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Management of nicotine dependence in patients with psychiatric disorders – recommendations of the Polish Psychiatric Association. Part I

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Summary

Smoking and nicotine dependence are still one of the main reasons for a number of serious and life-shortening somatic diseases. At the same time, they are more prevalent in mentally ill individuals than in the general population. This work, which constitutes the first part of recommendations of the Polish Psychiatric Association, presents the scale of the phenomenon in the general population and among people with psychiatric disorders, diagnostic criteria of nicotine dependence and nicotine withdrawal. It discusses the impact of smoking and exposure to cigarette smoke on the development and course of psychiatric disorders as well as on the treatment of psychiatric disorders, including interactions between nicotine and psychotropic medications. Many psychiatric patients can reduce smoking or achieve complete abstinence if they are offered adequate motivation and therapeutic support. Contrary to popular belief, smoking cessation and nicotine dependence treatment do not negatively affect the symptoms of psychiatric disorders; patients' mental conditions can improve following smoking cessation therapy. The best results in terms of maintaining abstinence are achieved with a treatment

approach that combines pharmacotherapy with psychotherapeutic intervention integrated into routine psychiatric care.

Key words: nicotine dependence, prevalence, health consequences, pharmacological treatment

Introduction

People with mental illness smoke cigarettes more often than those without psychiatric disorders. Despite the significant advances made in recent decades in terms of effective therapeutic approaches for nicotine dependence, patients with mental disorders are rarely offered appropriate therapy, and even when they eventually receive treatment, they are much less likely to quit smoking and maintain abstinence than those without mental illness. Treatment of nicotine dependence should, therefore, be an essential component of comprehensive psychiatric care. However, medical staff, including psychiatrists, most often do not address the smoking of patients under their care, presumably due to the belief that they will not be able to quit smoking successfully and that short-term tobacco abstinence will adversely affect their mental state.

The epidemiology of smoking

A 2018 World Health Organisation (WHO) report shows that smoking, including passive smoking, is a major public health problem worldwide and accounts for around 8 million deaths each year [1]. It is the most common cause of death among men in Poland (over 26%) and the second most common cause of death among Polish women (nearly 14%) [2]. According to a 2020 study by the National Institute of Public Health – National Institute of Hygiene, 23.1% of Polish men and 14.9% of women declared to smoke regularly, while the use of electronic products containing nicotine was declared by 10.8% of men and 7.1% of women [3, 4]. In October 2020, almost one in four Polish adults (23.7%) was an active consumer of nicotine, based on *Konsumpcja nikotyny – raport z badań ilościowych dla biura do spraw substancji chemicznych* [Nicotine consumption – a quantitative research report for the Chemicals Bureau], published in November 2020. Nicotine consumption is slowly but consistently declining, with the proportion of 'smokers' down by nearly 6 percentage points compared to 2018, with 32.6% of men and 15.8% of women declaring themselves to be smokers. The vast majority state that they smoke traditional cigarettes (21.5%), while the second largest group of nicotine consumers is made up of users of hand-rolled tobacco – currently 3.1%. Users of e-cigarettes with liquid are 1.4% of Polish adults, and the use of tobacco heating products is declared by 1.5% of Polish adults (a threefold increase compared to 2019). Smoking cigars/cigarillos or a pipe is incidental among adult Poles – regular use is currently reported by less than 1% of respondents [5]. According to WHO information, people with serious mental illnesses smoke tobacco more often than those

in the general population (61% vs 33%), consume more cigarettes per day and are less likely to stop smoking; it is also known that smoking is one of the main causes of premature death in people with psychiatric disorders, as in the general population [1].

The impact of smoking on somatic health

In the United States, cigarette smoking causes more than 480,000 deaths each year, i.e. more than human immunodeficiency virus (HIV), drugs, alcohol, traffic accidents, and gunshots combined [6]. More than 10 times as many US citizens have died prematurely from smoking than in all the wars fought by the United States. Around 90% of all lung cancer deaths are caused by smoking. Each year, more women die from lung cancer than from breast cancer [7]. The cause of approximately 80% of all deaths from chronic obstructive pulmonary disease (COPD) is smoking [6]. Cigarette use increases the risk of death from all causes in men and women. The risk of death from cigarette smoking has risen in the USA over the past 50 years. We do not have such detailed data from Poland.

Heart disease, stroke and lung cancer are significantly more likely to occur in smokers [6]. The risk of coronary heart disease and stroke in smokers increases by 2 to 4 times, while the risk of lung cancer by up to 25 times. The effects of smoking may include poorer overall health, increased absenteeism in the workplace and higher healthcare use and costs. Smokers are at greater risk of cardiovascular disease. Smoking may cause cancer almost anywhere in the body; the most common areas of increased cancer risk are the bladder, blood (acute myeloid leukaemia), cervix, colon/rectum, oesophagus, kidney/ureter, larynx, liver, throat, pancreas, and the stomach.

Another consequence of smoking may be pulmonary disease due to damage to the airways and alveoli. Smoking-related lung diseases also include COPD with emphysema and chronic bronchitis. Most cases of lung cancer are caused by cigarette smoking. In patients with bronchial asthma, tobacco smoke may trigger dyspnoea or exacerbate the disease. Smokers are 12 to 13 times more likely to die from COPD than non-smokers [6, 7].

Cigarette smoke mainly targets the respiratory epithelium, which acts as a barrier to inhaled toxic chemicals, while tobacco smoking, in general, impairs mucociliary clearance, as evidenced by prolonged transit time in the saccharine test. The development of COPD is promoted by persistent inflammation of the airways and lung parenchyma in response to several stimuli (e.g. cigarette smoke, bacterial and viral infections, air pollution, etc.).

The impact of smoking on the development of cardiovascular disease

Ageing and smoking are major risk factors for cardiovascular disease (CVD). Tobacco smoking and haemodynamic forces are both key stimuli for the onset of

vascular endothelial dysfunction. The effects of tobacco smoke exposure on blood vessels in the context of potential pro-inflammatory and atherosclerotic activity are well documented.

Poussin et al. [8] compared the effects of the aerosol of Tobacco Heating System 2.2 (THS; an electrically heated tobacco product) and reference cigarette smoke (3R4F CS) on processes that contribute to vascular pathomechanisms leading to CVD. The study confirmed the effect of 3R4F in accelerating the ageing of young human aortic smooth muscle cells (HAoSMCs) and enhancing the ageing effect of old HAoSMCs in vitro, confirming the risk of developing CVD from exposure to cigarette smoke. Compared to 3R4F CS, THS showed significantly reduced vascular effects, suggesting a lower risk of SMC-related vascular pathomechanisms leading to CVD [8].

Other studies suggest the potential for CVD development caused by long-term e-cigarette vaping to a degree similar to that caused by exposure to tobacco smoke, and the severity of this toxicity is believed to increase with the duration of exposure and the nicotine content [9].

Still, other research suggests that nicotine may alter vascular reactivity through endothelium-dependent and/or endothelium-independent mechanisms, leading to clinical symptoms in both cigarette smokers and e-cigarette users. Furthermore, nicotine is thought to induce vascular remodelling through its effects on the proliferation, migration and matrix production of vascular endothelial cells and vascular smooth muscle cells [10].

Potential health benefits of smoking cessation

Quitting smoking is one of the most important actions smokers can take to reduce their risk of CVD. Smoking cessation reduces the risk of CVD and death, lowers markers of inflammation and hypercoagulability, leads to a rapid improvement in high-density lipoprotein cholesterol (HDL-C) levels, suppresses the development of subclinical atherosclerosis and slows its progression over time. Discontinuation of tobacco smoke exposure reduces the risk of coronary syndromes (both acute and chronic, formerly known as coronary artery disease), with the risk dropping sharply in 1-2 years after cessation and then decreasing more slowly in the long term, reducing the risk of disease and death from stroke, which after cessation comes close to the risk for those that have never smoked. In addition, it reduces the risk of abdominal aortic aneurysm, with risk reduction increasing with time after cessation, and may reduce the risk of atrial fibrillation, sudden cardiac death, heart failure, venous thromboembolism and peripheral artery disease [6].

Smoking cessation decreases the likelihood of developing COPD and slows the progression by limiting the loss of lung function over time. Additionally, it alleviates respiratory symptoms (e.g. cough, sputum production, wheezing), reduces the frequency and severity of respiratory tract infections (e.g. bronchitis, pneumonia),

leads to improved lung function, symptom relief, and improved treatment efficacy in patients with bronchial asthma [6].

When exposure to tobacco smoke stops, the risk of the above-mentioned tobacco-related cancers is markedly diminished. The lifetime risk of cancer for heated tobacco products is expected to be below 10-5 (1/100,000), three orders of magnitude lower than for cigarettes [11].

Nicotine dependence

Pathogenesis

Nicotine is a substance that carries a high risk of addiction. The risk of becoming addicted to nicotine after trying it at least once is 32%. This is the highest rate among all known psychoactive substances. For example, the probability of developing an addiction to heroin after using it at least once is 23% and 17% for cocaine [12, 13].

The primary mechanism underlying nicotine dependence is related to its impact on the reward system. The mesolimbic dopaminergic pathway, which is a key link in the reward system, is modulated by a number of substances and neurotransmitters that are responsible for the brain's natural reinforcement of adaptive behaviour. Many exogenous substances affect dopamine concentrations in the reward system both directly and indirectly by influencing other neurons. Any substance that triggers significantly fast and rapid dopamine surges in the reward system (such as nicotine) will have a potentially addictive effect [14].

The mechanism leading to nicotine dependence comprises four factors:

1. Direct influence on postsynaptic alpha-4 beta-2 nicotinic acetylcholine receptors located on dopaminergic neurons increases dopamine levels in the nucleus accumbens.
2. Activation of presynaptic alpha-7 receptors located on glutamatergic neurons in the ventral tegmental area boosts dopamine release in the nucleus accumbens and dorsolateral prefrontal cortex.
3. The desensitisation of postsynaptic alpha-4 beta-2 receptors on GABAergic interneurons impairs GABAergic transmission, resulting in enhanced dopaminergic transmission in the nucleus accumbens [12, 14, 15].
4. Non-nicotine mechanism – it has been shown that type A and type B monoamine oxidase activity is inhibited in smokers compared to non-smokers, which contributes to the enhanced addictive effect of nicotine. The diminished monoamine oxidase activity in smokers is dose-dependent and is most evident in those who smoke more than 20 cigarettes per day. Monoamine oxidase, which is responsible for the catabolism of catecholamines, is inhibited by such components of tobacco smoke as beta-carboline alkaloids, salsolinol or terpinenes. This inhibition of dopamine catabolism thus enhances its effect on reward system structures [16-20].

Diagnosing nicotine dependence

Both the ICD-11 and DSM-5 classification systems place tobacco/nicotine dependence in the group of mental disorders. Nicotine/tobacco dependence syndrome is diagnosed when at least 3 out of 7 of the following symptoms are present:

1. Increasing nicotine tolerance
2. Tobacco abstinence syndrome
3. Greater than intended tobacco use and difficulty in controlling this behaviour
4. Continued smoking despite the desire to stop
5. A significant amount of time spent smoking
6. Tobacco use prioritised over other activities
7. Persistent smoking despite the awareness of existing related health and psychological problems.

Nicotine withdrawal syndrome

It is estimated that withdrawal symptoms occur in 50% of individuals who try to quit smoking. Predicting who will develop withdrawal symptoms is challenging. They appear a few hours after smoking cessation, reach maximum intensity within 24-48 hours, and then decrease and subside within 10 days. Withdrawal symptoms occur as a consequence of nicotine affecting the relevant receptors. It causes a rapid opening of alpha-4 beta-2 nicotinic receptors, resulting in a sharp boost of dopamine in the reward system. However, the nicotinic receptor becomes desensitised within a short time. Recovery of nicotine receptor sensitivity is associated with the onset of withdrawal symptoms. A chronic smoker shows an increase in alpha-4 beta-2 receptors due to 'up-regulation.' The recovery of sensitivity by more receptors in compulsive smokers after prior desensitisation is responsible for the appearance of withdrawal symptoms [21-23].

The most common withdrawal symptoms include:

1. Anxiety
2. Attention deficit disorder
3. Dysphoric or depressed mood
4. Increased appetite/weight gain
5. Irritability, frustration, anger
6. Restlessness
7. Changes in blood pressure and heart rate
8. Dry mouth.

Nicotine dependence in individuals with mental disorders

People with mental disorders smoke more cigarettes compared to the general population, are more likely to be diagnosed with nicotine dependence, and are less likely to choose to quit smoking. All this leads to a disproportionate health and financial burden as well as a higher risk of death, and smoking-related illnesses are estimated to contribute more to premature death in this group than mental illness alone [24]. Smoking-related diseases (CVD, respiratory diseases, cancer) are also the predominant cause of premature death in people with alcohol and other substance dependence [25]. Smoking rates among people with mental illness remain high, even though they are decreasing in the general population. For example, the smoking rate in the general population in Australia decreased from 26% to 19% between 1997 and 2010, and remained unchanged among persons with mental disorders. In 2007, 32% of Australians with mental illness smoked cigarettes as compared to 16% of mentally healthy people [26]. We do not have corresponding data in Poland. In England, 42% of cigarettes are smoked by people with mental health conditions, including addictions [27]. The Australian data suggest that the highest proportion of cigarette smokers is associated with patients who are addicted to other psychoactive substances (73%), and those with schizophrenia (70%), bipolar disorder (61%) and alcohol dependence (61%). This is followed by depression (38%) and anxiety disorders (33%) [28].

The causes for the higher frequency of smoking and nicotine dependence in patients with mental disorders are complex. A common genetic basis for nicotine dependence and schizophrenia has been identified. Variants in the genes encoding nicotinic acetylcholine receptors are associated with the quantity of smoking and the risk of schizophrenia; in patients with schizophrenia, G alleles of the opioid receptor gene are linked to lower sensitivity to nicotine and, consequently, with higher tobacco consumption [29]. A common biological susceptibility is also indicated by neuroimaging studies of patients with schizophrenia and neurotypical smokers [30].

Common environmental and stress factors that increase the risk of psychiatric disorders and predispose a person to nicotine dependence also play an important role. On the other hand, smoking can affect individual susceptibility to stress. In animal studies, prolonged exposure to nicotine has been shown to cause dysregulation of the stress axis and hypersecretion of cortisol, with consequent changes in monoaminergic transmissions. This effect normalises after nicotine withdrawal [27].

Some concepts highlight the role of nicotine in the self-treatment of patients with mental disorders. Patients with schizophrenia, for example, may use nicotine to relieve negative symptoms and anhedonia. Smokers receiving antipsychotics have less severe extrapyramidal symptoms and less frequently need anticholinergic agents [29]. Attention has also been drawn to the potential for improving cognitive function in patients with schizophrenia, elderly depression, Parkinson's disease, and during the early stages of Alzheimer's disease [31]. However, studies have been conducted on

heavy smokers with schizophrenia during short – and long-term abstinence and after relapse to smoking, with no changes in cognitive function reported. What is more, in schizophrenia, the dopaminergic effects of nicotine are associated with higher severity of positive symptoms, physical aggression and insomnia [29]. In patients with depression and anxiety disorders, symptomatic improvement under the influence of nicotine may be deceptive: an attempt to stop smoking results in withdrawal symptoms (including anxiety and mood disorders), while another cigarette provides relief. The withdrawal symptoms are mistakenly interpreted as symptoms of the underlying disease [27].

The excessive use of tobacco products by psychiatric patients is fuelled by the common myth that smoking cessation will worsen the patient's mental condition. Still, reliable meta-analyses have not confirmed this, and, at the same time, smoking cessation in people with addictions extends the period of abstinence from other substances and alcohol by approximately 25% [26]. Considering the significant impact of tobacco smoking on the somatic health and mental status of patients with psychiatric disorders, the diagnosis and treatment of nicotine dependence should be provided routinely as a part of psychiatric care.

The impact of smoking and exposure to tobacco smoke on the development and course of psychiatric disorders

Increasingly more studies are investigating the link between lifestyle, mental health and the development of psychiatric disorders. Firth et al. [32] conducted a systematic review of studies evaluating the impact of physical activity, sleep, dietary patterns and smoking on the risk and therapeutic outcomes of a number of mental disorders. Evidence has been found suggesting that smoking is a causal factor in the emergence of the most common mental disorders and severe mental illnesses, including major depression, bipolar disorder and schizophrenia. Smoking has been confirmed to increase the risk of mental illness and is also associated with an earlier age of onset [33]. Additionally, a significant and meaningful relationship between smoking and a higher risk of suicide attempts in people with psychosis has been evidenced [34]. People with mental illness smoke more, are more likely to become addicted to nicotine and have more severe symptoms when trying to quit. Despite this, motivation to quit smoking among people with mental illness and nicotine dependence is comparable to that of the general population [35].

Research confirms that smoking cessation is associated with a reduction in the symptoms of depression, anxiety, PTSD, and lower emotional lability. The inclusion of smoking cessation interventions in people with addictions resulted in a simultaneous 25% increase in the likelihood of maintaining abstinence from alcohol or drugs as compared to standard treatment. Prochaska et al. [35] demonstrated that the introduction of a smoking cessation intervention in a randomised trial involving psychiatric

inpatients who were smokers was associated with a significantly lower likelihood of rehospitalisation [35].

Exposure to second-hand smoke is associated with the development of depression, generalised anxiety disorder (GAD), attention-deficit/hyperactivity disorder (ADHD) and conduct disorders [36]. Passive smoking in closed premises by non-smokers is linked with higher rates of depression symptoms and stress [37]. Depression has been found to be more likely among women, but not among men. A study in a Canadian population showed that passive smoking exposure among non-smokers was associated with more frequent anxiety disorders and poorer subjective assessments of one's mental health and stress levels, but was not associated with mood disorders [38]. A review of studies and the results of a population-based study conducted in China showed that passive smoking might be considered an important risk factor for cognitive impairment in the elderly [39]. On the other hand, children exposed to second-hand smoke in the home showed an increased risk of ADHD. In Scotland, 15% of children, mostly from poverty-stricken areas, were exposed to second-hand smoke indoors and exhibited emotional and behavioural problems. These problems diminished when a ban on smoking in homes was introduced [40]. Stress, depression and suicidal ideations were more severe in adolescents as the intensity of passive smoking increased, even after adjusting for variables such as age, gender, father's and mother's education level, school performance, economic status, place of residence and alcohol use [41].

Smoking and sleep disorders

Reduction and then quitting smoking is a basic sleep hygiene recommendation. The relationship between smoking and sleep quality is bilateral. Increasing nicotine dependence has a negative impact on sleep, and poor sleep quality and sleep deprivation are one of the risk factors for developing nicotine dependence. The lifestyle of the developed world has been linked to the prevalence of sleep deprivation in society. The age groups that are most affected by sleep deprivation are young adults and adolescents, among whom the minimum recommended sleep duration of seven hours is regularly maintained by just over 50% [42]. One of the negative health consequences of sleep deprivation is increased consumption of stimulants such as caffeine and nicotine, which are among the most common measures for dealing with excessive daytime sleepiness. For this reason, sleep deprivation and the resulting excessive daytime sleepiness are associated with an increased risk of smoking in adolescents [42] and young adults. This is also true for e-cigarettes [43].

During the initial period of smoking, the beneficial aspects of nicotine's effect of reducing daytime sleepiness outweigh its negative impact on sleep. Significant shortening of sleep time, reduction in sleep efficiency and depth, and extended sleep latency (the time it takes a person to fall asleep) are only present in severely nicotine-dependent individuals [44]. This is most often connected to not being able to sleep

through the night without smoking or having a quick cigarette after waking up in the morning. Questions about waking up at night to smoke a cigarette and how soon after waking up the first cigarette is lit are the first two questions in the Fagerstrom test, which assesses the degree of nicotine dependence [45].

Smoking is most strongly associated with poorer sleep quality when one tries to stop. In nicotine withdrawal syndrome, increased insomnia symptoms are experienced by more than 40% of nicotine-dependent individuals. Non-pharmacological interventions consistent with the principles of cognitive-behavioural therapy for the treatment of insomnia and the short-term use of sleep medications are, therefore, important methods supporting smoking cessation attempts [46].

Interactions of nicotine and other substances contained in tobacco with drugs used to treat psychiatric disorders

Tobacco smoke contains more than 4,000 different, largely toxic chemical compounds, many of which interact with medicines taken by patients. The adverse impact of cigarette smoke on the effects of medicinal substances extends to active and passive smokers alike. Most of the interactions between tobacco smoke and medications take place during the pharmacokinetic phase, i.e. the metabolism in the liver. Numerous studies have shown that nicotine and polycyclic aromatic hydrocarbons formed during tobacco combustion (benzopyrene, benzofluorene, benzoanthracene), increase enzyme protein synthesis and induce cytochrome P-450 isozymes such as: CYP1A1, CYP1A2, CYP2E1 and certain UDP-glucuronosyltransferase (UGT) isoforms. By contrast, the cyanides and carbon monoxide present in tobacco smoke have an inhibitory effect through binding to the iron of the haem group of the CYP P-450 isozymes and, therefore, potentially elevate serum drug concentrations [47].

The interactions that occur in the pharmacodynamic phase between tobacco smoke and the drugs taken, on the other hand, rely on their antagonism or synergism towards the receptors they affect. This may result in the drug's efficacy being stimulated or attenuated, which may involve the risk of adverse effects as well as failure to achieve the intended therapeutic effect. Below are examples of psychotropic medications that most often interact with tobacco smoke in the pharmacokinetic phase (i.e. anxiolytics, antipsychotics, antidepressants, and procognitive drugs) [48].

A. Benzodiazepines

Lower therapeutic concentrations, as well as a shorter half-life and increased clearance, have been demonstrated during the use of benzodiazepines in smokers. Consequently, the presumed anti-anxiety activity is weaker, requiring higher doses of the medication. This leads to less effective or ineffective treatment. Smokers require higher doses of benzodiazepines, as, for example, administration of alprazolam in some smoking patients results in a 50% reduction in serum drug levels and a 35% t½ reduction compared to non-smokers. Additionally, smokers may show

decreased sedative and sleeping effects from benzodiazepines, probably induced by nicotinic stimulation of the central nervous system [49].

B. Antipsychotics

With atypical antipsychotics, there is a reduction in serum drug concentrations due to enhanced metabolism, meaning that smokers will require higher doses. Some examples of interactions with clozapine, olanzapine and haloperidol are given below.

Clozapine is mainly metabolised by CYP1A2 and has a narrow therapeutic index. In smokers, the serum concentration is about 68% of that achieved in non-smokers, and this may be the reason for the lack of efficacy in therapy. After smoking cessation, the dose of the drug should be reduced, especially if such side effects as hypotonia, drowsiness, or extrapyramidal symptoms intensify.

Olanzapine is metabolised by CYP1A2 and CYP2D6. The steady-state drug concentration (the state in which the rate of drug entry into the body equals the rate of elimination) is five times lower in smokers, and clearance increases even up to 98%. It is recommended that patients who smoke and are taking clozapine or olanzapine be treated with a prescribed dose adjustment factor of 1.5 for 2-4 weeks. Blood levels of such medications should be monitored in patients who have suddenly quit smoking.

Haloperidol has a higher clearance (44%) and approximately 20% lower serum concentration in smokers due to the induction of metabolising enzymes, mainly CYP2D6, CYP3A4, and CYP1A2. Smokers require higher doses, and their drug levels after smoking cessation must be monitored to prevent adverse effects, as with clozapine. At the same time, it should be noted that CYP2D6 is characterised by a genetic polymorphism that determines the effect of smoking on haloperidol concentrations, the result of which is that some patients show increased metabolism, while in other cases there are no differences between smokers and non-smokers [49].

C. Antidepressants

Smoking may increase the clearance of tricyclic antidepressants through the induction of CYP1A2, causing lower plasma concentrations. In the case of SNRIs (e.g. duloxetine), there may even be a 50% reduction in plasma drug concentrations. Fluvoxamine is metabolised by CYP1A2 and CYP2D6. Smokers demonstrate a reduction in maximum blood concentration (32%), the area under the curve (31%) and steady-state concentration (39%). A reduction in the therapeutic efficacy of other CYP2A1-metabolised antidepressants, including amitriptyline, clomipramine, mirtazapine, and agomelatine, has also been observed [49].

D. Procognitive drugs

Currently, there are no clear reports of clinically significant effects of interaction with nicotine, either during smoking or after abrupt cessation, for the new generation of drugs used in the treatment of Alzheimer's disease, such as donepezil, galantamine and rivastigmine (acetylcholinesterase inhibitors). Meanwhile, in the

case of memantine, nicotine is a risk factor for interaction, and it is recommended to increase the dose of the drug after smoking cessation. An attenuated therapeutic effect can be expected in smoking patients following cytochrome P-450 enzyme induction, so higher doses are recommended [50].

In conclusion, most interactions between cigarette smoke and medicinal substances take place at the metabolic stage in the liver following the induction of drug-metabolising enzymes – cytochrome P-450 isozymes and UGT – by nicotine and polycyclic aromatic hydrocarbons. They may impair or even completely eliminate the therapeutic effect of the drugs. A patient who smokes either traditional or electronic cigarettes containing nicotine should take a different dose of the drug from the commonly recommended dose to achieve an adequate therapeutic effect. Another crucial point is that after smoking cessation, the patient should be aware that the dose needs to be adjusted so that toxic concentrations of the drug do not occur, especially in the case of medications with a narrow therapeutic index.

Summary

Tobacco smoking is one of the most important health problems globally. It significantly affects the population of people with mental disorders by increasing the morbidity and mortality rate. Smoking and nicotine dependence are more prevalent in mentally ill individuals than in the general population, as many mental illnesses are risk factors for nicotine dependence, and, at the same time, smoking can promote the development of some psychiatric disorders. The significant prevalence of smoking and nicotine dependence in individuals with psychiatric disorders is linked to common genetic and neurobiological factors. Furthermore, patients with psychiatric disorders may experience improved mental functioning at an emotional and cognitive level as a result of the nicotine released from the tobacco used, with positive effects on cognition, mood and emotion control. Nicotine dependence is most commonly found in people with schizophrenia, depressive disorders, bipolar disorder and other substance dependence.

Many patients with psychiatric disorders are able to reduce smoking or achieve complete abstinence if they are offered adequate therapeutic support during treatment of the underlying disease. Contrary to popular belief, smoking cessation and nicotine dependence treatment do not negatively affect the symptoms of psychiatric disorders; in fact, patients' mental conditions can improve following smoking cessation therapy, regardless of maintaining abstinence. Many studies confirm the improvement in psychiatric symptoms during treatment for nicotine dependence. Banning smoking in hospitals and psychiatric wards is also helpful in terms of providing better protection for non-smoking patients and staff against passive smoking hazards.

Patients with psychiatric disorders smoke more during periods of exacerbation, and the success of various methods aimed at smoking cessation is severely limited among

this patient group. As nicotine dependence is a substance use disorder, mental health professionals are best qualified to provide interventions in this area. It is, in fact, their duty to do so, especially in view of the significant negative impact of smoking on health, psychotropic drug metabolism, morbidity and mortality. Creating and implementing training programmes to increase the awareness and skills of mental health professionals in identifying and treating nicotine-dependent individuals is, therefore, of great value.

References

1. World Health Organization. *European health report 2018: More than numbers – evidence for all.* World Health Organisation, Regional Office for Europe; 2018.
2. Murray CJL, Aravkin AY, Zheng P, Abbafati C, Abbas KM, Abbasi-Kangevari M et al. *Global burden of 87 risk factors in 204 countries and territories, 1990–2019: A systematic analysis for the Global Burden of Disease Study 2019.* Lancet 2020; 396(10258): 1223–1249.
3. Narodowy Instytut Zdrowia Publicznego – Państwowy Zakład Higieny [National Institute of Public Health – National Institute of Hygiene]. *Sytuacja zdrowotna ludności Polski i jej uwarunkowania* [Health status of Polish population and its determinants]. Warszawa: NIZP-PZH; 2020.
4. Bała M, Cedzyńska M, Balwicki Ł, Czajkowska-Malinowska M, Jankowska-Zduńczyk A, Jassem J et al. *Wytyczne leczenia uzależnienia od nikotyny* [Tobacco dependence treatment guidelines]. https://adst.mp.pl/s/www/pulmonologia/WytyczneZUN.pdf (retrieved: 22.07.2022).
5. *Konsumpcja nikotyny – RAPORT* [Nicotine consumption – REPORT]. file:///C:/Users/wum/Downloads/Konsumpcja_nikotyny_raport_popr.pdf (retrieved: 22.07.2022).
6. U.S. Department of Health and Human Services. *The Health Consequences of Smoking – 50 Years of Progress: A Report of the Surgeon General*. Atlanta: U.S. Department of Health and Human Services, Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health; 2014.
7. U.S. Department of Health and Human Services. *Women and Smoking: A Report of the Surgeon General.* Rockville, MD: U.S. Department of Health and Human Services, Public Health Service, Office of the Surgeon General; 2001.
8. Poussin C, Toorn van der M, Scheuner S, Piault R, Kondylis A, Savioz R et al. *Systems toxicology study reveals reduced impact of heated tobacco product aerosol extract relative to cigarette smoke on premature aging and exacerbation effects in aged aortic cells in vitro.* Arch. Toxicol. 2021; 95(10): 3341–3359.
9. El-Mahdy MA, Mahgoup EM, Ewees MG, Eid MS, Abdelghany TM, Zweier JL. *Long-term electronic cigarette exposure induces cardiovascular dysfunction similar to tobacco cigarettes: Role of nicotine and exposure duration.* Am. J. Physiol. Heart Circ. Physiol. 2021; 320(5): H2112–H2129.
10. Whitehead AK, Erwin AP, Yue X. *Nicotine and vascular dysfunction.* Acta Physiol. (Oxf.) 2021; 231(4): e13631.
11. Hirano T, Takei T. *Estimating the carcinogenic potency of second-hand smoke and aerosol from cigarettes and heated tobacco products.* Int. J. Environ. Res. Public Health 2020; 17(22): 8319.
12. Stahl SM. *Podstawy psychofarmakologii. Teoria i praktyka,* t. 4. Gdańsk: Via Medica; 2010.

13. Benowitz NL. *Cigarette smoking and cardiovascular disease: Pathophysiology and implications for treatment.* Prog. Cardiovasc. Dis. 2003; 46(1): 91–111.
14. Buchta WC, Riegel AC. *Chronic cocaine disrupts mesocortical learning mechanisms.* Brain Res. 2015; 1628(Pt A): 88–103.
15. Jiloha RC. *Biological basis of tobacco addiction: Implications for smoking-cessation treatment.* Indian J. Psychiatry 2010; 52(4): 301–307.
16. Fowler JS, Volkow ND, Wang GJ, Pappas N, Logan J, MacGregor R et al. *Neuropharmacological actions of cigarette smoke: Brain monoamine oxidase B (MAO B) inhibition.* J. Addict. Dis. 1998; 17(1): 23–34.
17. Leroy C, Bragulat V, Berlin I, Grégoire MC, Bottlaender M, Roumenov D et al. *Cerebral monoamine oxidase A inhibition in tobacco smokers confirmed with PET and [11C]befloxatone.* J. Clin. Psychopharmacol. 2009; 29(1): 86–88.
18. Shahi GS, Das NP, Moochhala SM. *1-Methyl-4-phenyl-1,2,3,6-tetra-hydropyridine-induced neurotoxicity: Partial protection against striato-nigral dopamine depletion in C57BL/6J mice by cigarette smoke exposure and by beta-naphthoflavone-pretreatment.* Neurosci. Lett. 1991; 127(2): 247–250.
19. Anthenelli RM, Tipp J, Li TK, Magnes L, Schuckit MA, Rice J et al. *Platelet monoamine oxidase activity in subgroups of alcoholics and controls: Results from the Collaborative Study on the Genetics of Alcoholism.* Alcohol Clin. Exp. Res. 1998; 22(3): 598–604.
20. Whitfield JB, Pang D, Bucholz KK, Madden PA, Heath AC, Statham DJ et al. *Monoamine oxidase: Associations with alcohol dependence, smoking and other measures of psychopathology.* Psychol. Med. 2000; 30(2): 443–454.
21. Hughes JR, Hatsukami D. *Signs and symptoms of tobacco withdrawal.* Arch. Gen. Psychiatry 1986; 43(3): 289–294.
22. Hughes JR, Hatsukami DK, Mitchell JE, Dahlgren LA. *Prevalence of smoking among psychiatric outpatients.* Am. J. Psychiatry 1986; 143(8): 993–997.
23. Hughes JR, Gust SW, Skoog K, Keenan RM, Fenwick JW. *Symptoms of tobacco withdrawal. A replication and extension.* Arch. Gen. Psychiatry 1991; 48(1): 52–59.
24. Williams JM, Steinberg ML, Griffiths KG, Cooperman N. *Smokers with behavioral health comorbidity should be designed a tobacco use disparity group.* Am. J. Public Health 2013; 103(9): 1549–1555.
25. Hurt RD, Offord KP, Croghan IT, Gomez-Dahl L, Kottke TE, Morse RM et al. *Mortality following inpatient addictions treatment. Role of tobacco use in a community-based cohort.* JAMA 1996; 275(14): 1097–1103.
26. Mendelsohn CP, Kirby DP, Castle DJ. *Smoking and mental illness. An update for psychiatrists.* Australas Psychiatry 2015; 23(1): 37–43.
27. Fluharty M, Taylor AE, Grabski M, Munafò MR. *The association of cigarette smoking with depression and anxiety: A systematic review.* Nicotine Tob. Res. 2017; 19(1): 3–13.
28. Cooper J, Mancusso SG, Borland R, Slade T, Galletly C, Castle D. *Tobacco smoking among people living with a psychotic illness: The second Australian Survey of Psychosis.* Aust. N. Z. J. Psychiatry 2012; 46(9): 851–863.
29. Sagud M, Peles AM, Pivac N. *Smoking in schizophrenia: Recent findings about old problem.* Curr. Opin. Psychiatry 2019; 32(5): 402–408.

30. Ward HB, Beermann A, Nawaz U, Halko MA, Janes AC, Moran LV et al. *Evidence for schizophrenia-specific pathophysiology of nicotine dependence.* Front. Psychiatry 2022; 13: 804055.
31. Hong SW, Teesdale-Spittle P, Page R, Ellenbroek B, Truman P. *Biologically active compounds present in tobacco smoke: Potential interactions between smoking and mental health.* Front. Neurosci. 2022; 16: 8885489.
32. Firth J, Solmi M, Wootton RE, Vancampfort D, Schuch FB, Hoare E et al. *A meta-review of "lifestyle psychiatry": The role of exercise, smoking, diet and sleep in the prevention and treatment of mental disorders.* World Psychiatry 2020; 19(3): 360–380.
33. Gurillo P, Jauhar S, Murray RM, MacCabe JH. *Does tobacco use cause psychosis? Systematic review and meta-analysis.* Lancet Psychiatry 2015; 2(8): 718–725.
34. Sankaranarayanan A, Mancuso S, Wilding H, Ghuloum S, Castle D. *Smoking, suicidality and psychosis: A systematic meta-analysis.* PLoS One 2015; 10(9): e0138147.
35. Prochaska JJ, Hall SE, Delucchi K, Hall SM. *Efficacy of initiating tobacco dependence treatment in inpatient psychiatry: A randomized controlled trial.* Am. J. Public Health 2014; 104(8): 1557–1565.
36. Bandiera FC, Richardson AK, Lee DJ, He JP, Merikangas KR. *Secondhand smoke exposure and mental health among children and adolescents.* Arch. Pediatr. Adolesc. Med. 2011; 165(4): 332–338.
37. Zeng YN, Li YM. *Secondhand smoke exposure and mental health in adults: A meta-analysis of cross-sectional studies.* Soc. Psychiatry Psychiatr. Epidemiol. 2016; 51(9): 1339–1348.
38. Asbridge M, Ralph K, Stewart S. *Private space second-hand smoke exposure and the mental health of non-smokers: A cross-sectional analysis of Canadian adults.* Addict. Behav. 2013; 38(3): 1679–1686.
39. Chen R, Hu Z, Orton S, Chen RL, Wei L. *Association of passive smoking with cognitive impairment in nonsmoking older adults: A systematic literature review and a new study of Chinese cohort.* J. Geriatr. Psychiatry Neurol. 2013; 26(4): 199–208.
40. Shiue I. *Correlations of indoor second-hand smoking, household smoking rules, regional deprivation and children mental health: Scottish Health Survey, 2013.* Environ. Sci. Pollut. Res. Int. 2015; 22(13): 9858–9863.
41. Lee E, Kim KY. *The association between secondhand smoke and stress, depression, and suicidal ideation in adolescents.* Healthcare (Basel) 2021; 9(1): 39.
42. Terry-McElrath YM, Maslowsky J, O'Malley PM, Schulenberg JE, Johnston LD. *Sleep and substance use among US adolescents, 1991–2014.* Am. J. Health Behav. 2016; 40(1): 77–91.
43. Kianersi S, Zhang Y, Rosenberg M, Macy JT. *Association between e-cigarette use and sleep deprivation in U.S. young adults: Results from the 2017 and 2018 Behavioral Risk Factor Surveillance System.* Addict. Behav. 2021; 112: 106646.
44. Hu N, Wang C, Liao Y, Dai Q, Cao S. *Smoking and incidence of insomnia: A systematic review and meta-analysis of cohort studies.* Public Health 2021; 198: 324–331.
45. Heatherton TF, Kozlowski LT, Frecker RC, Fagerström KO. *The Fagerström Test for Nicotine Dependence: A revision of the Fagerström Tolerance Questionnaire.* Br. J. Addict. 1991; 86(9): 1119–1127.
46. Patterson F, Grandner MA, Malone SK, Rizzo A, Davey A, Edwards DG. *Sleep as a target for optimized response to smoking cessation treatment.* Nicotine Tob. Res. 2019; 21(2): 139–148.

47. Delijewski M, Goniewicz ŁM. *Interakcje leków z dymem tytoniowym w praktyce farmaceuty* [Drug interactions with tobacco smoke in community pharmacy practice]. Farm. Prz. Nauk. 2010; 12: 43–59.

48. Jośko-Ochojska J, Spandel L, Brus R. *Interakcje alkoholu i dymu tytoniowego zlekami – wiedza potrzebna na co dzień* [Alcohol and tobacco smoke interactions with medications – indispensable everyday knowledge]. Hygeia Public Health 2015; 50(3): 474–481.

49. Desai HD, Seabolt J, Jann MW. *Smoking in patients receiving psychotropic medications: A pharmacokinetic perspective.* CNS Drugs 2001; 15(6): 469–494.

50. Pal A, Balhara YP. *A review of impact of tobacco use on patients with co-occurring psychiatric disorders.* Tob. Use Insights 2016; 9: 7–12.

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