CORRESPONDENCE

The Therapeutic Potential of Cannabis and Cannabinoids

by Dr. med. Franjo Grotenhermen und Prof. Dr. med. Kirsten Müller-Vahl
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Scientific Data Are Lacking

Using a substance that has been used as a medicinal remedy for millennia to treat cancer, immunodeficiency syndrome, and muscle spasms seems an obvious thing to do.

It does, however, seem completely unscientific to initiate a study of smoking cannabis in chronically ill patients because it seems to cause greater damage to the bronchi than does tobacco.

It's not new for a potentially hallucinogenic plant-derived drug to have found its way into treatment, but, in my view, more potent treatment options are available for patients with cachexia, pain, and nausea—including options gained from sufficient experience in the combination with opiates.

The problem in treating muscle spasms in underlying neurological disorders—and the authors indirectly point this out in their table—lies in the induction of neurological adverse effects, including delirium.

To assign responsibility for the risks to the patient alone is common practice only for self-medication.

It is entirely possible to remain below the hallucinogenic threshold, especially for single doses, but the pharmacodynamics cannot be reproduced without blood concentration monitoring. The article is lacking scientific data about this. As long as these data are not available, the only option for treatment-refractory symptoms is dosage adjustment in an in-patient setting.

In that scenario it seems likely that drug monitoring would be decided on, because in view of the efficacy-safety profile it seems entirely feasible that a therapeutic effect would be achieved.

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Conflict of interest statement

The author declares that no conflict of interest.

Limited Range of Indications for Cannabis

In my job as a neurologist and psychiatrist specializing in the relatively new discipline of pain medicine, a focus of my work has for many years been harm prevention—of nephropathy due to analgesics, gastrointestinal complications of NSAIDs such as hemorrhage of perforation, toxic hepatopathy, and drug-induced chronic headache with complications (1). Long-term treatment with opioid analgesics—after checking responsiveness and tolerability by means of regular and systematic follow-up—had far better results in this setting than did non-opioids (2). NSAIDs are effective in acute treatment and are the reasonable option in that setting, but they are associated with complications in the longer term.

For cannabinoids, important risks include triggering of psychosis, schizophrenia, and cognitive impairments (3), which the authors mentioned in their article (4). It should also be pointed out that cannabis and cannabinoids are effective in only a proportion of patients in possible indications such as permanent pain in multiple sclerosis or other neuropathic pain conditions or severe spasms.

This contingency (that which is not necessary, but which may be, or not be, possible), which runs as theme throughout pain medicine, can therefore not offer conclusions that follow a set pattern, such as “There is now clear evidence that cannabinoids are useful for the treatment of various medical conditions,” but only conclusions along the lines that cannabinoids may be useful. Furthermore, the authors state: “The use of such preparations may therefore be reasonable for patients in whom conventional treatment does not achieve adequate relief of symptoms such as spasticity, pain, nausea, vomiting, or loss of appetite.” This is correct in principle, but it does not include a definition of “conventional treatment.” The rational range of indications for cannabis/cannabinoids is therefore limited.

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In Reply:

Wörz mentions the much-discussed association between cannabis use and cognitive impairments or the triggering of psychosis. A recently published cohort study that is regarded as the most reliable study of the effects of cannabis on brainpower to date confirmed earlier results: while study participants who developed cannabis dependency before the 18th birthday showed notable impairments to memory, concentration, and brainpower, adults did not show any such impairments, even if they were heavy users (1). It may be assumed that cannabis can damage the adolescent brain, but not—in contrast to alcohol—the adult brain. According to the available evidence, treatment of adult patients with cannabinoid medications can be classified as harmless in terms of developing cognitive deficits.

The assessment for the occurrence of psychosis is similar: regular consumption of cannabis evidently doubles the risk of psychosis only if this happens before the physiological growth of the brain is completed. In the meantime, numerous factors have become known that increase the probability of psychosis. Double the risk of the disorders exists in children who grew up in large cities, compared with children growing up in a rural environment (2). Before treating children and adolescents with cannabis medications, a careful risk-benefit analysis is required.

Wörz rightly emphasizes that all medical drugs can cause adverse effects and that they may not be effective in all patients. Experts share the view of the US Institute of Medicine, according to which “Marijuana is not a completely benign substance. It is a powerful drug with a variety of effects. However, except for the harms associated with smoking, the adverse effects of marijuana use are within the range of effects tolerated for other medications.” (3). Cannabinoids are currently used particularly for those indications where established treatments do not result in any improvement or cause unacceptable side effects.

Hagmann points out the harms that smoking causes to the respiratory tract. According to the current evidence, smoking cannabis does in fact cause less

damage than smoking tobacco (4), but from a medical perspective patients should generally be advised against inhaling toxic combustion products. Since responsiveness to cannabinoids and the targeted plasma concentrations vary between individuals, measuring blood concentrations is neither necessary nor does it make sense. Relevant psychological side effects of cannabinoid medications are best avoided by gradual stepping up of the dosage and tailoring the dosage to the individual patient. Severe neurological side effects, such as Hagmann expresses concerns about, are immaterial in everyday clinical practice. For this reason, dosage adjustment in an in-patient setting is usually not required.

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Professor Müller-Vahl has received conference delegate fees as well as travel and hotel expenses from Astra-Zeneca and Lundbeck. She has also received honoraria for conducting commissioned clinical studies, and funding for a research project she initiated, from Boehringer Ingelheim. She serves on the executive board of the Arbeitsgemeinschaft Cannabis als Medizin e. V. (ACM, Germany's medical cannabis working group, reg assoc) and the International Association of Cannabinoid Medicines (IACM).