Dronabinol for the Treatment of Cannabis Dependence

BACKGROUND:

- Marijuana is the most commonly used illicit drug in the United States
- Cannabis dependence is the 3rd most prevalent substance dependence syndrome
- The investigation of pharmacotherapies for cannabis dependence remains limited and no effective medication has yet been identified
- The agonist substitution strategy has been effective for other substance use disorders
- Dronabinol is an orally bioavailable synthetic form of delta-9-tetrahydrocannabinol, a naturally occurring pharmacologically active component of marijuana
- It has been shown to reduce cannabis withdrawal symptoms in laboratory settings

OBJECTIVE:

- To evaluate the safety and efficacy of Dronabinol in treating cannabis dependence

METHODS:

- Randomized, double-blind, parallel-group, placebo-controlled,single-site, outpatient clinical trial
- Duration: 12 weeks total
- Inclusion criteria:
    - Between the ages of 18 and 60
    - Met DSM-IV-TR criteria for current cannabis dependence
    - Reported using marijuana at least 5 days a week during the past 28 days
    - Had a marijuana-positive urine drug screen on the day of study entry
- Exclusion criteria:
    - Met DSM-IV-TR criteria for a current significant and unstable Axis I psychiatric condition which required psychiatric intervention or in the investigators opinion would be disrupted by the study medication
    - Physiological dependence on any substances (other than nicotine) that would require a medical intervention
    - Current suicidal risk or history of suicidal or homicidal behavior during the last 2 years
    - History of seizures
    - Unstable physical condition (HTN, elevated transaminase levels, uncontrolled diabetes)
    - Clinically significant coronary vascular disease as indicated by history or suspected by abnormal ECG or history of cardiac symptoms
    - History of an allergic reaction to Dronabinol
    - Nursing, pregnant, or females unwilling to use an effective method of birth control
    - In professions in which even mild intoxication would be hazardous
    - Court mandated to treatment
- Total patients enrolled 156; Placebo Group (PBO) – 77, Dronabinol (DRO) – 79
- Dronabinol or Placebo: 2 capsules twice daily (total 4 capsules/day) on a flexible schedule
- Started at 10mg once daily and titrated up to max 20mg twice daily (target dose)
- Primary Outcome Measure
    - Two consecutive weeks of abstinence in weeks 7 and 8 (Primary)
- Secondary Outcome Measures
    - Retention in treatment (time to dropout)
    - Maximum number of consecutive days of abstinence
    - Average daily amount of marijuana use
    - Days per week of marijuana use
    - Per-visit marijuana withdrawal discomfort score
    - Abstinence during 2-week lead-out phase
- Data handling method used: intent to treat

RESULTS:

- A total of 99 patients completed the study; Placebo Group – 44, Dronabinol Group – 55
- The proportion of patients who achieved 2-weeks of continuous abstinence in weeks 7 and 8
    - Not significantly different between the DRO (17.7%) and PBO (15.6%) groups (P = .69)
    - Proportion of patients achieving 2 consecutive weeks of abstinence in their last two weeks of study participation were similarly low as for the primary outcome and did not significantly differ between DRO (21.3%, 16/76) and PBO (19%, 14/72)
- Retention in treatment (time to dropout)
    - Retention was significantly better on DRO (77% retained to week 8), compared to PBO (61% retained to week 8) group (P = .02)
- Maximum number of consecutive days of abstinence
    - not significantly different effects of treatment (P = .79)
    - The median maximum number of consecutive days of abstinence was 6 days for DRO (Interquartile range: 1–13 days), and 5 days for PBO (Interquartile range: 2–16 days)
- Average amount of marijuana use
    - significant three-way interaction across treatment, week and baseline amount (P< .001)
        - indicates treatment effect over time was different for varying baseline use
        - this difference diminished towards the end of the trial
            - as cannabis use and PBO were found to be comparable
- Days per week of use
    - Close to daily and did not differ between groups (P = .54)
    - significant effect of time (P < .001)but no significant interaction of treatment by time
        - indicating frequency of cannabis use decreased over weeks in the trial
- Marijuana withdrawal
    - significant treatment by time interaction (P = .02)
        - suggests that withdrawal symptoms decreased over time for both groups
        - but DRO group experienced significantly greater drop in WDS over time
- Abstinence during 2-week lead-out phase
    - Majority maintained abstinence: 92.9% (13/14) DRO group; 91.7% (11/12) PBO group

STRENGTHS:

- Government supported (NIDA)
- Sufficient sample size todetect clinically meaningful effect sizes (small to medium)
- Psychological component of substance dependence recognized and practically controlled for using a standardized psychotherapy platform
- Relevant conclusionsdrawn from results

LIMITATIONS:

- Voucher incentives – provided alternative motives for study participation
- Reliance on self-reporting to gather data
- Invalidated methods - modified TLFB approach developed by the authors
- Appropriateness of dosage and regimen itself difficult to evaluate
- Timing of outcome measures inappropriate

CONCLUSIONS:

Dronabinol for the treatment of cannabis dependence shows promise. Although this study didn't prove much statistical significance, success may be possible with further investigation. In the future, Dronabinol needs to be studiedat higher doses, for longer durations, in combinations,and as a more individualized therapy. Designing of regimens should be patient-specific with non-specific time frames. Cannabis dependence is a considerable public health problem, and no pharmacologic interventions have been successful in treating it. The results of this study are a stepping stone in the development of a clinically effective treatment.