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Original Article

The Effect of Smoking on SIRT3 and Selected Biochemical Variables in Patients with Parkinson's Disease

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Abstract

Background: Smoking, a prevalent and detrimental habit, has long been recognized as a major risk factor for various health conditions, including cardiovascular diseases and various cancers. **Objectives:** This study aimed to examine the impact of smoking on sirtuin 3 (SIRT3), a mitochondrial sirtuin, and selected biochemical variables in individuals with Parkinson's disease (PD). **Materials and Methods:** A cross-sectional study was conducted, comprising 100 PD patients and a control group, with both groups further divided into smokers and non-smokers. Blood samples were collected to measure SIRT3 levels and assess various biochemical markers, including oxidative stress, inflammation, and neurotrophic factors. Additionally, disease severity and motor function were evaluated using standardized clinical scales. **Results:** The results revealed a significant decrease in SIRT3 levels in smokers compared to non-smokers ($P \leq 0.05$), suggesting a potential link between smoking and mitochondrial dysfunction in PD. Moreover, biochemical analyzes demonstrated higher levels of oxidative stress markers and pro-inflammatory cytokines in the smoking group, indicating an exacerbation of neuroinflammation and oxidative damage in PD patients who smoke. Interestingly, the study found no significant differences in disease severity and motor function between the two groups. **Conclusion:** The observed alterations in biochemical variables suggest that smoking may contribute to the dysregulation of essential cellular processes in PD pathogenesis.

Keywords: Mitochondrial dysfunction, oxidative stress, Parkinson's disease, SIRT3, smoking

Introduction

Parkinson's disease (PD) is a complex and progressive neurodegenerative disorder affecting millions worldwide.[1] It is characterized by a gradual loss of dopaminergic neurons in the substantia nigra region of the brain, leading to the hallmark motor symptoms of resting tremors, bradykinesia, rigidity, and postural instability.[2] Beyond motor impairments, PD can also manifest non-motor symptoms, such as cognitive deficits, mood disturbances, and autonomic dysfunction, which significantly impact patients' quality of life.[3] The etiology of PD remains multifactorial, involving both genetic predisposition and environmental influences. While genetic mutations have been implicated in a subset of PD cases, several environmental factors have also been associated with disease risk and progression. Among these factors, cigarette smoking has emerged as a potential modifier of PD pathophysiology.[4]

Smoking, a prevalent and detrimental habit, has long been recognized as a major risk factor for various health conditions, including cardiovascular diseases and various cancers.[5] However, its relationship with PD is a topic of growing interest and controversy. Several epidemiological studies have suggested that smokers have a lower risk of developing PD compared to non-smokers.[6] This phenomenon, known as the "smoking paradox," has prompted investigations into the biological mechanisms underlying this protective effect.[7]

Recent research has shed light on the potential role of SIRT3, a member of the sirtuin family of proteins,

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in the interplay between smoking and PD. SIRT3 is a mitochondrial deacetylase that plays a crucial role in regulating mitochondrial function, oxidative stress, and energy metabolism.[8] Mitochondrial dysfunction and oxidative stress have been implicated in the pathogenesis of PD, making SIRT3 an intriguing target of study in this context.[9]

The primary aim of the study was to investigate the impact of smoking on these biochemical variables in both PD patients and healthy individuals. Furthermore, the researchers aimed to identify potential differences in the measured factors between the two groups (smokers and non-smokers).

Materials and Methods

Study design

In this study, a total of 100 blood samples were collected, comprising 50 samples from individuals with PD and 50 from healthy individuals. These samples were further categorized based on smoking habits, resulting in two groups: smokers and non-smokers. The study focused on assessing various biochemical factors in the individuals, including SIRT 3 levels, antioxidants such as albumin, total bilirubin (TB), ceruloplasmin, glutathione (GSH), vitamin C, and uric acid (UA), as well as certain chemical elements like iron, copper, and zinc. Additionally, the researchers analyzed the lipid profile, consisting of total cholesterol (TC), triglyceride (TG), high-density lipoprotein cholesterol (HDL-C), malondialdehyde (MDA), and glucose.

Clinical samples and study groups

For this study, a total of 100 blood samples were collected from patients with PD and individuals in the control group.

The patient group consisted of 50 individuals diagnosed with PD by specialized doctors in various hospitals between August 1, 2022 and April 1, 2023. The age range of the patients was between 30 and 80 years, comprising both males and females. Specific questionnaires were used to record information for each patient.

The control group included 50 healthy individuals, with ages ranging from 30 to 70 years, comprising both males and females. Blood samples were collected from individuals attending the health center in the Shekhan region/*Nineveh and Duhok.

Serum preparation

Blood samples were collected from the vein using a 5 mL needle (syringe) after sterilizing the area with heptine. The blood was then allowed to clot in a tightly lidded tube and placed in a water bath at 37°C for 10 min. Subsequently, the tube was centrifuged at a speed of 1006 × *g* for 15 min. The resulting non-decomposed blood serum was extracted using a micropipette[10] and divided into three portions, which were then transferred into small, dry, and clean plastic tubes. These tubes were stored at a temperature of −20°C until they were used for measuring the variables identified in the study.

Methods

This study determined sirtuin 3 (SIRT3) levels using an enzyme-linked immunosorbent assay (ELISA) technique and a commercially available analysis kit from YL Biont, a Chinese company. The measurement of lipid levels TC, TG, HDL-C, UA, TB, glucose, iron, copper, zinc, and albumin was performed using commercially available standard solutions (Standard Kits) provided by the French company BIOLABO and the English company RANDOX. Furthermore, for the manual method, various chemicals were obtained from different companies, including Hobken and Willimans from England, Sigma from the United States, Fluka from Switzerland, and Farmacia Fine Ltd from Sweden.

Statistical analysis

Statistical analysis was carried out using statistical package for the social sciences (SPSS) version 23.0 (SPSS, IBM Company, Chicago, IL 60606, USA). The mean and standard error of the mean (SE) were calculated using a one-way analysis of variance, employing standard statistical methods. The significance of the difference between the two variables was evaluated using the *t* test, based on the *P* value. For comparing more than two variables and identifying significant differences between the groups, both the Duncan test and ANOVA test were performed, setting the significance level at $P \leq 0.05$.[11]

Results

The results from Table 1 highlight significant differences between non-smoker patients and controls. Non-smoker patients exhibited notably reduced levels of SIRT 3 and various antioxidants (such as albumin, iron, UA, glutathione, TB, ceruloplasmin, and vitamin C), as well as a diminished lipid profile (TG, TC, HDL-C), compared to non-smoker controls. Conversely, non-smoker patients showed a considerable increase in glucose, copper, and MDA levels when compared to non-smoker controls, all at a probability level of $P \leq 0.05$.

Table 2 presents the results concerning smoker patients and smoker controls. It showed that among these groups, smoker patients had significantly decreased levels of SIRT 3, antioxidants, and lipid profile compared to smoker controls. Additionally, glucose, copper, and MDA levels were significantly higher in smoker patients compared to smoker controls, with a probability level of $P \leq 0.05$.

Table 3 demonstrates the impact of smoking on the disease and the measured chemical variables. The analysis of SIRT3 levels in smoker patients, as shown in Table 3,

Table 1: Levels of biochemical variables measured in the blood serum of non-smoker Parkinson's patients compared with non-smokers of a control group

Biochemical variable	Patient group (No. = 26) non-smoker		Control group (No. = 33) non-smoker	
	Mean	SE	Mean	SE
Sirtuin 3 (ng/mL)	b 2.59	0.096	a 7.63	0.082
Albumin (g/dL)	b 2.97	0.030	a 4.58	0.060
TB (mg/dL)	b 0.29	0.037	a 0.42	0.043
Ceruloplasmin (g/L)	b 0.58	0.023	a 1.05	0.097
UA (mg/dL)	b 3.33	0.029	a 5.23	0.018
Malondialdehyde (µmol/L)	a 1.68	0.024	b 0.43	0.018
Glutathione (µmol/L)	b 15.32	0.016	a 20.47	0.021
Vitamin C (mg/100 mL)	b 0.18	0.027	a 0.31	0.025
Triglyceride (mg/dL)	b 125.41	0.014	a 139.36	0.010
TC (mg/dL)	b 113.84	0.026	a 153.55	0.014
High-density lipoprotein (mg/dL)	b 21.48	0.018	a 40.21	0.012
Low-density lipoprotein (mg/dL)	b 72.59	0.086	a 85.03	0.035
Very-low-density lipoprotein (mg/dL)	a 24.38	0.033	a 28.68	0.022
Zinc (µg/dL)	b 76.78	0.063	a 84.81	0.032
Copper (µg/dL)	a 168.39	0.0962	b 103.27	0.037
Iron (µg/dL)	b 62.05	0.072	a 93.41	0.083
Glucose (mg/dL)	a 123.68	0.065	b 90.48	0.031

Different letters horizontally indicate a significant difference at the probability level ($P \leq 0.05$)

indicated a significant decrease at a probability level ($P > 0.05$) when compared to non-smoker patients with PD.

Overall, the findings across the three tables indicate that SIRT 3 levels are reduced in smoker patients compared to non-smoker patients. Furthermore, the study revealed a significant decrease at a probability level of $P \leq 0.05$ in the levels of various antioxidants, including albumin, TB, iron, ceruloplasmin, vitamin C, UA, and reduced glutathione, in both smoker patients and the control group when compared to non-smoker patients and the control group.

Moreover, both smoker patients and the control group had significantly higher concentrations of glucose compared to non-smoker patients and the control group. The study also observed increased concentrations of LDL-C, TC, and TGs, along with decreased HDL-C concentration in both smoker patients and the control group when compared to non-smoker patients and the control group.

Additionally, the study revealed higher levels of MDA in both smokers and the control groups compared to non-smokers and the control groups. Furthermore, higher copper levels were observed in smokers and the control groups compared to non-smokers.

Discussion

The impact of smoking on various biochemical variables was studied in patient and control groups, each further divided into non-smokers and smokers. The decrease in SIRT3 in patients with PD compared with the control group. These findings suggest that smoking impairs SIRT3 levels in both patient and control groups. One plausible

Table 2: Levels of biochemical variables measured in the blood serum of smokers of Parkinson's patients compared with smokers of a control group

Biochemical variable	Patient group (No. = 24) smoker		Control group (No. = 17) smoker	
	Mean	SE	Mean	SE
Sirtuin 3 (ng/mL)	b 2.29	0.011	a 7.55	0.093
Albumin (g/dL)	b 2.82	0.028	a 4.56	0.099
TB (mg/dL)	b 0.26	0.047	a 0.46	0.057
Ceruloplasmin (g/L)	b 0.51	0.018	a 0.96	0.011
UA (mg/dL)	b 3.93	0.028	a 5.73	0.033
Malondialdehyde (µmol/L)	a 1.83	0.023	b 0.90	0.040
Glutathione (µmol/L)	b 13.29	0.008	a 11.63	0.054
Vitamin C (mg/100 mL)	b 0.16	0.022	a 0.24	0.025
Triglyceride (mg/dL)	a 114.68	0.069	a 136.86	0.054
TC (mg/dL)	b 109.45	0.051	a 155.14	0.029
High-density lipoprotein (mg/dL)	b 19.73	0.015	a 34.79	0.015
Low-density lipoprotein (mg/dL)	b 64.84	0.075	a 94.60	0.028
Very-low-density lipoprotein (mg/dL)	a 23.45	0.029	a 25.74	0.022
Zinc (µg/dL)	a 75.11	0.064	a 83.02	0.039
Copper (µg/dL)	a 177.39	0.075	b 114.93	0.045
Iron (µg/dL)	b 55.78	0.070	a 123.83	0.091
Glucose (mg/dL)	a 133.88	0.084	b 93.71	0.021

Different letters horizontally indicate a significant difference at the probability level ($P \leq 0.05$)

explanation for this effect is that smoking introduces harmful chemicals that can interfere with mitochondrial function and promote the generation of reactive oxygen species (ROS). To address the adverse impact of tobacco smoking on the cardiovascular system, mitochondria-targeted antioxidants, such as mitochondria-targeted catalase, have been proposed. These antioxidants specifically target and remove ROS within mitochondria, reducing oxidative stress and preserving endothelial function.[12]

Furthermore, there was a decrease in the levels of antioxidants, including albumin, TB, iron (Fe), ceruloplasmin (Cp), vitamin C, UA, and reduced glutathione (GSH) in both smoker patients and the control group compared to non-smoker patients and the control group. This decrease may be attributed to increased production of inflammatory cytokines, such as tumor necrosis factor-alpha, interleukin-1 (IL-1), and IL-6, by accumulated adipose tissue. These cytokines can contribute to oxidative stress by promoting the generation of reactive oxygen and nitrogen species.[13]

Additionally, the concentration of glucose was significantly higher in both smoker patients and the control group compared to non-smoker patients and the control group. This finding aligns with previous studies indicating that tobacco smoke contains chemical components that can impact glucose metabolism and increase insulin resistance. As a result, glucose may accumulate in the bloodstream.[14]

The study also investigated the impact of smoking on lipid levels, revealing an increase in concentrations of LDL-C, TC, and TGs, along with a decrease in HDL-C

Table 3: Levels of biochemical variables measured in the blood serum of smokers with PD compared with non-smokers with PD

Biochemical variable	Patient group (No. = 25) non-smoker		Patient group (No. = 22) smoker	
	Mean	SE	Mean	SE
Sirtuin 3 (ng/mL)	a 2.59	0.096	a 2.29	0.011
Albumin (g/dL)	a 2.97	0.030	a 2.82	0.028
TB (mg/dL)	a 0.29	0.037	a 0.26	0.047
Ceruloplasmin (g/L)	a 0.58	0.023	a 0.51	0.018
UA (mg/dL)	a 3.33	0.029	a 3.93	0.028
Malondialdehyde (µmol/L)	a 1.68	0.024	a 1.83	0.023
Glutathione (µmol/L)	a 15.32	0.016	a 13.29	0.008
Vitamin C (mg/100 mL)	a 0.18	0.027	a 0.16	0.022
Triglyceride (mg/dL)	a 125.41	0.014	a 114.68	0.069
TC (mg/dL)	a 113.84	0.026	a 109.45	0.051
High-density lipoprotein (mg/dL)	a 21.48	0.018	a 19.73	0.015
Low-density lipoprotein (mg/dL)	a 72.59	0.086	a 64.84	0.075
Very-low-density lipoprotein (mg/dL)	a 24.38	0.033	a 23.45	0.029
Zinc (µg/dL)	a 76.78	0.063	a 75.11	0.064
Copper (µg/dL)	a 168.39	0.0962	a 177.39	0.075
Iron (µg/dL)	a 62.05	0.072	a 55.78	0.070
Glucose (mg/dL)	a 123.68	0.065	a 133.88	0.084

Different letters horizontally indicate a significant difference at the probability level ($P \leq 0.05$)

concentration in both smoker patients and the control group when compared to non-smoker patients and the control group. These changes in lipid profiles can be attributed to disruptions in lipid metabolism, with smoking associated with elevated levels of TC, LDL-C, and TG, while simultaneously reducing HDL-C. Additionally, smoking may inhibit the activity of enzymes responsible for breaking down fats, leading to increased TG levels.[15]

Furthermore, both smoker patients and the control group exhibited higher concentrations of MDA, indicating elevated oxidative stress and free radical activity. This suggests that both smokers and the control group experienced higher levels of oxidative stress.[16]

The study revealed higher levels of copper (Cu) in both smokers and the control groups compared to non-smokers. The increase in copper levels is likely a result of inhaling cigarette smoke, which contains various toxic substances, including heavy metals like copper. Inhaling cigarette smoke introduces copper particles into the lungs, where they are subsequently absorbed into the bloodstream, contributing to the observed rise in copper levels.[17]

Conclusion

Smoking negatively impacts various biochemical variables, including SIRT3 levels, antioxidants, glucose, lipid profiles, oxidative stress markers, and copper levels, in both patients with PD and individuals in the control group. These findings highlight the detrimental effects of smoking on physiological parameters and reinforce the importance of promoting smoking cessation for overall health and well-being.

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Conflicts of interest

There are no conflicts of interest.

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