

Narang S, Gibson D, et al. Efficacy of Dronabinol as an Adjuvant Treatment for Chronic Pain Patients on Opioid Therapy. J Pain 2008;9(3):254-264.

Design: Randomized clinical trial

Brief summary of results:

- 30 patients (16 women, 14 men, mean age 43) taking stable doses of opioids for more than 6 months for chronic noncancer pain were eligible for entry into a study of the analgesic effects of dronabinol in Boston
- They were ineligible if they had cancer pain, had been using transdermal fentanyl or intrathecally administered opioids, needed opioid dosing more often than every 8 hours, had current substance abuse by self-report, were involved in litigation, compensation, or disability issues, or had depression and/or anxiety
- They entered a double-blinded, single dose phase (Phase I) in which each patient received each of three treatments: placebo, 10 mg dronabinol, or 20 mg dronabinol, in a sequence which was determined randomly
- Each of the three treatments was administered when the patients came to the clinic in the morning, took one dose of the assigned treatment for that day, and remained in the clinic for the remainder of the day, together with their morning dose of the regular opioid medication
- The primary efficacy measure was total pain relief (TOTPAR) 8 hours after the dose of study medication; this was scored on a scale of 0=no relief of pain to 10=complete relief of pain
- The use of breakthrough medication (presumably an opioid) was allowed during the 8 hour period of observation, but further study measurements were stopped after the breakthrough medication was taken
- After Phase I, the patients were invited to an open-label Phase II, in which they were given a 4 week supply of dronabinol and titrated their own use, taking as little as 5 mg once a day or as much as 20 mg tid, while keeping a pain diary at home
- The primary outcome for Phase II was the change in pain intensity from baseline to the average pain intensity during week 4 of Phase II; at the end of week 4, patients who wished to continue taking dronabinol were referred to their treating physicians for further care
- In Phase I, TOTPAR was 31.1 for placebo, 39.7 for 10 mg dronabinol, and 41.7 for 20 mg dronabinol; the latter two scores were statistically significant compared to placebo ($p<.05$ and $p<.01$ respectively)
- In Phase II, average pain intensity decreased from about 6.9 to about 5.3 (graphical display only), with $p<.001$ for week 4 compared to baseline
- Side effects were frequent and were dose-related; drowsiness, dry mouth, and dizziness were the most frequent, but subsided on average within 2 hours of dosing

Authors' conclusions:

- Dronabinol may be a useful adjunct to opioids in the treatment of chronic pain, and may improve quality of sleep as well

Comments:

- The reporting of the main outcome, TOTPAR, is not clear; it is measured on a scale of 1 to 10, but the TOTPAR reported in Table 3 range from 31.1 to 41.7
- TOTPAR is said to be calculated when “integral relief scores” were “summed”
- If summation were done, then the score of 41.7 would be the sum of the 30 patients for whom the summation was done, and would be only about 1.4 points on average
- When only p values are reported, the effect size of the compared treatments is not well characterized
- The only phase of the trial with a comparison was Phase I, in which the administration was done in the clinic, with blood levels and pain scores elicited on site; this appears to be in part a study of the pharmacokinetics of the drug, and the administration of the drug was under conditions that would not characterize the use of the drug outside that setting
- Presumably the “rescue” medication taken in clinic was an opioid, but it is not clear that some patients may be regularly scheduled to take an opioid more than once per day; it is possible that the “breakthrough” drug could have been their regularly scheduled medication dose

Assessment: Inadequate for evidence of dronabinol as an analgesic (main outcome is poorly reported, and administration of the study medication was under highly artificial conditions)