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Attenuated opioid analgesia to experimental pain in cannabis users

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To the Editor:

We read with interest the finding of Twardowski et al¹ that people who regularly used cannabis required significantly higher amounts of sedatives when undergoing an endoscopic procedure compared with nonusers.

An unanticipated finding from our ongoing study ([NCT02945293](#)) examining opioid analgesia and side effects in people who regularly consume alcohol and a subset who also reported using cannabis is in line with the findings from Twardowski et al.¹ The major goal of our study is to examine the effects of aging and alcohol use on opioid analgesic response. Older adults (aged ≥ 60 years) and middle-age adults (aged 35–59 years) who self-reported alcohol use were enrolled. The amount of alcohol consumed over the past 30 days was characterized by self-report, a blood-based biomarker, and self-reported cannabis use. For the laboratory study visit, participants were asked to refrain from alcohol and pain medications (including cannabis) for 24 hours before the study visit. Participants underwent baseline assessments that included an experimental pain stimulus, the cold pressor test (CPT), which involves placing a hand in cold water ($\pm 1^\circ\text{C}$). Participants then received 10 mg of oxycodone. The CPT was repeated 90 minutes later during the peak opioid effect. The typical response to the CPT under the influence of an opioid is increased time (seconds) before the first sensation of pain (threshold) and increased time before hand withdrawal (tolerance). No alcohol was administered during the study day.

A mixed, linear effect model revealed that, independent of recent alcohol use, participants who used cannabis did not show the typical and anticipated increase in pain threshold and tolerance compared with nonusers on the CPT (Figure). These findings suggest that regular cannabis use may attenuate analgesic effects of opioids, which is consistent with the findings of Twardowski et al.¹

Results are limited by a small sample size (N=128) and lack of detailed cannabis use information (eg, frequency and form). Nonetheless, the use of an experimental model, rather than uncontrolled clinical data, suggests that cannabis use be examined further with regard to its possible effect on pain medication efficacy, which may be an important piece of information for physicians to consider in the future. (doi:[10.7556/jaoa.2020.070](#))

Reference

1. Twardowski MA, Link MM, Twardowski NM. Effects of cannabis use on sedation requirements for endoscopic procedures. *J Am Osteopath Assoc*. 2019;119(5):307–311. doi:10.7556/jaoa.2019.052

Figure.

Results of the cold pressor test 90 minutes after oxycodone dose comparing people who regularly use marijuana with people who do not. Typical response was an increased amount of time before (A) sensation of pain (threshold) and (B) removal of hand (tolerance). Error bars represent 95% CI. ^a $P < .001$. Typical response on the cold pressor test (CPT) under the influence of an opioid is increased amount of time for threshold and tolerance relative to pre-drug baseline. An attenuated response was observed in regular marijuana users, indicating reduced analgesia in response to experimental pain in marijuana users.