage and cancer secondary to the carcinogenic properties of the drug (Hall et al., 2005). Also, in most states, prescribing or suggesting marijuana for CINV treatment is complicated because of the obvious legal implications and difficulty obtaining the drug legally.

One thing to keep in mind when suggesting oral THC for CINV is its side-effect profile. The increased psychoactive effects such as decreased motor control, limited concentration, dizziness, dysphoria, and paranoia are unacceptable to many patients who refuse to continue taking THC or even participate in studies (Hall et al., 2005). However, all drugs have their own unique side-effect profiles, and patients must determine whether the side effects can be tolerated.

More studies should be done with increased sample sizes comparing oral THC and serotonin receptor antagonists to further validate findings. Additional trials should be conducted comparing oral THC and aprepitant in the treatment of delayed CINV. Employing oral THC in a trial comparing the current protocol of dexamethasone, dolasetron (or other serotonin receptor antagonist), diphenhydramine, and lorazepam to the same protocol substituting oral THC for dolasetron for treatment of severe CINV also may prove advantageous.

## Conclusion

This review of studies has shown that cannabinoids are more effective than placebo and are at least comparable to antiemetics such as prochlorperazine and ondansetron. Cannabinoids have great potential as adjuvant medication, and nurses should feel supported by the literature to suggest oral THC for treatment of CINV to their patients and physician colleagues. As with any medication, side-effect profiles should be reviewed with patients prior to taking the medication and potential medication interactions should be investigated. The addition of the cannabinoids to existing antiemetic regimens may provide increased relief of CINV, resulting in better QOL and overall health of patients with cancer.

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Digital Object Identifier: 10.1188/09.ONF.345-352

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## Journal Club Questions

This article has been chosen as particularly suitable for reading and discussion in a journal club format. The following questions are posed to stimulate thoughtful critique and exchange of opinions, possibly leading to changes on your unit. Formulate your answers as you read the article. Photocopying of this article for group discussion purposes is permitted.

1. How significant is the issue of nausea and vomiting control with our patients?
2. How successful are our current nausea and vomiting protocols in controlling these side effects of chemotherapy?
3. Is synthetic tetrahydrocannabinol (THC) available in our hospital formulary?
4. What experience has anyone had with patients who take synthetic THC or who smoke marijuana specifically to relieve chemotherapy-related nausea and vomiting?
5. Based on information in the article or direct experience with this drug, what specific concerns should be addressed when administering this medication?
6. What specific concerns should staff or patients have regarding the use of this specific drug?

At the end of the session, recap the discussion and make plans to follow through with suggested strategies.