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Introduction

Cannabis is the most commonly used illicit drug of abuse in New Zealand (NZ); in 2008 15% of those aged 16-64 years of age reported having used it in the past 12 months [1]. Long term cannabis use can be associated with the development of dependence, which is manifest by a withdrawal syndrome on cessation [2,3]. During withdrawal, relapse to cannabis use is common as it relieves the symptoms of withdrawal [3]. The association between cannabis use and mental health problems (in particular anxiety, depression, and schizophrenia) and a number of other adverse life outcomes (such as poor educational outcomes and life satisfaction) has been reported [4]. Chronic use of cannabis also has adverse effects on pulmonary and cardiac health [5,6]. Survey evidence shows that frequent cannabis users (who do not smoke tobacco) are more likely to experience many of the respiratory problems that chronic tobacco smokers experience [8].

Many tobacco users also misuse cannabis, vice versa [9,10]. While there are differences in the way people use both substances (some roll their own tobacco and cannabis 'cigarettes', others make 'joints' comprising of only cannabis), the concurrent use of cannabis and tobacco can add to the health burden experienced by such individuals, and may increase the potential for substance-induced harm over and above that caused by using one substance on its own [10]. Therefore, an intervention that can reduce the harm caused by both substances could be highly cost-effective, and would have immediate and long-term health benefits for individuals, irrespective of their age or current state of health.

Varenicline has demonstrated efficacy as a smoking cessation aid [11]. It is a partial agonist at the $\alpha_4\beta_2$

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be significantly more effective than placebo in reducing the severity of cannabis withdrawal symptoms

quit smoking tobacco, but not cannabis, and so there was no external pressure to alter their use of the latter. Furthermore, all participants were enrolled in the Auckland Methadone Service and attended CADS for regular outpatient treatment, but did not report receiving any current treatment for tobacco or cannabis use. Cannabis use is common among methadone maintained patients [25] but has been found to have no measurable effect on treatment outcomes. Scavone and colleagues [27] reported that while cannabis use was relatively high during induction onto methadone, it dropped significantly following stabilisation. Participants in this study were not undergoing methadone induction and so therefore it is unlikely that the reported reductions in cannabis use could be attributed to the effect of methadone treatment.

Ending that all participants stopped taking varenicline prior to completion of the 12 week course of the treatment is disappointing. Participants reported a variety of side effects whilst taking varenicline. Headache and vomiting, feeling fat, feeling nauseated and vomiting, and feelings of anger and being short tempered were attributed to taking the drug by four participants. None of these reports of adverse effects is surprising. Data from clinical trials show that gastrointestinal symptoms (commonly nausea) and fatigue were amongst the most common side effects reported (occurring at the rate of 1%, and incidence higher than placebo [20]. More recently, varenicline has been implicated in violence towards others, which may manifest as anger [28], but there are few other reports of this effect.

Conclusion

Findings from these cases suggest a link between the administration of varenicline and a reduction in the enjoyment experienced from using cannabis and reduction in the amount of cannabis used. We postulate that the probable mechanism responsible for this effect is the action of varenicline at the nAChR, which is a common receptor target for both varenicline and THC. Indeed the nAChR has been implicated, through in vivo animal studies, as a possible target for pharmacological agents to treat cannabis abuse [17]. As far as the authors are aware, these results are the first to demonstrate this phenomenon in humans, but there is a need for larger controlled studies to more definitively demonstrate this phenomenon. These future studies will also need to monitor the incidence of side effects, in particular nausea that might affect induction onto varenicline and ultimately success of using this drug for this purpose. Furthermore, alcohol is also known to target nAChRs [29]. Recent early human trials have shown that varenicline reduces alcohol craving, and the rewarding effects and quantity of alcohol consumed [30-32], and therefore alcohol consumption should also be monitored.

Given that many tobacco smokers also smoke cannabis [16] we argue that the availability of a therapeutic intervention, such as varenicline, that has the potential to target the misuse of both substances would confer significant health benefits for these individuals.

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