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Assessment of patients hospitalized in the Clinical Toxicology and Cardiology Department in Lublin due to poisoning with Cannabis derivatives as a voice in the discussion on the legalization of marijuana

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A – Research concept and design, B – Collection and/or assembly of data, C – Data analysis and interpretation, D – Writing the article, E – Critical revision of the article, F – Final approval of the article.

Abstract

The article aims to discuss the justification for the legalization of cannabinoids based on the analysis of data from countries where marijuana has been legalized for both medical and recreational use, as well as a retrospective analysis of the medical documentation of patients from the Clinical Toxicology and Cardiology Department and Internal Diseases of the Provincial Specialist Hospital named after Stefan Cardinal Wyszyński in Lublin (years 2020-2024).

During the analysis of hospital documentation, a slight upward trend in the number of hospitalizations due to cannabinoid poisoning was observed over the years 2020-2024. In 2024, 54 cases of hospitalization due to poisoning with Cannabis derivatives were recorded, with an average length of hospitalization of 3 days. The vast majority of patients were men (83%) under the age of 26. In 78% of patients, co-occurrence of poisoning with other psychoactive substances was noted, with the most common being alcohol (29 cases), LSD (12 cases), and benzodiazepines (11 cases).

44 patients required consultation with a psychologist or psychiatrist. Suspected suicide attempts were noted in 12 patients. In 38 patients, psychomotor agitation occurred, with pharmacological sedation required in 34 patients. In 22 cases, there was a significant increase in creatine levels, which may indicate an increased risk of rhabdomyolysis.

Press analysis showed that the legalization of marijuana does not lead to immediate and significant changes in public health indicators, except for issues related to road safety. Shortly after the legalization of recreational marijuana in some U.S. states and Canada, an increase in consultations with doctors was observed, caused by both acute and chronic effects of cannabinoid poisoning. Due to the short time since marijuana was legalized, research and statistical analyses are still incomplete and often lead to various, contradictory conclusions.

Keywords: Cannabis, marijuana, health, legalization, healthcare.

1. Introduction

Cannabinoids have been known to humans for hundreds of years, the first mentions of their properties can be found in records of Chinese medicine from 2700 BC. The most common of these is 9-tetrahydrocannabinol (THC), which is a highly psychoactive substance, and cannabidiol (CBD), which does not exhibit psychoactive properties(1). Other compounds belonging to this group, also found in plants from the Cannabis family, include: cannabigerol, cannabichromene, cannabidivarin and tetrahydrocannabivarin(2). These substances were previously obtained from Indian hemp (phytocannabinoids) but with the development of science, they began to be synthesized in laboratory conditions.

Both the growing access to information about cannabinoids and the noticeable trend towards increasing availability of marijuana are causing a rise in public interest in this substance. Many countries are opting for decriminalization or various forms of legalization of marijuana, both for medical and recreational use. However, the short period since the introduction of marijuana legalization and the few studies on its impact on society after legislative changes make it impossible to gather complete data regarding the understanding of the consequences of legalization.

The article aims to discuss the justification for the legalization of cannabinoids based on the analysis of data from countries where marijuana has been legalized for both medical and recreational use. It also includes a retrospective analysis of medical documentation of patients from the Clinical Toxicology and Cardiology Department and Internal Diseases of the Provincial Specialist Hospital named after Stefan Cardinal Wyszyński in Lublin (years 2020-2024).

The action of cannabinoids is most often described as an influence on mood and perception. The mechanism of action of these substances is based on the inhibition of adenylate cyclase. The human brain has cannabinoid receptors coupled with G-proteins, classified as type 1 (CB1) and type 2 (CB2)(3), where the most abundant variant in the central nervous system (CNS) is CB1(4). After discovering the aforementioned receptors, science focused on defining endogenous compounds that were their primary ligands. Research has managed to isolate two

endogenous cannabinoids: anandamide (AEA) and 2-arachidonoylglycerol (2-AG). Due to the mass use of cannabis for medical and recreational purposes, research on the action of cannabinoids has deepened, revealing a new group of receptors, so-called non-CB1 receptors, which are not coupled with G-proteins. These include GPR18, GPR55, and GPR119 receptors. A thorough investigation of the structure and mechanisms of cannabinoid receptors has allowed for the development of synthetic compounds with applications as drugs.

However, despite the potential therapeutic benefits, the use of cannabinoids may have a negative impact on human health. Smoking marijuana can contribute to the induction of chronic inflammation in the respiratory tract, cause cough, and excessive cell proliferation, which consequently increases the risk of lung cancer (5–7). Additionally, the use of cannabinoids may have a negative impact on reproductive health – in men by lowering testosterone levels (8) and in women by inhibiting the luteinizing hormone and prolactin. Cannabinoids may also negatively affect fetal development and contribute to low birth weight in newborns. Furthermore, cannabinoids have an inhibitory effect on the secretion of TSH and growth hormone.(9,10) Besides, the use of cannabinoids is associated with cognitive function disorders and ataxia. (11) Moreover, the use of cannabinoids is associated with an increased risk of developing schizophrenia or psychotic disorders and worsened prognosis in these disorders. (12–14) Combining cannabinoids with medications or alcohol may have hepatotoxic effects. This is observed through an increase in alanine aminotransferase or aminotransferase asparaginase levels. At the same time, it disrupts the pharmacokinetics of drugs significantly affecting the effectiveness of therapy with all drugs metabolized by the liver. (15) Additionally, cannabinoids interact with numerous neurotransmitters, including opioids, dopamine, GABA, and glutamate. They may also interact with drugs and compounds (including ethanol) that are metabolized by cytochrome P450 and CYP2C19, CYP3A4, 5'-diphosphoglucuronosyltransferases (UGT) UGT1A7, UGT1A9, and UGT2B7.

The use of cannabinoids in medicine is discussed in the context of neurological treatment and oncological, especially in patients receiving palliative treatment. The Food and Drug Administration (FDA) has approved one cannabis-derived drug - Epidiolex and synthetic drugs based on their natural prototypes: Nabilone, and Dronabinol. Synthetic analogs are used in oncology patients to minimize the side effects of chemotherapy - mainly nausea and vomiting(1). Another application of THC-based drugs in oncology is their administration to patients with cachexia or anorexia (also in patients with AIDS-related anorexia). However, both the FDA and EMA have not approved any of the drugs for use in the treatment of cancer pain. (2)

Cannabinoids have found application in alleviating the symptoms of neurodegenerative diseases such as Alzheimer's disease (AD) and Parkinson's disease. The use of THC and CBD-containing drugs in patients with AD has shown a significant reduction in symptoms associated with this disease such as anxiety, depression, agitation, or cognitive disturbances. (16) Additionally, Nabilone is used in the treatment of neuropathic pain, chronic spasticity, and spasms resulting from multiple sclerosis (MS) and spinal cord injury. There are high hopes for the use of CBD preparations to reduce seizures in children with refractory epilepsy.

Even though cannabinoids have several properties that are or could be used in medicine, their use is associated with many side effects.

The side effects of cannabinoid use can manifest differently depending on individual tolerance. The most commonly reported side effects are hypotension accompanied by bradycardia or tachycardia, more frequent respiratory infections, severe psychotic incidents, disturbances in the time perception, depressive or anxious states, or inappropriate increases in drive and mood, which is supported by data collected during the analysis of medical

documentation from the Clinical Toxicology and Cardiology Department and Internal Diseases of the Provincial Specialist Hospital in Lublin.

Detailed information on the use of cannabinoids, interactions, and side effects will be presented in the further part of the article.

2. Research Methodology

The aim of the analysis of the justification for the legalization of cannabinoids was to collect data from patients in the Clinical Department of Toxicology and Cardiology and Internal Diseases of the Provincial Specialist Hospital named after Stefan Cardinal Wyszyński in Lublin, THAT WERE hospitalized due to cannabinoid intoxication (ICD10 - T40.7 Intoxication with Cannabis derivatives) in 2024. Additionally, the number of hospitalizations due to cannabinoid intoxication from 2020 to 2024 was assessed. The collected data were analyzed using statistical programs, and the obtained results are presented in the further part of the article. This data was compared with information obtained during the analysis of medical literature and available news about the effects of cannabinoid legalization in other countries.

3. Results

The statistical data presented in the article comes from the analysis of hospital documentation of the Clinical Department of Toxicology-Cardiology and Internal Diseases of the Provincial Specialist Hospital named after Stefan Cardinal Wyszyński in Lublin. The aim of the analysis and discussion on the justification for introducing cannabinoids into the market was to analyze 54 cases of hospitalization of patients diagnosed with poisoning from Cannabis derivatives (ICD10 – T40.7 Poisoning from Cannabis derivatives) in 2024.

These poisonings account for 54 admissions to the Emergency Department (which constitutes 46 patients, as 5 patients were hospitalized more than once due to cannabinoid intoxication in the analyzed year) in 2024. No significant upward trends were observed when analyzing the number of patients hospitalized due to intoxication with psychoactive substances from 2020 to 2024. Attention should also be paid to the issues of reliability in assessing trends from 2019 to 2021 due to the ongoing COVID-19 pandemic.

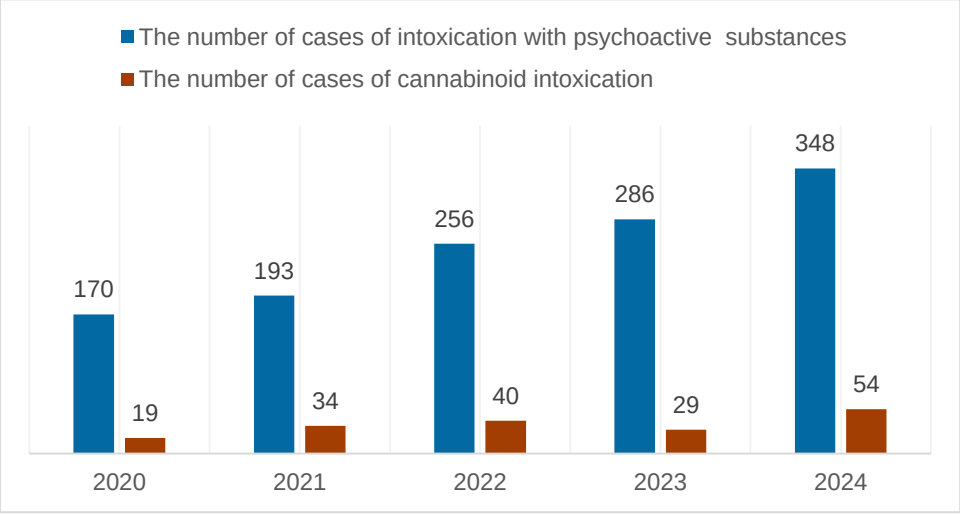

Chart 1. Comparison of the number of patients hospitalized due to cannabinoid intoxication and other psychoactive substances in the Clinical Toxicology-Cardiology and Internal Medicine Department from Internal Medicine from 2020 to 2024.

The collected data shows that the majority of admissions – 63% (34 cases) occurred on weekdays, i.e., from Monday at 07:00 to Friday at 17:59. In contrast, during weekends, i.e. from Friday at 18:00 to Monday at 06:59, 37% of patients were admitted (20 cases). Considering the time of patient admissions to the Emergency Department, a greater number of admissions occurred during nighttime, i.e. from 18:00 to 06:59. These admissions accounted for 57.4% of all cases (31 cases). Meanwhile, daytime admissions, i.e. from 07:00 to 17:59, accounted for 42.6% of all cases, corresponding to 23 admissions.

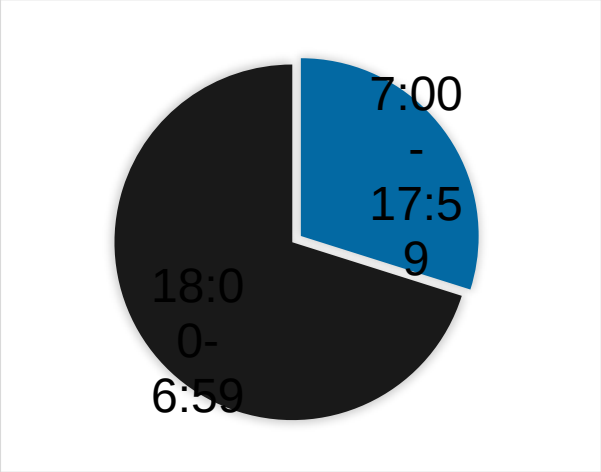

Chart 2. Time of admission of patients due to poisoning with Cannabis derivatives to the Hospital Emergency Department Emergency in the year 2024.

The average length of hospitalization was 3.07 days – the shortest stay in the department was 1 day and the longest was 15 days. In 57% (31 cases), hospitalization did not last longer than 2 days.

Among the 54 cases recorded in the Department, a decisive majority – 83% (45 cases) were male patients compared to 17% (9 cases) female patients.

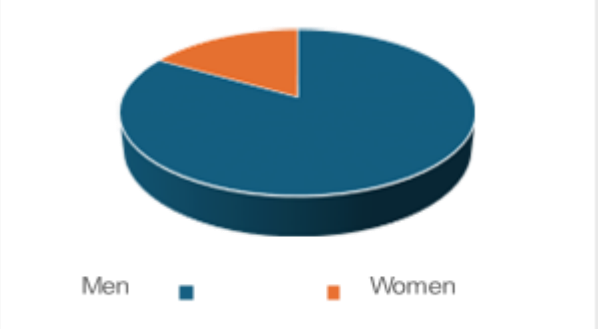

Chart 3. Gender representation among patients hospitalized due to poisoning with derivatives of Cannabis in 2024.

Among the patients admitted to the Department in 2024, those under 25 years of age dominated (57.4% of cases) – the median age of patients is 22 years, with:

- 29.6% (16 cases) are patients under 18 years of age,
- 27.8% (15 cases) of patients aged 19-25,
- 20.4% (11 cases) of patients between 26 and 35 years of age,
- 20.4% (11 cases) of patients between 36 and 45 years of age,
- only one patient was over 45 years old, which constitutes 1.9%.

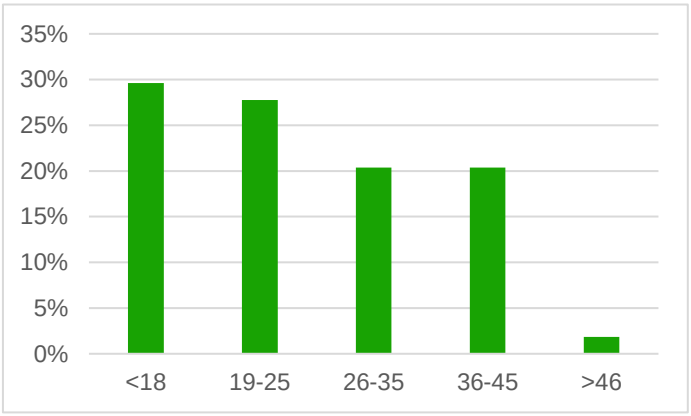

Chart 4. Age of patients admitted due to poisoning with Cannabis derivatives in 2024. The predominance of patients under 18 years of age (16 cases), followed by 15 patients aged 19 to 25 years, 11 patients aged 26 to 35 years, and one patient over 46 years of age.

39% of patients reported a history of comorbidities. Among the comorbid diseases and mental disorders, patients reported:

- Depressive disorders - 5 cases,
- bipolar affective disorder - 4 cases,
- alcohol dependence syndrome - 3 cases,
- schizophrenia - 2 cases,
- anxiety disorders - 2 cases,
- delusional disorders - 1 case.

Among the reported other coexisting chronic diseases:

- hypertension was reported 3 times,
- rhabdomyolysis reported 2 times,
- 1 case:
- of type II diabetes,
- of polyneuropathy,
- of osteonecrosis,
- of ulcerative colitis,
- of acute kidney injury, of fatty liver,
- of bronchial asthma,
- of hypertransaminasemia of peroneal nerve palsy of the lower limb.

In most cases, poisoning occurred after the consumption of cannabinoids for recreational purposes - 38 hospitalizations. In 12 cases, a suicide attempt was suspected, while 4 cases required police intervention to bring the patient to the Emergency Department.

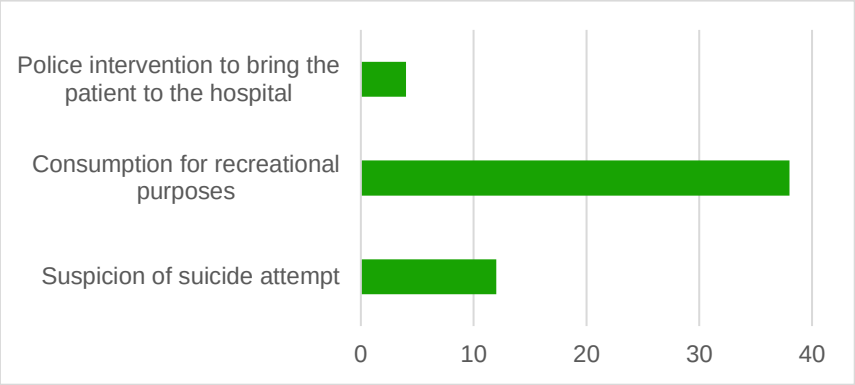

Chart 6. Circumstances of patient admission due to poisoning with Cannabis derivatives to the Hospital
Emergency Department in 2024.

In most cases (78%, 42 cases) there was co-occurring poisoning with other psychoactive substances:

- Alcohol poisoning: 54% (29 cases)
- LSD poisoning: 22% (12 cases)
- Benzodiazepine poisoning: 20% (11 cases)
- Mephedrone and cathinone poisoning: 15% each (8 cases each)
- Amphetamine poisoning: 13% (7 cases)
- Poisoning with tricyclic antidepressants: 6% (3 cases)
- Poisoning with fentanyl, carbamazepine, valproic acid, cocaine, methaqualone, and tramadol: 4% each (2 cases each)
- Poisoning with methadone, oxycodone, opioids, and ecstasy: 2% each (1 case each)
- Poisoning with other drugs: 13% (7 cases)

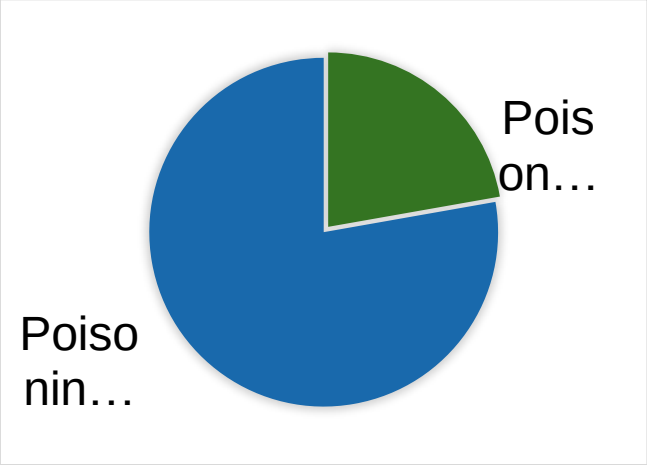

Chart 7. Distribution of patients based on the potential co-occurrence of poisonings with other substances psychoactive substances other than poisoning with Cannabis derivatives.

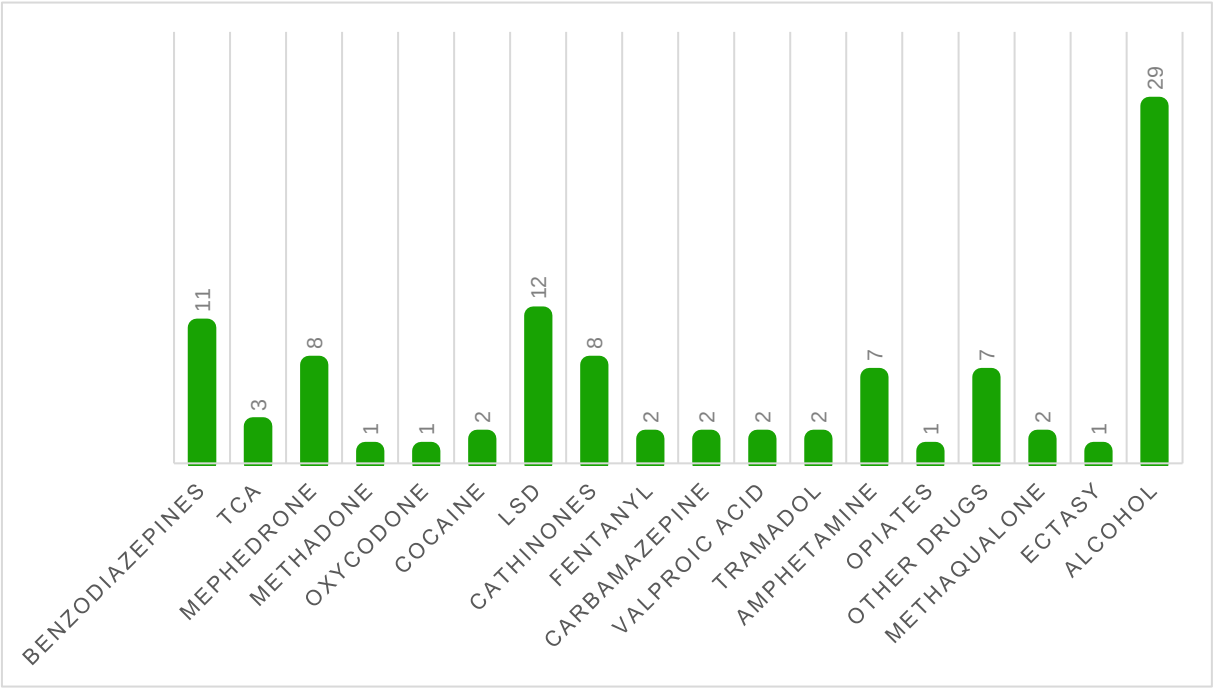

Chart 8. Presentation of detected psychoactive substances accompanying poisoning with derivatives Cannabis in patients admitted to the Clinical Toxicology and Cardiology Department and Internal Diseases

Due to the influence of cannabinoids on resting heart rate, the heart rate of patients upon admission to the Emergency Department was compared.

The average heart rate is 98.3 beats per minute. The measurement results are as follows:

- 46.3% of patients (25 cases) had an elevated heart rate, above 100 beats per minute, but not exceeding 120.
- 9.3% of patients (5 cases) had a heart rate above 120 beats per minute.
- 37.0% of patients (20 cases) had a heart rate in the range of 70-99 beats per minute.
- 7.4% of patients (4 cases) had a heart rate in the range of 50-69 beats per minute.

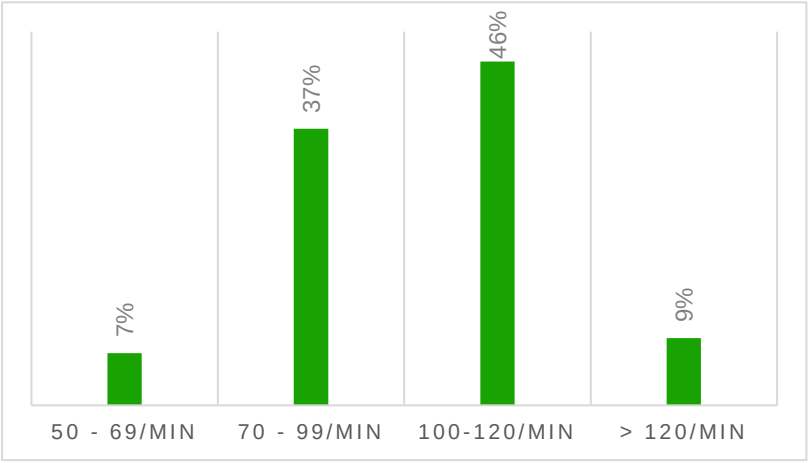

Chart 9. Comparison of heart rates of patients with cannabis derivative intoxication upon admission to the Hospital Emergency Department.

During hospitalization, urine tests for the presence of THC metabolites were performed using the immunochromatographic method with a cutoff threshold of 50 ng/ml. In the case of a positive result, cannabinoid metabolites in urine were measured using the semi-quantitative immunoenzymatic EMIT method with a cutoff point of 50 ng/ml. The results were presented in terms of metabolite concentrations expressed in ng/ml. The EMIT test results showed that:

- Values higher than 2000 ng/ml were recorded in 4% (2 cases), with the highest concentration exceeding 10000 ng/ml.
- 500-1000 ng/ml was recorded in 13% (7 cases).
- 200-500 ng/ml – 7% (4 cases).
- 100-200 ng/ml was identified in almost half – 43% (23 cases).
- Lower values, i.e.: 50-100 ng/ml were observed in 20% (11 cases).

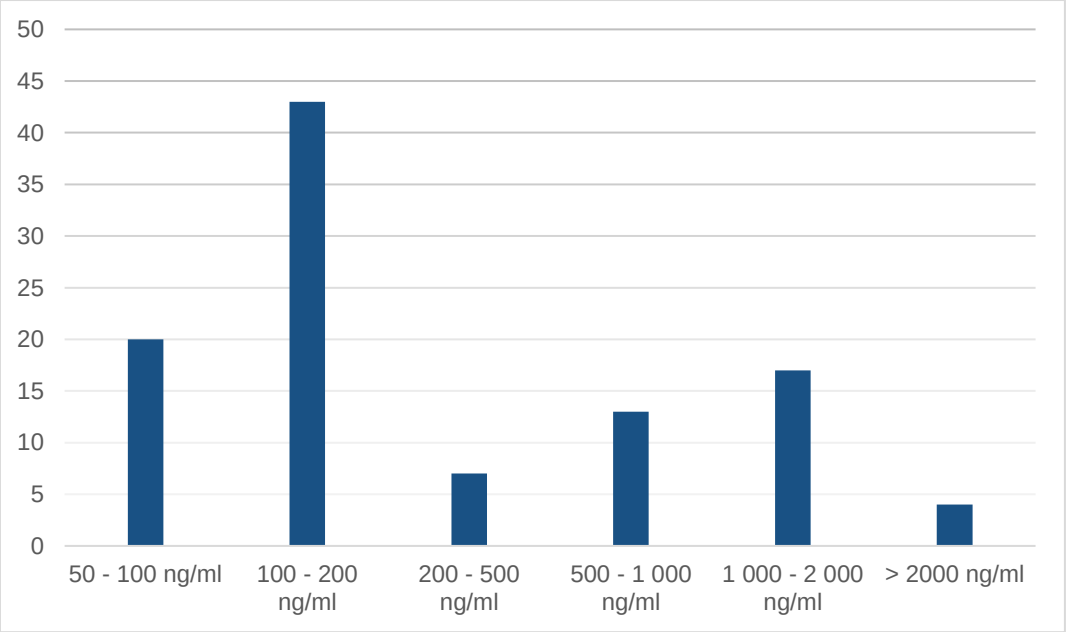

Chart 10. Highest cannabinoid concentrations in urine (ng/ml) in patients admitted to the Clinical Department of Toxicology, Cardiology, and Internal Diseases.

One of the most serious complications of cannabinoid poisoning is rhabdomyolysis. To determine the risk of its occurrence, patients underwent a test for creatine kinase levels in urine. Normal values for men are 20-195 IU/l while for women 24-170 IU/l. An increase in kinase levels was observed in 41% (22 cases), which may indicate a high risk of developing rhabdomyolysis syndrome.

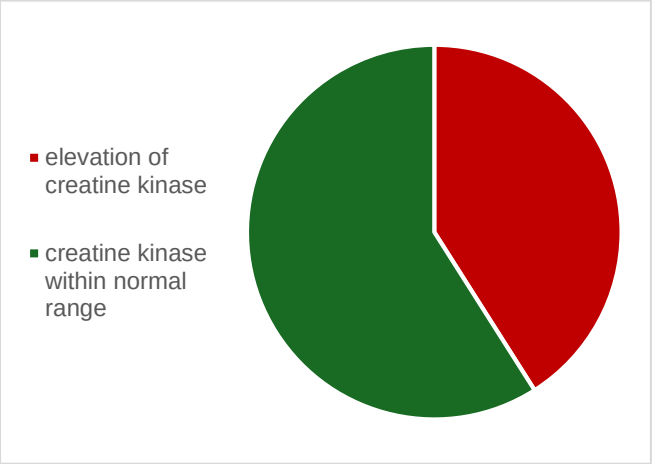

Chart 11. Creatine kinase levels in urine of patients with poisoning from Cannabis derivatives.

The occurrence and exacerbation of pre-existing mental disorders also constitute a serious complication of cannabinoid poisoning. During hospitalization, 81% (44 cases) of patients required psychological or psychiatric intervention. The risk of suicide attempts was noted in 22% (12 cases). Additionally, the majority of patients were psychomotorically agitated – 70% (38 cases) and required pharmacological sedation using propofol, midazolam, and diazepam – 63% (34 cases). Furthermore, a significant majority of patients were recommended detoxification – 81% (44 cases). This data is presented in the following chart 12.

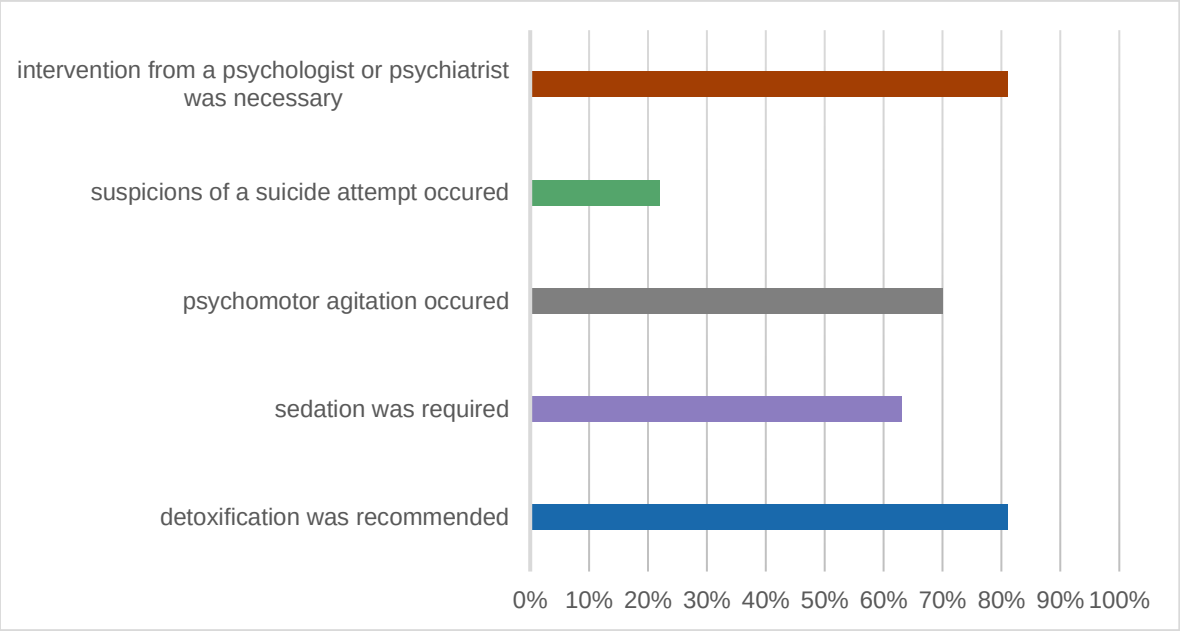

Chart 12. Patients who required intervention from a psychologist or psychiatrist – 44. Suspected suicide attempts were noted in 12 patients. 38 patients exhibited motor agitation, of which 34 patients required pharmacological sedation.

36 patients were hospitalized in the Toxicology–Cardiology Department due to intoxication with psychoactive substances once. The highest number of hospitalizations was 5 per person in the case of 2 patients.

4. Discussion

The described statistics concern cases of hospitalization due to poisoning with Cannabis derivatives in the Clinical Toxicology-Cardiology and Internal Medicine Department of the Provincial Hospital in Lublin in 2024. Cannabinoid poisonings accounted for 3.98% of all hospitalizations (54 cases out of 1358 cases). Among the patients who were hospitalized for this reason, the majority were men (83%), with an average age of 26.1 years. Most hospitalizations occurred on weekdays and during nighttime hours. In 70.3% of patients, poisoning occurred after the use of cannabinoids for recreational purposes. While literature analysis suggests that smoking marijuana can induce feelings of relaxation, it should be noted that it also causes a range of acute and chronic negative effects on mental health. These include slowed thinking, fatigue, euphoria, and, in some individuals, anxiety and delusions.

According to a study published by the Dutch Statistical Office in October 2010, marijuana users have mental health problems twice as often as those who do not use it. In contrast, the physical health of users and non-users of marijuana differed to a lesser extent. The most reported mental health issues among marijuana users are anxiety, melancholy, sadness, and impatience. Determining the direct effects of long-term use is difficult because this condition cannot be studied experimentally for ethical reasons.

Nevertheless, the statistical analysis of patients hospitalized in the Clinical Toxicology-Cardiology and Internal Medicine Department indicates that 81% of patients after using Cannabis derivatives required psychological or psychiatric intervention due to exacerbated mental disorders, which seems to confirm these conclusions. The severity of symptoms related to Cannabis derivative intoxication is underscored by the fact that the majority of patients in the Toxicology Department in Lublin required sedative treatment (63%) due to significant psychomotor agitation. It is also worth noting that 22% of patients were at risk of suicide, which is a significant element in assessing health risks in individuals poisoned with cannabinoids.

The use of cannabis is one of the environmental factors associated with increased risk and worsening prognosis of schizophrenia, and some data suggest that there is a causal relationship between the use of cannabinoids and the onset of schizophrenia and affective disorders, as presented in Moore's meta-analysis. The results indicate that the risk of psychosis is increased by about 40% among cannabis users. However, for affective disorders, the results were not as clear-cut. (12)(13)(14) 5–15% of long-term cannabis users reported experiencing isolated psychotic symptoms. Among patients hospitalized in the Toxicology Department in Lublin, cases of schizophrenia (2 cases), bipolar affective disorder (4 cases), depressive disorders (2 cases), and anxiety disorders (2 cases) were recorded, which often correlated with the intensification of their clinical complaints.

As many as 41% of patients had elevated creatine kinase levels, which may indicate the risk of rhabdomyolysis. 30 individuals also had elevated heart rates (above 100 beats per minute), which may indicate a negative impact of the substance on the cardiovascular system, as confirmed in the literature (17). The collected statistical data indicate serious health consequences associated with cannabinoid abuse and also emphasize the need for a comprehensive approach to patient treatment, including both medical interventions and psychological and psychiatric support.

Urine tests of patients in the Toxicology Department showed a variety of concentrations of cannabinoids; the lowest recorded value in urine was 50-100 ng/ml, while the highest was over 2,000 ng/ml. The varying dynamics of metabolizing this substance in patients' bodies may suggest the co-occurrence of intoxication with other psychoactive substances and significant diversity in the study group in terms of gender and age. Furthermore, analysis of the literature

indicates that smoking marijuana reduces the rate of drug metabolism and inactivation by the liver and accelerates the progression of fibrosis. (18)(19)

Cannabinoids interact with numerous neurotransmitters, including opioids and amine, Cannabinoids interact with neurotransmitters such as GABA and glutamate and interact with compounds that are metabolized by cytochrome P450 and CYP2C19, CYP3A4, 5'-diphosphogluconolactonyltransferase (UGT) UGT1A7, UGT1A9, and UGT2B7. The cytochrome P450 found in the liver is one of the main enzymes that metabolize steroid hormones, cholesterol and its derivatives, vitamin D, bile acids, and eicosanoids(20), but above all, it is the main enzyme determining the pharmacokinetics of drugs and the response to these drugs. (15) Hytocannabinoids (especially THC and CBD), as well as synthetic cannabinoids, are substrates for various CYP enzymes, which means that using them alongside drugs metabolized by these enzymes may lead to ineffective therapy. (21) The competition of cannabinoids with drugs for cytochrome may cause an increase in drug concentrations in plasma, raising their therapeutic concentration to toxic levels and prolonging their action. Individuals using synthetic cannabinoids, as well as phytocannabinoids, should check the metabolic pathway of other medications they are taking, as it may be necessary to reduce the dose taken to keep their concentration within the therapeutic window. Special attention should be paid when using CBD and THC simultaneously with amiodarone, fluoxetine, ketoconazole, and other antifungal medications, cotrimoxazole, macrolides, verapamil, warfarin, phenobarbital, rifampicin, clobazam, carbamazepine, or phenytoin. Similar effects are caused by the combination of ethyl alcohol with cannabinoids, competing for the same cytochrome, which enhances each other's effects and increases their hepatotoxicity. For this reason, it is not recommended to combine both substances simultaneously. (22)

The active ingredients of marijuana, especially THC, act on the nervous system in a similar way to addictive drugs, enhancing the feeling of reward and euphoria. Regular use of marijuana leads to changes in the functioning of the reward system in the brain, which reduces the motivational strength of natural rewards and can lead to addiction. 70% of patients hospitalized in the Toxicology Department in Lublin were admitted with suspected intentional use of cannabinoids for recreational purposes. Analysis of the available literature indicates that repeated stimulation of the reward system causes changes in neurons that reinforce addictive behaviors (23)(24). This can be confirmed by the obtained statistical data – 10 patients were hospitalized more than once in the Toxicology Department due to intoxication with psychoactive substances. Furthermore, patients did not comply with recommendations for undergoing detoxification.

Among patients hospitalized in 2024 in the Clinical Cardiology-Toxicology and Internal Diseases Department, in 42 cases (78%), co-occurrence of intoxication with other psychoactive substances was noted, with the most common substance accompanying cannabis-related intoxication being alcohol (54%). Among other detected substances are LSD, benzodiazepines, and other drugs. Prospective studies indicate that early use of marijuana often marks the beginning of using other drugs (25)(26), while long-term use of marijuana leads to subtle and selective cognitive function impairments. These include difficulties in attention concentration and filtering out irrelevant information, which intensify with prolonged use. Marijuana use also worsens work performance, especially in tasks requiring cognitive engagement and decision-making. Additionally, smoking marijuana leads to problems with working memory and psychomotor slowing. It also increases the risk of accidents and injuries at work, especially in individuals with other risk factors. (11)

The side effects of cannabinoid use can manifest differently depending on personal tolerance. The most reported adverse effects are hypotension accompanied by bradycardia or

tachycardia, more frequent respiratory infections, severe psychotic incidents, disturbances over time, depressive states, anxiety, or inappropriate increases in drive and mood.

Within the respiratory system, smoking marijuana causes chronic cough, induces a state of inflammation in the airways, and contributes to cell proliferation (5–7), which may contribute to the development of lung cancer. Although studies do not clearly show a higher risk of lung cancer in marijuana smokers compared to tobacco smokers, lung damage caused by smoking marijuana, unlike tobacco, is not reversible after cessation of use. In individuals infected with the virus (17), marijuana use may lead to higher mortality.

THC and CBD significantly reduces testosterone production in men, which leads to the disruption of sperm production. Studies conducted on pregnant rats showed that CBD and THC resulted in higher embryo lethality and lower birth weight of live offspring, characterized by neurological defects and cognitive-behavioral disorders. (8) In preclinical studies, cannabinoids showed inhibitory effects on luteinizing hormone, prolactin, growth hormone, and TSH, with a slight impact on follicle-stimulating hormone, indicating a possible negative effect on women's reproductive health. Women who smoke marijuana during pregnancy have a higher risk of giving birth to low birth-weight children. The impact of maternal marijuana use on infant development has not been systematically studied, but the lipid solubility of THC allows it to quickly pass into breast milk, where it accumulates and can be transferred to the infant. (9,10)

Additionally, in the case of male embryos as well as young men, marijuana use increases the risk of developing testicular germ cell tumors (TGCT). The authors of the study observed a 70% higher risk of TGCT associated with current marijuana use, and this risk was particularly elevated in the case of regular use (especially when started during adolescence). (25)

Negative effects of long-term (over 10 years) and frequent (more than 5 times daily) smoking of cannabis on human neural tissue have also been documented. Marijuana users have bilaterally reduced volumes of the hippocampus and amygdala – with changes in the hippocampus being more pronounced. (12)

However, one cannot forget the possible positive effects of cannabinoid use. The effects of Nabilone – a synthetic cannabinoid drug – are observed in neuropathic pain chronic spasticity and ramps resulting from multiple sclerosis (MS) and spinal cord injury. (4) In particular, the CB1 receptor is defined as a receptor with a major role in the analgesic action of cannabinoids. (27) Furthermore, there is increasing evidence that cannabinoids not only affect symptoms caused by MS but may also influence the inhibition of disease progression by acting in an anti-inflammatory, neuroprotective mechanism and even slowing down the demyelination processes of neurons in the central nervous system.

Cannabinoids have also found application in neurodegenerative diseases such as Alzheimer's Disease (AD) and Parkinson's Disease (PD). AD is caused by deposits of amyloid-beta containing hyperphosphorylated tau proteins and reduced activity of acetylcholinesterase. In animal models, it has been proven that cannabinoids reduce oxidative stress and tau protein phosphorylation through CB2 receptors. Furthermore, CB2 activation weakened inflammation due to the release of neurotoxic and pro-inflammatory mediators by reactive astrocytes and microglial cells, thereby modulating unclear processing, and stimulating the proliferation and migration of microglia. (1)

One of the greater successes of treatment with CBD is the reduction of seizures in children with refractory epilepsy. In a randomized, double-blind, placebo-controlled study, CBD reduced seizures in patients with epilepsy associated with Lennox-Gastaut syndrome, who were also receiving clobazam, valproate, lamotrigine, levetiracetam, or rufinamide. Seizures were significantly shortened, and the interval between them was extended. (8) However, further research is needed to draw more accurate conclusions.

The growing awareness of the effects of cannabinoids, their increasing availability, and the potential health issues arising from their use should prompt adjustments to regulations and legal acts to address health situations.

In Poland, in 2017, cannabis with a THC content above 0.3% was legalized, but only for medical use. Polish law does not provide for the possibility of legally purchasing marijuana for recreational purposes. Currently, marijuana can only be obtained legally based on a prescription. There is no reimbursement for these types of medical products, and availability in pharmacies is very limited. In 2019, the first preparations were introduced to the pharmacy market, and the price of medical marijuana in pharmacies is about 65 PLN for 1g.

Among adults, legalization in Canada, the USA, and Uruguay had a small immediate impact on health indicators. In the USA, in states where marijuana was legalized for both medical and recreational purposes, a significant increase in its usage frequency was recorded. However, higher rates had already been noted in these states earlier, indicating that legalization may intensify already existing trends. (28)(29)(30)

Additionally, in Colorado, after legalization, an increase in the number of accidental poisonings was observed with cannabinoids in children under 9 years old(31) and an increase in its usage frequency among adolescents who accessed it through their parents. (32)(33) With cannabinoids in children under 9 years old (31) and an increase in its usage frequency among adolescents who accessed it through their parents. (32)(33)

However, in the first two years after legalization, the most significant impact on health was a public increase in the number of consultations with doctors, caused by both the acute and chronic effects of cannabinoids. This phenomenon was reported in Canada and several states in the USA. Moreover, the largest increase in the frequency of emergency room visits was recorded in places where the sale of food products containing marijuana was allowed and in places where there was an increase in demand and supply of these products. In some places, the upward trends were only temporary. Meanwhile, the number of individuals with cannabinoid addiction who reported to hospitals or outpatient care facilities did not change significantly after legalization.

In the vast majority of places where the use of cannabinoids was legalized, an increase in the number of cases of driving under the influence of marijuana was recorded as well as an increased number of car accidents resulting in injuries and fatalities. This may be due to impairments in cognitive functions, attention concentration, and psychomotor slowing, which are adverse effects of cannabinoid use. This trend was observed in the USA and Paraguay – however, it was not recorded in Canada.

In studies conducted in Washington State and Colorado, a slight increase in the number of newborns with congenital disabilities was also recorded. (34)(35) In Colorado, an increase in the number of premature births was additionally observed – which may be related to the effects of cannabinoids on pregnant women; however, there is a lack of studies regarding this complication in other places. (36)

In discussions about the legalization of cannabinoid use, its possible impact on the reduction in the frequency of opioid use (37) – due to the potential to reduce pain and induce a state of euphoria through the use of cannabinoids. However, the results of studies regarding opioid use after marijuana legalization are inconsistent. Some studies indicate a decrease in the monthly number of deaths from opioid overdoses in states where the use of cannabinoids was legalized compared to states with bans or legalization only of cannabinoid-based medications. (38) Conversely, other studies observed a decrease in the number of prescriptions for opioid medications, but compared to states where legalization did not occur, the differences were not significant. (39)(40)

Finally, legalization does not seem to have any short-term impact on the occurrence of symptoms such as excessive vomiting, psychosis, or self-harm in adults. It may, however, be associated with a decrease in the number of poisonings with synthetic cannabinoids.

5. Conclusions

The discussion regarding the justification for marijuana legalization is still a current topic in the public sphere. Analyzing medical data obtained from the Clinical Toxicology-Cardiology Department At the Department of Internal Medicine in Lublin, a gradual increase in hospitalizations due to cannabis-related poisonings has been observed. From the interviews, it is known that in 70% of cases, poisoning occurred after intentional consumption of marijuana for recreational purposes, even though marijuana has been legalized in Poland only for medical use since 2017. Patients admitted to the ward exhibited psychomotor agitation (70%), often requiring sedation (63%) and psychological or psychiatric assessment (81%). Upon admission to the Emergency Department, most patients showed tachycardia (55% of patients had a heart rate exceeding 100 beats per minute) and elevated creatine kinase levels (41%). Additionally, recurrent admissions of previously hospitalized patients due to psychoactive substance intoxication were frequently observed. None of these patients adhered to the recommendation to undergo addiction therapy that they received during their previous stay.

The collected data indicates that it is not possible to assess the direction that the population will take after the legalization of marijuana for both medical and recreational use. The legalization of marijuana does not lead to immediate and significant changes in public health indicators, except for significant issues related to road safety. However, there are potential benefits arising from legislative changes, such as better education for adult users about health risks through warnings on labels and greater freedom to discuss health issues related to marijuana with healthcare professionals. While reducing exposure to synthetic cannabinoids may be beneficial, this may be offset by an increase in health problems associated with natural cannabinoids. However, further detailed studies are needed to obtain a bigger picture of the effects of marijuana legalization.

5. After Conclusions

- **Author's conclusions**

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- **Data Availability Statement**

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Authors declare there is no conflicting interest.

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