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INTRODUCTION: There is significant evidence that cannabinoids may be involved in the modulation of pain, especially of neuropathic origin. HIV-related painful peripheral neuropathy is a significant medical problem with unsatisfactory treatment options. Based on the effects of cannabinoids in preclinical models of neuropathic pain and anecdotal case reports, a controlled trial of smoked cannabis was conducted.

METHODS: Following a 16 patient open-label pilot proof-of-concept phase that suggested a beneficial clinical effect of seven days of smoked cannabis, a follow-on randomized, placebo-controlled trial was conducted. Fifty participants with painful HIV-related neuropathy and baseline pain scores > 3 on a 10 point visual analog scale were admitted to the General Clinical Research Center for a 7-day inpatient stay. Participants smoked one 3.56% tetrahydrocannabinol containing cigarette or a matching placebo three times daily for five days. In addition to the effect of smoked cannabis on the subjects’ chronic clinical pain, the impact on an experimental heat/capsaicin pain model was also evaluated. The primary endpoints were the reduction and relative reduction in neuropathic pain as assessed by average daily pain scores as well as the effect of smoking on acute experimental pain. A >30% reduction in pain was considered to be significant for this analysis. Reduction in experimental pain was a secondary outcome measure.

RESULTS: Fifty of the 56 randomized participants (43 men, 7 women, mean age 48 years) completed the placebo-controlled trial; 25 on each arm. Patients had an average of 6 years of neuropathic pain. In 17 cases the neuropathy was felt to be secondary to HIV alone, in 26 secondary to HIV medications and to both in 7. Baseline characteristics were well-matched across study arms. Thirteen of the 25 patients who were randomized to marijuana cigarettes reported greater then 30% reduction in pain during the intervention phase, compared with 6 of the 25 patients receiving placebo cigarettes (p=0.04). The pain reduction was greater in the group receiving marijuana (34%) than in the group receiving placebo (16.7%). The marijuana group also experienced a similar significant reduction in response to the experimental pain model compared to placebo recipients. Adverse events were not appreciated in this trial.

CONCLUSION: Smoked marijuana is effective in reducing chronic ongoing neuropathic pain as well as acute pain in the experimental pain model. The magnitude of the response of the neuropathic pain is similar to what is seen with gabapentin, a widely used therapeutic intervention for HIV neuropathy.

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