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THE IMPORTANCE OF MEDICAL CANNABIS FOR SOLVING THE PROBLEM OF PROVIDING ANALGESIA TO PALLIATIVE PATIENTS IN UKRAINE

Lekhan V.M.

Dnipro State Medical University, Dnipro, Ukraine

One of the ways to solve the problem of pain relief for palliative patients in Ukraine is to expand the arsenal of painkillers through the use of medical cannabis. In many palliative diseases, cannabis is able to alleviate other symptoms that accompany patients with incurable diseases at the end of their lives: nausea, lack of appetite, seizures, anxiety, depression. The procedure for the legalization of medical cannabis in Ukraine is coming to an end, which is a timely decision of the legislators and the government. Before the full-scale medical cannabis war, 2.3 million patients were needed. Since its inception, this need has increased to 5.5–6 million. The Ukrainian agricultural market and the pharmaceutical industry will eventually be able not only to provide the country with the necessary amount of plant raw materials for the production of medicines and other cannabis products, but also to earn profits from exports, providing part of the growing demand for cannabis in Europe in other countries of the world. But this will require good conditions for investors and a consistent state policy in the adoption of by-laws and the practical implementation of already adopted laws. The medical effects of herbal cannabis and preparations containing it depend on the content of the narcotic TetraHydroCannabinol (THC) and the non-narcotic CanaBiDiol (CBD). Consumer preferences for recreational cannabis are gradually flooding the market with high-THC, low-CBD herbal cannabis, which increases the risk of faster addiction, the frequency and severity of cannabis side effects such as psychotic disorders and cardiovascular crises. Ukraine needs to be prepared for the increase in the use of illicit recreational cannabis along with the increase in the use of medical cannabis, including among children and adolescents, and to counter these phenomena. But even despite these risks, significant positive medical and social consequences can be expected from the legalization of medical cannabis for palliative patients and war victims with post-traumatic stress disorders.

Keywords: *chronic pain, hospices, narcotic painkillers, non-narcotic painkillers, PTSD.*

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In Ukraine, the problem of depriving palliative patients of chronic pain is unresolved [1–3], which negatively affects the quality of life of patients. One of the possible solutions is to expand the arsenal of painkillers due to medical cannabis, which also has a sedative, anti-nausea effect, reduces intraocular pressure, which is important for the treatment of glaucoma. Medical cannabis can significantly alleviate the chronic pain of approximately 1 million cancer patients in the country after chemotherapy, restore their appetite, which is absent due to intoxication, and reduce the convulsive manifestations of the disease. Professional medical associations of the world are in favor of expanding the study of the effects of cannabis and recognize its great therapeutic potential.

The use of cannabis to relieve physical and mental pain is over 5,500 years old. Thus, the rite of smoking cannabis at funerals among the Scythians helped to reduce the sense of loss. In ancient India, Greece, and Rome, cannabis was used to treat fever, leprosy, gout, arthritis, and dysentery. In the modern world, the medical effects of cannabis have been studied in relation to Alzheimer's disease, Parkinson's disease, epilepsy, multiple sclerosis, amniotrophic lateral sclerosis, HIV/AIDS, cancer and many other diseases. In most countries of the world, in connection with the need to fight against the illegal circulation of narcotic substances, a ban on the cultivation of cannabis was introduced by the middle of the 20th century. However, later some countries legalized its use for medical purposes. And some countries (the USA, the Netherlands, Canada, Uruguay, Mexico) are also for recreation. According to UN data, as of 2015, there were more than 181 million cannabis users in the world [4].

The history of attempts to legalize cannabis for medical purposes in Ukraine dates back three decades. For a long time, the conservatism of society, the opposition

of tobacco companies, the inconsistency of medical reform, and other factors stood in the way of legalization. The last attempt of the lawmakers in 2022 led to the legalization of medical cannabis in Ukraine, but it will remain prohibited for recreational purposes. Patients will receive it via electronic prescriptions. Only legal entities that have a license and a GMP certificate will be able to grow cannabis. They must provide round-the-clock video surveillance of a closed greenhouse for growing raw materials, control the movement of each hemp bush with an individual code from the producer to the patient. In December 2021, 60 out of 149 pharmaceutical manufacturers of Ukraine declared their readiness to produce cannabis preparations under such conditions. But it is likely that the first preparations with a cannabis content of 0.3% of Ukrainian production will be made from foreign raw materials [5].

But later, Ukraine will be able to make a profit from the trade of technical hemp due to the quota volume of sales to EU countries (every fifth grown kilogram) and also without restrictions from sales to countries that do not have quotas. It is also possible to export medical cannabis (marijuana) with a high TetraHydroCannabinol (THC) content [6]. According to the calculations of business analysts, the profitability of growing hemp in Ukraine can reach 50%, the income from each hectare of land is 500–2000 USD. At the same time, Ukraine can satisfy a significant part of the European cannabis market, which has been growing rapidly for the past 10 years. In general, provided that growth rates are maintained, this market will reach an annual turnover of 115.7 billion euros by 2028.

On the eve of the completion of the legalization procedure in Ukraine, we must study the possible social consequences of increasing the consumption of cannabis. First, there is a risk of increased recreatio-

nal consumption, including by young people. The second, it is the risk of consuming cannabis together with alcohol. Thirdly, it is insufficient experience of medical professionals who will meet more patients who use medical and recreational cannabis, but will not have the appropriate training to work with such patients. To forecast events related to the consequences of the legalization of medical cannabis in Ukraine, it is advisable to also take into account the experience of other countries that legalized cannabis earlier.

The effect of cannabis on the human body is mostly determined by the narcotic substance TetraHydroCannabinol (THC). Plants of the hemp family (*Cannabaceae*) contain over hundreds of phytocannabinoids that enhance each other's effects and stimulate the endocannabinoid system. The human endocannabinoid system regulates metabolism, individual links of immunity, appetite, fertility, pain sensation, mood, emotions, memory, coordination of movements [7]. In a study by de Melo Reis R.A. et al. (2021) [8] determined the relationship between the operation of this system and the quality of human life.

When using cannabis recreationally, it is necessary to take into account the risks of its side effects: the appearance of symptoms of anxiety, depression, hallucinations, the development of addiction, the risks of vascular crises and respiratory arrest. These risks increase with higher THC content in marijuana [9]. According to the meta-analysis of Cascini F. et al. (2012) [10] THC content in cannabis is on average 5%, but the maximum content can reach 15–17%. Such a concentration is extremely dangerous. Especially if at the same time as the high content of THC in the plant there is a low content of non-narcotic CanaBi-Diol (CBD), which mitigates the negative effect of THC. Quite often, the selection of cannabis crops is aimed specifically at increasing the THC content, which is often

accompanied by a decrease in the CBD content [11]. The recreational marijuana market is responding quickly to user preferences. An analysis of marijuana offered by "coffeeshops" in the Netherlands (2014) [12] revealed an average content of THC in herbal cannabis at the level of 15%, CBD – 1%. The shift in consumer preferences towards cannabis with a higher THC content indicates an increase in the risks of its recreational use in the WHO European Region. As of 2012, cannabis was the top drug for which users sought medical attention for the first time in the region.

In the countries of Oceania (Australia, New Zealand) since the beginning of the century, a similar trend of increasing demand for cannabis with a higher THC content and lower CBD content has been noted. This is associated with an increase in the number of psychoses and a decrease in fertility [13]. In the US, THC content in illicit cannabis has gradually increased from 3.7% in 1993 to 12.6% in 2013 due to increased circulation of sinsemilla. An increase in the number of hospitalizations caused by drug use has been associated with the change in cannabis user preferences [14].

In palliative medicine, the analgesic, anti-nausea, anxiolytic, antidepressant and anticonvulsant effects of cannabis are necessary. Before the full-scale war in Ukraine, 2.3 million patients needed medical cannabis. Most of them were palliative patients with chronic pain. During the war, the number of patients requiring cannabis tripled from military and civilian patients with Post-Traumatic Stress Disorder (PTSD) [15]. PTSD encourages risky behavior, abuse of psychoactive substances, increases the risk of hypertension, angina pectoris, stomach ulcers, gastritis, arthritis, and depression. In turn, deaths from cardiovascular and oncological diseases increase more than 1.5 times.

Medical risks from the use of cannabis with a high THC content support the scien-

tific debate in the world about the feasibility of legalization and influence government restrictions [16]. As of mid-2023, this discussion has led to the identification of benefits over risks in Ukraine and in 55 other countries around the world. What is important is the relatively low cost of cannabis with sufficient potential for pain relief. The pain relief needs of palliative patients in low- and middle-income countries are easier to meet with domestically produced drugs, which in many countries makes it easier to obtain budget funding.

In Ukraine, the assessment of the need for medical cannabis correlates with the assessment of the need for hospice and palliative care by Nesterenko V.G. et al. (2021–2023), which is also several times more than the actual coverage of patients [17–19]. From a formal point of view, in order to legalize cannabis, it will be removed from the register of prohibited substances and registered in the register of substances under strict control. The development and registration of new dosage forms and medical preparations containing cannabis with a defined list of indications for use will take place. Cannabis will begin to be used for medical, industrial, scientific and technical purposes. It is also planned to include drugs containing cannabis in the list of drugs of the "Affordable Medicines" program with reimbursement of part or all of their cost by the National Health Service of Ukraine [20].

As already mentioned, among the risks of using cannabis, the occurrence of addiction is mentioned, which is less compared to opiates [21]. Teenagers are a risk group for the rapid onset of addiction, so age restrictions on the sale of cannabis exist in all countries that have legalized it. Other possible risks in young cannabis users are also vascular crises (strokes and heart attacks), psychotic disorders (with the occurrence of hallucinations), reduced learning ability [22; 23].

The legalization of marijuana in the years 2010–2020 in the United States led to an increase in its smoking by children and adolescents. Jones E.L. & Rozenman M. (2024) emphasize [24] that the recreational use of cannabis by young people reduces their chances of employment, obtaining higher education, and having children. In addition, early initiation of marijuana smoking correlates with aggressive behavior and more delinquency. Despite the strong focus on youth cannabis use, the majority of cannabis users in Europe and North America are middle-aged and older. The study of Orhurhu V. et al. (2020) [25] on cannabis consumption in the United States showed a high adherence to the drug in patients over 45 years of age, with low-income households, women, tobacco dependents, patients after trauma and failed spine surgery. A decrease in cannabis adherence has also been reported in patients who consistently take opioids for pain relief. The study was conducted in the period 2011–2015 on a large number of patients (248 thousand people) and with high reliability of results (from $p < 0.0001$ to $p = 0.03$).

Among all the studies on the risks of cannabis use, the most famous is the work of Nutt D.J. et al. (2010) [26], in which the total harm from the use of various psychoactive substances is compared. According to the results of the study, this harm is less from the use of cannabis compared to tobacco and cocaine by approximately $\frac{1}{4}$, compared to heroin – by $2\frac{3}{4}$, compared to alcohol – by 3.5 times. In addition, in a state of cannabis intoxication, its users are approximately 10 times less likely to show aggression towards others, than in the case of alcohol intoxication.

Conclusions

The study of the medical properties of cannabis allows us to consider it a promising tool for solving the problem of insufficient analgesia in palliative patients in low- and middle-income countries. The

legalization of medical cannabis in Ukraine is timely and expected both by the medical community and by patients with chronic pain, Alzheimer's, Parkinson's, multiple sclerosis, epilepsy, cancer patients, etc. Growing cannabis is a promising area of agricultural and pharmaceutical business in

Ukraine. The issue of growing cannabis and the production of drugs containing it should be subject to strict control. An increase in the recreational use of cannabis, especially by children and adolescents, cannot be allowed.

Conflict of interest is absent.

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Лехан В.М.

ЗНАЧЕННЯ МЕДИЧНОГО КАНАБІСУ ДЛЯ ВИРІШЕННЯ ПРОБЛЕМИ ЗАБЕЗПЕЧЕННЯ ЗНЕБОЛЕННЯМ ПАЛІАТИВНИХ ХВОРИХ В УКРАЇНІ

Одним з шляхів вирішення проблеми знеболення у паліативних пацієнтів в Україні є розширення арсеналу знеболюючих засобів за рахунок використання медичного канабісу. При багатьох паліативних захворюваннях канабіс здатний пом'якшити й інші симптоми, що супроводжують пацієнтів із невиліковними захворюваннями наприкінці їх життя: нудоти, відсутності апетиту, судом, тривоги, депресії. Це коротке наукове повідомлення написано у час, коли процедура легалізації медичного канабісу в Україні добігає кінця, що є своєчасним рішенням законодавців та уряду. До повномасштабної війни медичного канабісу потребували 2,3 млн пацієнтів. Від її початку ця потреба збільшилася до 5,5–6 млн. Український сільськогосподарський ринок та фармацевтична індустрія згодом зможуть не тільки забезпечити країну необхідною кількістю рослинної сировини для виробництва ліків та інших виробів із канабісу, але й зможе отримувати прибуток від експорту, забезпечивши частину зростаючого попиту на канабіс у Європі на інших країнах світу. Але для цього будуть потрібні хороші умови для інвесторів та послідовна державна політика у прийнятті підзаконних актів та практичній реалізації у життя вже прийнятих законів. Медичні ефекти трав'яного канабісу та препаратів з його вмістом залежать від вмісту наркотичного Тетрагідроканабіолу (ТГК) та ненаркотичного Канабі-Діолу (КБД). Вподобання споживачів рекреаційного канабісу призводять до поступового наповнення ринку трав'яним канабісом із підвищеним вмістом ТГК та зниженим вмістом КБД, що підвищує ризики швидшого звикання, частоти появи та сили прояву таких побічних дій препаратів канабісу як психотичні розлади та серцево-судинні кризи. Україні потрібно бути готовою до збільшення вживання забороненого рекреаційного канабісу разом із збільшенням використання медичного канабісу, у тому числі серед дітей та підлітків, та протистояти цим явищам. Але навіть попри ці ризики можна очікувати значних позитивних медико-соціальних наслідків від легалізації медичного канабісу для паліативних хворих та постраждалих від війни із посттравматичними стресовими розладами.

Ключові слова: *хронічний біль, хоспіси, наркотичні знеболювальні, ненаркотичні знеболювальні, ПТСР.*

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Information about the author:

Lekhan Valery M. – MD, DMedSc, Professor of the Department of Social Medicine, Public Health and Health Care Management, Dnipro State Medical University.

Postal address: Ukraine, 49044, Dnipro, Yavornytskyi Ave., 24.

E-mail: v.n.lexan@gmail.com

ORCID: 0000-0003-2953-3292.