

A pilot study on the plasma concentration-effect relationship of tetrahydrocannabinol/cannabidiol oromucosal spray in patients with multiple sclerosis.

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ABSTRACT

Objectives: We aimed to assess the potential relationship between intrasubject 9-tetrahydrocannabinol/cannabidiol (THC/CBD) oromucosal spray plasma profiles and clinical effects elicited by subacute dosing in chronically treated patients with multiple sclerosis (MS).

Methods: The patients were challenged with a morning test dose of two THC/CBD sprays at a 15-minute interval. Venous blood samples were collected before the first spray administration and every 30 minutes after the second spray, until 240 minutes post-dosing. Patients rated their spasticity by the Numerical Rating Scale (NRS) simultaneously with blood drawings. Postural and motor tests were performed before the first spray and 90 and 180 minutes thereafter. The study design was pilot, single center, open and prospective.

Results: Twelve patients were recruited. Peak plasma concentrations of THC/CBD largely varied among patients, from 0.60 to 13.29 ng/mL for THC and 0.55 to 11.93 ng/mL for CBD. Time to peak plasma concentrations ranged from 150-240 minutes for THC and 90-240 minutes for CBD. Patients' NRS serial scores decreased after dosing, from a median value of 6 to 3.5 ($p<0.001$). A significant inverse correlation was observed between median intrasubject repeated NRS scores and corresponding median values of both THC ($p<0.01$) and CBD ($p<0.002$) plasma concentrations. No

significant effect of cannabinoids dosing could be appreciated according to posturographic and motor tests.

Conclusion: Our kinetic-dynamic findings from THC/CBD oromucosal spray are the first obtained in real MS patients. Although preliminary, they suggest that subacute dosing might elicit a subjective clinically significant effect on MS related spasticity, paralleling cannabinoids measurable plasma concentrations.