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Bio-basierte Ökonomie
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Certification

I confirm that I follow the issue of the medical use of cannabis and cannabinoids since 1994 and am aware of all relevant publications concerning vaporization of cannabis and cannabinoids since this time. Since the preparation of my review for Storz & Bickel and my last certification of July 18, 2018 four relevant new studies on this issue came to my attention. The objective of my literature review was to detect new data on the use of the Volcano Medic, the Mighty Medic or other vaporizers for the administration of cannabinoids in humans. The primary focus was studies on safety issues. One study reviewed the effects of cannabis in asthmatic patients.The second study presented results from a mouse model of aerosol exposure by using a vaporiser to study health effects of cannabis inhalation. The third showed that most fibromyalgia patients in Israel smoke medicinal cannabis, but that a large number prefers vaporisation. The fourth analysed cannabis metabolites in urine after different routes of administration.

1. Review on the medical use of cannabis in asthmatic patients

Investigators of the Hadassah-Hebrew University School of Medicine in Jerusalem, Israel, reviewed the knowledge of cannabis effects on asthmatic patients (Jarjou'i & Izbicki 2020). They showed that cannabis has a bronchodilator effect on the airways and might have an anti-inflammatory effect on asthmatic patients. They noted that "harmful effects on the lungs are mainly attributed to smoking and include airway irritation and the development of chronic bronchitis symptoms." They concluded that smoking should be avoided and inhalation by vaporiser may be better, but they claimed more research "to determine the harmful effects of vaporizers as well as inhalers."

2. Development of a mouse model of aerosol exposure by using a vaporiser to study health effects of cannabis

Researchers of the Northeastern University in Boston, USA, investigated acute neuroradiological, behavioral, and physiological effects of nose-only exposure to vaporized cannabis in mice (Farra et al. 2020). To facilitate the assessment of risks associated with cannabis inhalation, they developed and

characterized a method for exposing mice to cannabis in a way that mimics the delivery of the drug to the airways of smokers. Cannabis (10% THC, 0.05% CBD) was vaporized to generate aerosols with a reproducible particle profile. Aerosols were acutely delivered to male, adult mice via a nose-only exposure system. Serum THC levels were measured for increasing cannabis doses. Blood pressure and heart rate were recorded at baseline and following exposure. Behavioral response to cannabis inhalation in the open field was documented. Awake neurological activity upon cannabis exposure was monitored using BOLD fMRI. Cannabis aerosols contained particles with count median diameter of 243 ± 39 nm and geometric standard deviation of 1.56 ± 0.06. They observed THC specific effects in the animals and concluded that "animal models of aerosol exposure will be instrumental for uncovering the health outcomes of chronic cannabis use."

3. Many fibromyalgia patients prefer the use of a vaporiser for administration of medicinal cannabis

Israeli investigators from the Department of Medicine of Laniado Hospital in Netanya and the Technion, Israel institute of Technology, evaluated the characteristics of cannabis use among patients with fibromyalgia (Habib & Levinger 2020). For this purpose all patients with fibromyalgia who were followed up at Laniado Hospital in Netanya and at the Nazareth Hospital in Nazareth, in addition to all patients followed at the different health service organizations by the first author were located and contacted regarding a large number of parameters. One-hundred and one patients completed the study. 54% smoked pure cannabis, 18% used vaporized cannabis only and 3 participants only used cannabis oil. The rest used a variety of combinations. The mean minimal daily frequency of cannabis consumption was 4 times and the mean maximal daily frequency was 8 times. Mean improvement in sleep and pain was slightly more than 77% with less improvement in other parameters. Cannabis treatment enabled nearly half of the patients to discontinue any treatment for fibromyalgia and all participants recommended cannabis treatment for their loved ones in case they develop severe fibromyalgia.

4. Analysis of cannabinoid metabolites in urine after smoking, vaporising and oral cannabis intake

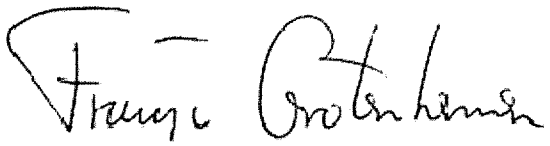
Investigators of the National Institute on Drug Abuse of the National Institutes of Health in Baltimore, USA, and other scientific institutions within the US and Sweden analysed all urine specimens from 11 frequent and 9 occasional cannabis users for 11 cannabinoids for up to 85 h following controlled smoked, vaporized or oral 51 mg THC in a randomized, placebo-controlled, within-subject dosing design (Huestis et al. 2020). No cannabidiol, cannabinol, cannabigerol, tetrahydrocannabivarin THCV, THC, 11-hydroxy-THC, tetrahydrocannabinolic acid were detected in urine. Median THCCOOH-glucuronide maximum concentrations (Cmax) differed considerably between the 3 administration routes in occasional users but not in frequent users. They were 68 µg/L after smoking, 27 µg/L after vaporisation and 360 µg/L after oral intake for occasional and 378, 248 and 485 µg/L for frequent users. The reason of the higher concentrations in frequent users compared with occasional users after smoking and vaporising cannabis may be a more efficient inhalation.

Summary:

The study by Jarjou'i & Izbicki (2020) confirms that many asthmatic patients profit from cannabis inhalation and that smoking should be avoided due to its harmful effects. Authors suggest more research into possible harmful effects of vaporisation. The article on the study by Farra et al. (2020) presents results from an animal model of cannabis vaporisation, which may be feasible to analyse effects from cannabis inhalation. The study by Habib & Levinger (2020) confirms that while smoking is still the preferred method of medicinal cannabis administration in Israel vaporisation is becoming

increasingly popular. The study by Huestis et al. (2020) shows that smoking cannabis results in higher THC-COOH concentrations in urine than vaporising the same amount of THC.

I declare that literature quoted in this review reflects current state-of-the-art, that references in this review are taken from recognized scientific publications, and that this review is outcome of a study according to scientific principles.



Dr. F. Grotenhermen

Literature

Farra YM, Eden MJ, Coleman JR, Kulkarni P, Ferris CF, Oakes JM, Bellini C. Acute neuroradiological, behavioral, and physiological effects of nose-only exposure to vaporized cannabis in C57BL/6 mice. Inhal Toxicol. 2020 Apr;32(5):200-217. doi: 10.1080/08958378.2020.1767237. Epub 2020 Jun 1.

Habib G, Levinger U. [CHARACTERISTICS OF MEDICAL CANNABIS USAGE AMONG PATIENTS WITH FIBROMYALGIA]. [Article in Hebrew] Harefuah. 2020 May;159(5):343-348.

Huestis MA, Sempio C, Newmeyer MN, Andersson M, Barnes AJ, Abulseoud OA, Blount BC, Schroeder J, Smith ML. Free and Glucuronide Urine Cannabinoids after Controlled Smoked, Vaporized, and Oral Cannabis Administration in Frequent and Occasional Cannabis Users. J Anal Toxicol. 2020 May 5:bkaa046. doi: 10.1093/jat/bkaa046.

Jarjou'i A, Izbicki G. Medical Cannabis in Asthmatic Patients. Isr Med Assoc J. 2020 Apr;22(4):232-235.

Abstracts of the cited literature, which are all available in the database PubMed

Isr Med Assoc J. 2020 Apr;22(4):232-235.

Medical Cannabis in Asthmatic Patients.

Jarjou'i A(1), Izbicki G(1).

Author information: (1)Pulmonary Institute, Shaare Zedek Medical Center, affiliated with the Hadassah-Hebrew University School of Medicine, Jerusalem, Israel.

BACKGROUND: With the increased use of cannabis in the medicinal and recreational domains, it is becoming more important for physicians to better understand its harmful and beneficial effects. Although medical cannabis comes in several forms, the preferred route of administration is smoking or inhalation. After caring for three asthmatic patients who were treated with medical cannabis and who reported improvement in their symptoms, we decided to review the available data on the effects of medical cannabis on asthmatic patients. OBJECTIVES: To review the known effects of medical cannabis on asthmatic patients. METHODS: A thorough search was conducted of the MEDLINE and PubMed databases as well as the internet for publications about the effects of medical cannabis on asthmatic patients. RESULTS: Cannabis has a bronchodilator effect on the airways and might have an anti-inflammatory effect on asthmatic patients. However, harmful effects on the lungs are mainly attributed to smoking and include airway irritation and the development of chronic bronchitis symptoms. CONCLUSIONS: Cannabis has some benefit, yet there are many harmful effects on the lungs. Additional research is needed to determine the harmful effects of vaporizers as well as inhalers.

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Acute neuroradiological, behavioral, and physiological effects of nose-only exposure to vaporized cannabis in C57BL/6 mice.

Farra YM(1), Eden MJ(1), Coleman JR(2), Kulkarni P(2), Ferris CF(2), Oakes JM(1), Bellini C(1).

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Objective: The rapid increase of cannabis consumption reinforces the need to elucidate the health hazards of this practice. The presence of fine particulate matter in cannabis smoke and vapor poses a major concern, as it may contribute to cardiopulmonary disease. To facilitate the assessment of risks associated with cannabis inhalation, we developed and characterized a method for exposing mice to cannabis in a way that mimics the delivery of the drug to the airways of smokers. Materials and Methods: Cannabis (10.3% THC, 0.05% CBD) was vaporized to generate aerosols with a reproducible particle profile. Aerosols were acutely delivered to male, adult C57BL/6 mice via a nose-only exposure system. Serum THC levels were measured for increasing cannabis doses. Blood pressure and heart rate were recorded at baseline and following exposure. Behavioral response to cannabis inhalation in the open field was documented. Awake neurological activity upon cannabis exposure was monitored using BOLD fMRI.Results and Discussion: Cannabis aerosols contained particles with count median diameter of 243 ± 39 nm and geometric standard deviation of 1.56 ± 0.06. Blood serum

THC levels increased linearly with aerosolized mass and peaked at 136 ± 5 ng/mL. Cannabis inhalation decreased heart rate and blood pressure but promoted anxiety-like behavior. Observed differences in BOLD activation volumes linked cannabis to increased awareness to sensory stimuli and reduced behavioral arousal.Conclusions: Quantified physiological, behavioral, and neurological responses served as validation for our mouse model of cannabis inhalation. Animal models of aerosol exposure will be instrumental for uncovering the health outcomes of chronic cannabis use.

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[CHARACTERISTICS OF MEDICAL CANNABIS USAGE AMONG PATIENTS WITH FIBROMYALGIA].

[Article in Hebrew]

Habib G(1)(2), Levinger U(3).

Author information: (1)Rheumatology Unit and Department of Medicine C, Laniado Hospital, Netanya. (2)Technion, Israel institute of Technology. (3)Department of Medicine C, Laniado Hospital, Netanya, Israel.

INTRODUCTION: Medical cannabis (MC) is becoming more and more popular among patients with chronic pain syndromes. In this study we evaluated the characteristics of MC use among patients with fibromyalgia. METHODS: All patients with fibromyalgia who were followed up at Laniado Hospital in Netanya and at the Nazareth Hospital in Nazareth, in addition to all patients followed at the different health service organizations by the first author were located and contacted regarding a large number of parameters. The data included demographic information, duration of fibromyalgia symptoms and diagnosis, duration of MC use, monthly consumption of MC, frequency of daily use, number of species of MC currently used, number of species previously used, types and features of MC supplied, methods of MC consumption, delay in MC supply, symptoms of cannabis withdrawal during delay in supply or shortage of MC, familiarity with the content of (-)- trans-Δ^9-tetrahydrocannabinol (THC) and Cannabidiol (CBD) of the current species used. Furthermore, information was retrieved on current medications for fibromyalgia and medications for fibromyalgia stopped after starting MC consumption, discontinuation of MC treatment, companies growing and supplying the currently consumed MC, names of current MC species, dominance of Sativa or Indica of the current MC species, and the impact of MC on clinical parameters such as pain, sleep, anxiety, depression, memory, concentration and weight. In addition, questions were presented regarding work, outdoor leisure time, driving, sharing their own MC with other people, opinion on the reform of MC in Israel and adverse effects of MC. RESULTS: One-hundred and one patients completed the study; 73% of the participants were female with a mean age of 45±11.8 years. The mean duration of fibromyalgia symptoms and diagnosis were 8.39±6 and 4.69±3.9 years, respectively. The mean duration of MC consumption was 15.3±12.6 months and the mean monthly consumption amount was 28.6±10.2 g. 54% smoked pure cannabis, 18% used vaporized cannabis only and 3 participants only used MC oil. The rest used a variety of combinations. The mean minimal daily frequency of MC consumption was 4.11±2.9 times and the mean maximal daily frequency was 7.9±5.6 times. The mean number of current daily MC species was 2.11±1 and the mean number of tried species was 6.7±5.2 for each participant; 47% of all the participants stopped any other treatment for fibromyalgia and 51% reduced the dose or the number of other medications for fibromyalgia. One patient only stopped MC treatment. Tikun Olam was the manufacturing company with the largest number of clients and its most popular species for daytime was "Alaska" and "Erez" for night-time. Mean improvement in sleep and pain was slightly more than 77% with less improvement in other parameters; 36% of the patients reported weight gain, while 16% reported weight loss; 51% reported

having more leisure time outdoors. Nearly all patients refused sharing any amount of their MC with friends or family members, and all patients recommended MC treatment for their loved ones once they develop severe fibromyalgia; 61% of the participants were against the reform of MC and 11% were in favor of it. Nearly one quarter of the patients reported mild adverse effects and one patient developed a psychotic attack (was consuming 70 gram of MC monthly). CONCLUSIONS: MC is an effective treatment for fibromyalgia, with nearly zero % withdrawal from this treatment. The mean daily amount consumed was relatively low, less than 1 gram, and the main method of consumption was smoking with a huge variety in the frequency of smoking during the day and night among the participants. MC treatment enabled nearly half of the patients to discontinue any treatment for fibromyalgia and all participants recommended MC treatment for their loved ones in case they develop severe fibromyalgia. Most participants were against the reform of MC in Israel. Mild adverse effects were reported in nearly a quarter of the patients but did not result in discontinuing its consumption.

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Free and Glucuronide Urine Cannabinoids after Controlled Smoked, Vaporized, and Oral Cannabis Administration in Frequent and Occasional Cannabis Users.

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BACKGROUND: Total urinary 11-nor-9-carboxy-tetrahydrocannabinol (THCCOOH) concentrations are generally reported following cannabis administration. Few data are available for glucuronide and minor cannabinoid metabolite concentrations. METHODS: All urine specimens from 11 frequent and 9 occasional cannabis users were analyzed for 11 cannabinoids for up to 85 h by LC-MS-MS following controlled smoked, vaporized or oral 50.6 mg Δ9-tetrahydrocannabinol (THC) in a randomized, placebo-controlled, within-subject dosing design. RESULTS: No cannabidiol, cannabinol, cannabigerol, tetrahydrocannabivarin (THCV), THC, 11-OH-THC, Δ9-tetrahydrocannabinolic acid were detected in urine. Median THCCOOH-glucuronide maximum concentrations (Cmax) following smoked, vaporized and oral routes were 68.0, 26.7 and 360 μg/L for occasional and 378, 248 and 485 μg/L for frequent users, respectively. Median time to specific-gravity normalized Cmax (Tmax) was 5.1-7.9 h for all routes and all users. Median Cmax for THCCOOH, THC-glucuronide and 11-nor-9-carboxy-Δ9-THCV (THCVCOOH) were less than 7.5% of THCCOOH-glucuronide Cmax concentrations. Only THC-glucuronide mean Tmax differed between routes and groups, and was often present only in occasional users' first urine void. Multiple THCCOOH-glucuronide and THCCOOH peaks were

observed. We also evaluated these urinary data with published models for determining recency of cannabis use. CONCLUSIONS: These urinary cannabinoid marker concentrations from occasional and frequent cannabis users following three routes of administration provide a scientific database to assess single urine concentrations in cannabis monitoring programs. New target analytes (CBD, CBN, CBG, THCV and phase II metabolites) were not found in urine. The results are important to officials in drug treatment, workplace and criminal justice drug monitoring programs, as well as policy makers with responsibility for cannabis regulations.

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