Journal Watch

Multicenter, Double-Blind, Randomized, Placebo-Controlled, Parallel-Group Study of the Efficacy, Safety, and Tolerability of THC:CBD Extract and THC Extract in Patients With Intractable Cancer-Related Pain

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Abstract:

Objective: This study compared the efficacy of a tetrahydrocannabinol: cannabidiol (THC:CBD) extract, a nonopioid analgesic endocannabinoid system modulator, and a THC extract, with placebo, in relieving pain in patients with advanced cancer.

Methods: In total, 177 patients with cancer pain, who experienced inadequate analgesia despite chronic opioid dosing, entered a two-week, multicenter, double-blind, randomized, placebo-controlled, parallel-group trial. Patients were randomized to THC:CBD extract (n = 60), THC extract (n = 58), or placebo (n = 59).

Results: The primary analysis of change from baseline in mean pain Numerical Rating Scale (NRS) score was statistically significantly in favor of THC:CBD compared with placebo (improvement of – 1.37 vs. -0.69), whereas the THC group showed a nonsignificant change (-1.01 vs. -0.69). Twice as many patients taking THC:CBD showed a reduction of more than 30% from baseline pain NRS score when compared with placebo (23 [43%] vs. 12 [21%]). The associated odds ratio was statistically significant, whereas the number of THC group responders was similar to placebo (12 [23%] vs. 12 [21%]) and did not reach statistical significance. There was no change from baseline in median dose of opioid background medication or mean number of doses of breakthrough medication across treatment groups. No significant group differences were found in the NRS sleep quality or nausea scores or the pain control assessment. However, the results from the European Organisation for Research and Treatment of Cancer Quality of Life Cancer Questionnaire showed a worsening in nausea and vomiting with THC:CBD compared with placebo (P = 0.02), whereas THC had no difference (P = 1.0). Most drug-related adverse events were mild/moderate in severity.

Conclusions: This study shows that THC:CBD extract is efficacious for relief of pain in patients with advanced cancer pain not fully relieved by strong opioids.

Comments:

Strength/Uniqueness:

This trial is one of the first multicentre, double-blind, randomized, placebo-controlled, parallel-group study to examine the efficacy, safety, and tolerability of cannabinoids products in cancer pain . It is an adequately powered study. The endpoints of this study were clearly defined as change from baseline in NRS pain score and use of breakthrough analgesia. The definition of clinically meaningful NRS reduction is reasonably defined (at least 30 % on a pain NRS). This definition is based on chronic pain trials.

Weakness:

1) This study was sponsored by a pharmaceutical company.
2) The patients appeared to be recruited from number of different facilities with probably very small number of participants from each facility. This may impact on the generalizability of the result.
3) The course of trial is relatively short in two weeks to provide any conclusion for safety of this product in this population.
4) The definition of intractable pain is clearly stated though it is questionable for the generalizability (NRS>4 for two days after at least 1 week of strong opioid treatment for cancer pain).
5) The information for the pain classification appeared to be rather limited to the patho-physiologies of cancer pain.
6) Considering the cognitive side effects of cannabinoids (including memory and concentration were assessed as a part of outcome measurement) ,no information of participant's base line cognitive status and objective changes after use of cannabinoids products were provided. It is unclear how the cognitive decline influenced on participants NRS. It is possible that cognitive effect benefited these participants by making them being less aware of their problems. impairment

Relevance to Palliative Care:

This trial may provide information to the palliative care clinicians for unconventional analgesic approach when dealing with difficult pain syndrome, intractable to conventional pain management methods. However the results should be cautiously interpreted due to the potential cognitive side effects in a p[population who are at high risk for developing delirium.