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The Influence of Smoking Behavior on Dopamine Level Increase in the Blood of Active and Passive Smokers at Kwala Bekala Market, Medan

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ABSTRACT

Cigarette is responsible for the death of 6 million people worldwide each year, with approximately 600,000 deaths related to exposure to secondhand smoke (World Health Organization (WHO)). A molecular biomarker in smoking behavior is the high level of dopamine in the blood. Therefore, this study aimed to analyze the differences in the blood dopamine levels between active and passive smokers. This comparative study consisted of 80 respondents, comprising 40 active and 40 passive smokers. The blood samples of 3 cc were taken from the vein and taken to the laboratory for measurement of dopamine level using the ELISA method. The results showed that the average dopamine level in active smokers was higher, at 70.48±21.89, while passive smokers at 65.98±25.30, with an average difference of 4.5 pg/ml. This suggested that smoking behavior could influence dopamine level in the blood of both active and passive smokers. Consequently, public awareness should to be raised about the health impacts of smoking, and the enforcement of smoking bans in public places such as Smoke-Free Areas (KTR/KUTARO) was essential to protect others from the dangers of exposure to cigarette smoke.

Keywords: Active Smokers, Nicotine, Dopamine, Passive Smokers, ELISA

ABSTRAK

Rokok menyebabkan kematian dari 6 juta orang di seluruh dunia setiap tahunnya dan sekitar 600.000 kematian terkait dengan paparan asap rokok pada perokok pasif *(World Health Organization* (WHO). Salah satu biomarker molekular dalam perilaku merokok adalah adanya kenaikan kadar dopamin dalam darah. Penelitian ini bertujuan untuk menganalisis perbedaan kadar dopamin dalam darah perokok aktif dan perokok pasif. Penelitian ini adalah studi komparatif dengan total sampel sebanyak 80 responden terdiri atas 40 perokok aktif dan 40 perokok pasif. Pada sampel dilakukan pengambilan darah sebanyak 3cc melalui vena dan dibawa ke laboraturium dan diukur kadar dopaminnya menggunakan metode ELISA. Hasil penelitian menunjukkan rerata kadar dopamin perokok aktif terlihat lebih tinggi yaitu 70.48±21.89 sedangkan pada perokok pasif 65.98±25.30 dengan selisih rerata sebesar 4,5 pg/ml. Berdasarkan hasil tersebut dapat disimpulkan perilaku merokok dapat mempengaruhi kadar dopamin dalam darah perokok aktif dan pasif. Oleh karena itu, kesadaran masyarakat perlu ditingkatkan tentang dampak merokok terhadap kesehatan dan menegakkan aturan larangan merokok di tempat umum seperti Kawasan Tanpa Rokok (KTR) untuk melindungi orang lain dari bahaya paparan asap rokok.

Kata kunci: Perokok Aktif, Nikotin, Dopamin, Perokok Pasif, ELISA

1. Introduction

Smoking behavior is the act of inhaling the smoke of burning cigarette wrapped in nipah leaves or paper and exhaling it back out (WHO, 2018). Data from the Basic Health Research (Riskesdas) in 2018 showed that the average proportion of smokers in Indonesia was 28.8%, with the prevalence age of 10-18 years increasing from 7.2% in 2013 to 9.1% in 2018 [1]. Smokers can be categorized into two types, namely active and passive. Active smokers are those who smoke and inhale cigarette regularly for more than 6 months. Passive smokers are those who do not smoke but inhale or are exposed to cigarette smoke from others, family, or the surrounding environment [2].

Generally, smoking is considered a behavior in substance use disorders, observable through behavioral, molecular, and neurological biomarkers. Behavioral biomarkers include addictive behavior, anxiety, depression, stress reactions, and several impulsive components. Molecular biomarkers can be observed from several components of neurotransmitters such as dopamine, glutamate, gamma-aminobutyric acid (GABA), and nicotinic receptors. Meanwhile, neurological biomarkers include the numerous neural circuits engaged in substance abuse that lead to addiction. These biomarkers identify smoking as substance abuse [3,4].

The high prevalence of smokers is caused by the addictive substances found in cigarette, which consist of 4,000 harmful chemical components. In cigarette, three substances are the most dangerous to the body, namely tar, nicotine, and carbon monoxide [5]. Nicotine is a toxic substance causing psychological addiction because it enters the brain very quickly after smoking in 10 seconds compared to others that take 30 to 60 seconds. This rapid entry causes changes in brain neurotransmitters, particularly dopamine playing a role in addictive behavior. According to Lande, nicotine is a toxic alkaloid that is very active and affects the neurophysiological system in the brain [4]. This makes nicotine difficult for active smokers to quit smoking, contributing to the high prevalence of smokers [6].

One of the molecular biomarkers in smoking behavior is an increase in dopamine level, a neurotransmitter that controls pleasurable feelings, body movement, behavior, motivation, attention, learning, and mood. All substance use disorders is coordinated by the limbic system in the brain, specifically the mesolimbic dopamine pathways. This include dopamine neurotransmitters in ventral tegmental area (VTA) of the midbrain and located in nucleus accumbens (NAc) [7,8].

Investigations into dopamine function among chronic smokers, conducted before and after extended periods of cessation, included measuring dopamine production capacity index in 30 male smokers dependent on nicotine and 15 non-smokers using positron emission tomography. The results showed a 15-20% decrease in dopamine production capacity in active smokers compared to non-smokers. This suggested that dopamine could serve as a potential biomarker for cigarette dependence [9]. Dopamine is a key neurotransmitter, playing a significant role in various neurological functions such as mood regulation, motivation, and movement coordination. Several investigations have predominantly focused on dopamine effects on the central nervous system and its association with conditions such as mood, attention-deficit, and movement disorders. The influence on oral health is mediated indirectly through overall health and individual behaviors. Dopamine is essential in managing stress responses and nicotine dependence among active smokers. The impact of nicotine on dopamine release in the brain potentially represents a mechanism through which the brain adapts to stress [10].

Active smokers tend to have problems with their gums such as bleeding, receding, and damage to the supporting tissues of the teeth. The correlation between smoking and periodontal disease is complex, as smokers are known to show more severe forms of gum disease compared to non-smokers. This is due to the propensity of smoking to foster plaque and calculus accumulation, causing poor gingival health and receding gums. Stress can increase these conditions by raising inflammation in the oral cavity, thereby worsening the severity of periodontal disease, which is higher in active smokers compared to non-smokers. This condition can damage the bone supporting the teeth, causing loss [11,12].

Dopamine function was examined in chronic smokers before and after long-term cessation. This was performed by measuring the index of dopamine production capacity in 30 nicotine-dependent male smokers and 15 non-smokers using positron emission tomography. The results showed a 15-20% reduction in dopamine production capacity in active smokers compared to non-smokers. This suggested that dopamine could be a marker for cigarette abuse [12]. A previous study also showed that an increase in dopamine levels produced

by cigarette smoking could be detected in cortical brain regions in humans using [11C]-FLB-457 PET imaging. Activation of these brain regions has been associated with cigarette craving, cognition, and relapse in fMRI (functional Magnetic Resonance Imaging) studies, showing the need for further investigation in larger and more diverse samples. [11C]-FLB-457 PET imaging has been proven to be a useful tool to investigate individual differences in cigarette addiction severity and relapse vulnerability in relation to cortical dopamine function [13].

2. Materials and Methods

This comparative study was carried out using a cross-sectional design to compare two groups, observe the effect, and measure the variables simultaneously for two groups. The experiment conducted in Kwala Bekala Market Area of Medan City was approved by the Health Research Ethics Committee of Universitas Sumatera Utara (No. 728/KEPK/USU/2024). The blood samples were taken in the market with the assistance of laboratory personnel who came to the study location. The population was active and passive smokers in Kwala Bekala Market area of Medan City, including employees, cleaning staff, and traders in the market. Subjects were individuals aged above 16 years and samples were obtained using the purposive sampling method. The sample size calculation was determined using the hypothesis formula for the mean of one population. Furthermore, the sample size for the blood dopamine level test was 37 individuals. Since the survey consisted of two groups, the total required sample was 80 smokers, comprising 40 active and 40 passive. The blood collection from the subjects started from 8 AM to 12 PM, followed by immediate transfer to the laboratory by the staff.

The inclusion criteria for active smokers were individuals who directly and regularly smoke a minimum of 10 cigarettes per day, as well as smoking for more than 1 year. These individuals must be between the ages of 16 and 65, willing to undergo an examination, complete the informed consent form, and participate in the study process. Meanwhile, for passive smokers, the criteria were individuals exposed to cigarette smoke daily in their environment, home, workplace, and surrounding areas. Passive smokers must also be willing to complete the informed consent form and participate in the study process.

The exclusion criteria for active smokers were individuals who have been using prescription medications regularly in the last 6 months, have physical or mental health conditions, including substance abuse (such as alcohol, narcotics, and other illegal drugs), smoke fewer than 10 cigarettes per day, and have been smoking for less than a year. For passive smokers, the exclusion criterion is not in the same room or environment as active smokers.

The blood samples from respondents were taken using 1.5 cc tubes, where tubes 1 and 2 contained EDTA to extract plasma. Meanwhile, the third sample was placed in a microcentrifuge tube without EDTA to extract serum. This was followed by immediate transfer to the laboratory and stored in a storage cabinet to maintain sterility. The blood samples were centrifuged to separate the blood plasma and serum from the blood cells. The samples can be stored for up to 6 hours at a temperature of 2-8°C and for longer storage (up to 6 months) at -20°C. The reagents used were prepared, starting with a wash buffer followed by an enzyme solution. The sample preparation process started with the blood plasma, followed by extraction and isolation processes to accumulate 50 µL of plasma dopamine, which was measured by using ELISA Fast Track.

3. Results

The results showed that the majority of active smokers were males, totaling 27 individuals (67.5%), and 30 (75%) passive smokers were females. Based on age groups, the majority of both groups fell in the 46-55 years, with 19 active (47.5%) and 25 passive (62.5%) smokers. Generally, active smokers were mostly traders, totaling 24 individuals (60%), while 16 (40%) were employees. Among passive smokers, 37 (92.5%) were traders, while 3 (7.5%) were employees (Table 1).

Table 1. Characteristics of Active and Passive Smoker Samples

Characteristic	n	Active smoker (n=40)		Passive smoker (n=40)	
		n	%	n	%
Gender					
Male	37	27	67.5	10	25.0
Female	43	13	32.5	30	75.0
Age (years)					
17-25	5	2	5.0	3	7.5
26-45	31	19	47.5	12	30.0
46-65	44	19	47.5	25	62.5
Occupation					
Trader	61	24	60.0	37	92.5
Employee	19	16	40.0	3	7.5

The average dopamine levels in active smokers at 70.48±21.89 was higher compared to passive group at 65.98±25.30. However, the analysis results showed no significant variation in dopamine levels between active and passive smokers, with a mean difference of 4.5 pg/ml (p=0.140) (Table 2).

Table 2. Average Dopamine Levels in Active and Passive Smokers

Smokers	Average Dopamine Levels			p
	mean	SD	Mean difference	
Active Passive	70.48 65.98	21.89 25.30	4.5	0.140

4. Discussion

Based on the study conducted using questionnaires, the majority of active smokers were males (67.5%) compared to females (32.5%). Among passive smokers, there were more females, with 30 individuals (75%) compared to only 10 males (25%). Chinwong reported a higher prevalence of smoking among males than females, although the prevalence varied across different countries. In Thailand, the prevalence of smoking was approximately 15-20 times higher among males than females based on the survey [10]. Another explanation could be social and cultural patterns where males showed a high tendency to smoke actively in domestic or occupational environments, potentially due to socializing with fellow smokers leading to nicotine addiction [14].

The study on dopamine levels in the blood of active and passive smokers showed an average difference of 4.5 pg/ml. The p-value (0.140) was greater than the significance threshold ($p < 0.05$). Dopamine levels in active smokers were 70.48 ± 21.89, while in passive smokers had 65.98 ± 25.30. These results did not show a significant difference due to the primary action mechanism of nicotine. The influencing factors include the frequency of passive smokers exposure to smoke, such as in their work, environment, or at home [15,16]. The acquisition phase of smoking addiction includes understanding how nicotine modifies neural pathways. Therefore, animal model could be used to provide insight into nicotine impact on dopaminergic and cholinergic signaling in key nodes of the reinforcement circuitry, namely the ventral tegmental area, NAc, amygdala, and hippocampus. Based on mechanisms that subserve natural rewards, nicotine activates midbrain dopamine neurons directly and indirectly. It also caused dopamine release in very broad target areas in the brain, including NAc, amygdala, and hippocampus. Additionally, nicotine is responsible for local changes in those target structures, altering the release of virtually all major neurotransmitters, and primes the nervous system to the influence of other addictive drugs [21].

The analysis results showing no significant difference ($p > 0.05$) was due to the primary action mechanism of nicotine related to dopamine release in the brain, rather than directly in the bloodstream. Dopamine can be converted to norepinephrine (noradrenaline) through metabolic processes in certain non-

brain cells that possess the appropriate enzymes. Therefore, the mechanism by which dopamine affects the body through the bloodstream is more related to its influence on the central nervous system and the role of metabolism in forming dopamine-related compounds affecting the blood system [17].

As a neurotransmitter, studies on dopamine have focused primarily on CNS (central nervous system). However, experimental results show that dopamine has important physiological functions in the immune system [18]. Dopamine interacts with other immune-modulatory pathways, such as the adrenergic system (norepinephrine) and hypothalamic-pituitary-adrenal (HPA) axis. These interactions help maintain a balance between immune activation and immune regulation. Dopamine is also included in neurotransmission and plays an essential role in regulating immune responses. It influences immune cell function, cytokine production, and migration, showing the importance of both inflammatory and regulatory processes. Previous reported that dopamine's modulation of immune responses played a significant role in maintaining immune homeostasis and therapeutic purposes in diseases. Calabresi et al. reported the modulation of behavior and cognition such as voluntary movement, motivation, punishment and reward, inhibition of prolactin production, sleep, dreaming, mood, working memory, and learning. Dopamine is known as the "feel-good" hormone, which releases a sense of pleasure and motivation to carry out various activities. As humans, the brains are hard-wired to determine behaviors that release dopamine in the reward system [22,23].

Based on this study, dental practitioners should be proactive in educating patients about the risks of smoking on oral health and encouraging them to participate in cessation programs. Regular dental check-ups and professional cleanings should be emphasized, particularly for smokers, to prevent and manage periodontal diseases effectively [19].

Despite not smoking directly, passive smokers are still exposed to cigarette smoke, which contains nicotine and other hazardous substances. Therefore, community service initiatives, such as Smoke-Free Areas (KTR/KUTARO) education, should be carried out to promote awareness about health and environmental issues. Government support is essential, including the development of policies that facilitate smoking cessation, raise cigarette taxes, mandate ID verification for purchases, and engage dentists in training on motivational strategies and solutions for smokers [5,20].

5. Conclusion

In conclusion, this study showed that dopamine levels in active smokers (70.48 ± 21.89 pg/ml) were higher than in passive smokers (65.98 ± 25.30 pg/ml) because direct inhalation of smoke activates dopamine. Overall smoking behavior could influence dopamine levels in the blood without showing significant differences. This showed the importance of considering individual variability and other factors capable of affecting the blood dopamine levels. The lack of significant difference ($p>0,05$) between the two groups suggested that exposure to cigarette smoke posed similar risks to both active and passive smokers. Therefore, public awareness should be increased regarding the health impacts of smoking and enforcing smoking bans in public places such as KTR to protect others from the dangers of exposure to cigarette smoke.

6. Acknowledgements

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7. Conflict of Interest

The authors declare no conflicts of interest to disclose concerning this study.

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