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Baclofen in the management of cannabis dependence syndrome

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Abstract: Cannabis is the most commonly used illicit drug in the world. However, only few studies have shown the efficacy of pharmacologic agents in targeting cannabis withdrawal symptoms or reducing the reinforcing effects of cannabis. Baclofen has been shown to reduce cannabis withdrawal symptoms and the subjective effects of cannabis. We think that the clinical utility of baclofen for cannabis dependence is a reasonable approach. A case report using baclofen is presented and provides preliminary support for the use of baclofen in the management of cannabis dependence.

Keywords: Cannabis dependence, baclofen, cannabis withdrawal

Introduction

Studies have unequivocally documented the occurrence of a cannabis dependence syndrome by demonstrating that cannabis has reinforcing properties in nonhuman primates and that abstinence from the drug causes withdrawal in humans [Tanda and Goldberg, 2003; Fattore *et al.* 2008]. This withdrawal syndrome can last from 1 to 3 weeks after cannabis cessation [Budney and Hughes, 2006]. The risk of relapse after a period of abstinence is significant [Perkonig *et al.* 2008]. Haney and colleagues have demonstrated that Oral Delta-9-THC seemed to ameliorate substantially symptoms of cannabis withdrawal and could decrease physiological and subjective effects of cannabis withdrawal [Haney *et al.* 2010]. Other treatments such as clonidine and rimonabant have also been demonstrated to decrease physiological and subjective effects, but none of these treatments have been successful in treating cannabis dependence or self-administration behavior [Hart, 2005].

Clinical studies have examined several treatment options and despite their limitations, they have suggested that treating cannabis withdrawal can improve the likelihood of prolonged abstinence [Clapper *et al.* 2009]. Nevertheless there is currently no recognized pharmacological treatment for the management of withdrawal syndrome or relapse prevention in cannabis dependent patients and clinical research with GABA-B

compounds is warranted given this important objective as stated by Vandrey and Haney [Vandrey and Haney, 2009]. Baclofen, a selective GABA-B agonist, has already been studied for alcohol and cocaine withdrawal and relapse prevention [Addolorato *et al.* 2006; Shoptaw *et al.* 2003]. Its safety and tolerability have been confirmed in several studies [Addolorato *et al.* 2002; Stallings and Schrader, 2007] and the low potential for abuse of baclofen must be regarded as a major factor in pharmacological treatment of substance addiction [Addolorato *et al.* 2000].

Few data are available today regarding the use of baclofen in the treatment of cannabis dependence. To the best of the authors' knowledge there was only a single clinical study that has associated baclofen with a cannabinoid under controlled laboratory conditions [Haney *et al.* 2010]. This study shows that baclofen significantly decreased self-reported ratings of 'High' and 'Want Marijuana' but had no impact on cannabis self-administration in a relapse model of cannabis use. There was also a case study of six patients with cannabis and nicotine dependence that shows that baclofen, at a standard dose of 40 mg/day, could reduce the signs and symptoms of cannabis withdrawal and facilitated abstinence [Nanjayya *et al.* 2010].

In a recent study, Lile and colleagues suggests that GABA-B receptor subtype could be involved

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in the abuse-related effects of delta-9-THC and that GABA-B receptors may be implicated in cannabinoid-related behaviors [Lile *et al.* 2012]. They emphasize that baclofen could enhance the effects of delta-9-THC or produce comparable effects alone, so could decrease some of the symptoms associated with cannabis withdrawal.

We hypothesized that baclofen could be an effective treatment in reducing the symptoms of cannabis withdrawal and in decreasing craving.

Case report

Mr P, an administrative executive aged 40, was monitored by our outpatient addiction department during 2012. He had been using cannabis (in herbal form) at home, every evening, for about 15 years with no abstinence of more than 2–3 days. He used cannabis to reduce symptoms of irritability and severe insomnia. He told us about his inability to stop his cannabis consumption, as well as growing problems at home and work, which he thought were related to use of the drug. Apart from occasionally drinking alcohol, he said that he did not consume any other drug or substance. He used to smoke 5 or 6 joints between 18:00 and 22:00 at home alone in his den. He met the criteria for cannabis abuse and dependence of DSM-IV and ICD-10, and had no symptoms of other psychopathological illnesses. He acknowledged finding it difficult to stay focused on specific tasks for a long time and sometimes had a hard time keeping up. Neuropsychological assessment showed no symptoms of attention deficit hyperactivity disorder (ADHD), but found that cognitive performance was impaired for auditory working memory and short-term memory. He never felt the urge to smoke cannabis at his work place, but tended to consume more at the weekend and on vacation (an average of 8–10 joints per day). Although convinced that his cannabis allowed him to control his impulsivity, to be less irritable and therefore behave better when with the family, he agreed to come for a consultation when forced to by his wife. She could no longer support seeing him remote, without interest in his children when he was at home, preferring to isolate himself and smoke joints in his own corner of the house. He finally recognized that his behavior at home and with his family was directly related to his consumption of cannabis. When we offered him medication to help with cannabis

withdrawal, he was ambivalent about the goal, hesitating between only reducing and completely stopping his cannabis use. No medication is currently recognized in the management of cannabis withdrawal and given the anxiolytic effects of this drug we decided to propose treatment with baclofen, a drug that we also commonly use, off label, in our addiction department for the treatment of alcohol dependence. Before starting treatment and after informing the patient and obtaining his consent, we carried out a somatic and biological assessment which showed no abnormality and a urine screen attested to the consumption of cannabis. The Cannabis Withdrawal Scale (CWS) [Allsop *et al.* 2011] score was 79/190 and the Cannabis Abuse Screening Test (CAST) [Legleye *et al.* 2012] score was 6/6. We then initiated treatment with baclofen at a dose of 15 mg/day divided into three doses of 5 mg (given in the morning, afternoon and evening). The dose was then increased by 15 mg each week to reach a maximum dose of 60 mg per day after 4 weeks of monitoring (20 mg in the morning, 20 mg at noon and 20 mg in the evening). During the first 2 weeks of treatment with baclofen, the consumption of cannabis did not change, and the patient felt no adverse effects of the treatment. CWS score was 50/190. In the third week he described a decreased desire to consume cannabis, and a decrease in his usual evening impulsiveness, being manifested by an increase in activity with his children and a slight improvement in relations with his wife. After 4 weeks of treatment, he had decreased his consumption of cannabis by more than half during the week, but he still persisted with notable consumption for the weekend and especially for sleep disorder. A biological assessment was taken after 1 month of treatment and no disorder was observed compared with the baseline taken before starting treatment with baclofen. The CWS score was then 37/190. The dose of baclofen was increased to 70 mg for the weekend (20 mg in the morning, 20 mg at noon and 30 mg in the evening) and this dose was maintained during the week. After six weeks of treatment with baclofen the patient consumed no cannabis at all, said he felt more relaxed and no longer complained of sleep disorder. The consumption of alcohol was not noted during the monitored period. We continued treatment with baclofen at the same dose and continued monitoring and consultation. At 16 weeks after the start of treatment the patient felt calmer, less anxious and was still not consuming cannabis.

Conclusion

This case report provides preliminary support for the use of baclofen in the management of cannabis dependence, especially for heavy cannabis users, with long-term and significant consumption. Nevertheless, further investigations are needed and randomized controlled trials are necessary to confirm that baclofen could be recommended as an efficient treatment for cannabis dependence.

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Conflict of interest statement

The author declares that there is no conflict of interest.

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