Research

The adverse effects of cannabinoids: implications for use of medical marijuana

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In the current issue of CMAJ, Wang and colleagues present a systematic review of the research on adverse effects of medical cannabis use. They included 23 randomized controlled trials and 8 observational studies of cannabinoids and cannabis extracts for various medical indications. The authors found that most of the adverse events (96.6% [4615/4779]) reported in the randomized clinical trials were not serious; dizziness was the most common of these (15.5% [714/4615]). They found that, although the rate of nonserious adverse events was higher among participants assigned to medical cannabinoids than among controls, the rates of serious adverse events did not differ significantly between the 2 groups (rate ratio 1.04, 95% confidence interval 0.78–1.39).

These findings support the conclusions of the Institute of Medicine, that short-term use of cannabinoids for medical purposes has an acceptable safety profile. This provides reassurance on the safety of prescribing cannabinoids and the newer cannabis extract for the short-term symptomatic relief of nausea and vomiting in cancer treatment and for the relief of acute pain (e.g., postoperatively). However, the review by Wang and colleagues is unable to provide information on the long-term use of cannabinoids for chronic disorders, such as multiple sclerosis, because the available trials were of relatively short duration (8 hours to 12 months).

None of the trials involved the smoking of cannabis. Observational population-based cohort studies of recreational cannabis users provide some indication of what the adverse events of long-term cannabis smoking may be. These studies have largely examined the effects in adolescence and early adulthood of sustained recreational use of cannabis among young people. More rarely, they have examined rates of long-term adverse health effects, such as cancer, that may arise from prolonged exposure to carcinogens contained in cannabis smoke. It is not clear whether medical use of cannabis among older adults would lead to the psychosocial outcomes that occur in younger adults. The consequences that are of most concern to clinicians and patients are the risks of developing cannabis dependence, exacerbation of cardiovascular disease, precipitation of psychotic disorders and cancers. Cannabis dependence can develop, but the evidence on risk factors for dependence comes primarily from studies that are of relatively short duration (8 hours to 12 months).
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involving recreational users who began using cannabis in adolescence and early adulthood and who use the most potent products. These users smoke cannabis with a greater frequency and intensity than older adults who would use smaller doses for symptom relief.11 We know nothing of the risks of incident cannabis dependence in the context of long-term, supervised medical use.

There has been concern about an association between cannabis use and psychosis, with evidence suggesting that cannabis may precipitate psychotic symptoms or disorders in people vulnerable to such symptoms.12 However, this evidence also comes from studies involving recreational users. There are currently no data on the extent of risk for psychotic symptoms among medical users, but those who are vulnerable to psychosis because of personal or family history would be ill-advised to use cannabis heavily for any reason.12,13

The risk of cardiovascular disease is potentially more concerning given that the population using cannabis for medical purposes probably has a higher prevalence of cardiovascular problems.14 There is little evidence on the extent of risk for adverse cardiovascular outcomes among cannabis users with pre-existing conditions. In a recent exploratory study, Mukamal and colleagues15 found that people who used cannabis heavily (in addition to heavy use of tobacco and alcohol) and who had higher elevated risk factors for adverse outcomes were at slightly elevated risk for death at later follow-up, but deaths were not related to cardiovascular causes. More research on this topic is needed. The risk factors for cancer associated with cannabis smoking remain uncertain given inconsistent findings: some studies have suggested no increased risk, whereas case–control studies have suggested some elevation of risk with heavy long-term use.8,9

The findings from Wang and colleagues16 review that, based on the current data, the risk of adverse events associated with short-term medical use of cannabinoids and cannabis extracts are minor. The risk seems to be marginally greater with oral use of Δ-9-tetrahydrocannabinol than with oral use of combined Δ-9-tetrahydrocannabinol–cannabidiol.8 These differences matter because the cannabis plant contains hundreds of cannabinoids, and cannabidiol may counteract some of the adverse effects of Δ-9-tetrahydrocannabinol.16 We need better information on the adverse effects of more sustained use of cannabinoids and cannabis preparations from follow-up studies involving patients who use these preparations.

There is a more pressing need for follow-up studies involving patients who smoke cannabis for medical purposes, to assess the risk for cannabis dependence and cardiovascular disease. These studies should involve Canadian patients authorized to use herbal cannabis (2261 as of October 200717), who have been willing to do so despite their doctors’ limited capacity to provide detailed information on the magnitude of risks associated with such use.

Competing interests: None declared.

Contributors: Both of the authors contributed to the conception and design of the manuscript, drafted and revised the article and approved the final version for publication.

Acknowledgements: The National Drug and Alcohol Research Centre is funded by the Australian Government Department of Health and Ageing. Louisa Degenhardt is the recipient of an Australian National Health and Medical Research Council Senior Research Fellowship. In 2000–2001, Wayne Hall was the Chair of the Working Party on the Use of Cannabis for Medical Purposes in New South Wales, Australia. Louisa Degenhardt was the Research Officer for the Working Group.

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