Synthetic Tetrahydrocannabinol (THC) is a Safe Adjunct to the Treatment of Postoperative Pain after Arthroscopic Knee Surgery: A Pilot Randomized Safety Trial

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INTRODUCTION:

Effective pain management after arthroscopic surgery often depends on opioids, which may introduce risks of overdose and diversion. Alternatives like multimodal pain protocols can reduce opioid use, but they can be complex. Dronabinol, a synthetic tetrahydrocannabinoid, has shown potential as a safer option, with studies suggesting it may reduce hospital stay and opioid use without affecting pain scores. This pilot study aimed to assess Dronabinol's safety when added to postoperative management following knee arthroscopy and later determine effectiveness in pain control.

METHODS: After IRB approval in November 2021, eligible and consenting patients over 18 years undergoing arthroscopic knee surgery were randomized to receive either Dronabinol or placebo alongside standard multimodal pain management. Exclusion criteria included patients under the age of 18, patients unable to provide consent, patients who are pregnant, breastfeeding, or trying to become pregnant, patients with an allergy to any of the study drugs, patients undergoing revision surgery or open surgery, patients with a history of mania, depression, or schizophrenia, patients currently diagnosed with alcohol or drug abuse, patients who cannot or will not abide by the medication regimen, or patients taking any of the following drugs: anticholinergic agents, benzodiazepines, central nervous system depressants, droperidol, hydroxyzine, levomepromazine, methotrimeprazine, monoamine oxidase inhibitors, ritonavir, selective serotonin reuptake inhibitors, sympathomimetics, St. John's Wort. Primary outcome for this pilot study was safety of the test drug with the secondary outcome being pain control and number of opioid tablets (hydrocodone-acetaminophen 5-325mg) consumed at 3 different time intervals: 24 hours, 48 hours, and 7 days post-op. Continuous variables were tested for normality and assessed using parametric or non-parametric 2 sample tests, as appropriate. Categorical variables were reported as count and percentage and assessed using Fisher exact tests.

RESULTS:

Among patients in the Dronabinol group, none reported side effects, while 2 out of 7 patients in the placebo group did (ie. dizziness, drowsiness, confusion, dry mouth). At 24 hours postoperatively, zero patients in the Dronabinol group reported using opioid medication (mean 0.00 half-tablets of Norco), compared to a mean of 0.75 half-tablets in the placebo group ($p = 0.299$). At 48 hours, opioid consumption remained lower in the Dronabinol group (mean 0.00 half-tablets of Norco) compared to the placebo group (mean 1.29 half-tablets), although the difference was not statistically significant ($p = 0.1563$). Use of non-opioid analgesics was similar between groups. By day 7, both groups reported no opioid use, but the Dronabinol group showed slightly higher mean use of non-opioid medications, including ASA (2.00 vs. 1.50, $p = 0.5714$), naproxen (2.00 vs. 1.00, $p = 0.3143$), and study caplets (1.50 vs. 0.75, $p = 0.3143$).

The primary endpoint—safety and side effects—showed no significant adverse events, with a lower, though not statistically significant, incidence of reported side effects in the dronabinol group ($p = 0.470$). The secondary outcome—opioid consumption—also favored the dronabinol group at 24 and 48 hours postoperatively, though the differences were not statistically significant ($p = 0.299$ and $p = 0.1563$, respectively).

DISCUSSION AND CONCLUSION:

Dronabinol appears to be a safe addition to postoperative multimodal pain management. Although our pilot study found no differences in side effects and opioid consumption between patients who received Dronabinol and those who received a placebo, the expansion study will hope to confirm these findings and to explore the potential role of dronabinol in other surgical contexts.