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Effects of Nicotine withdrawal on the Plasma Lipid Profile of Wistar Rats fed with High-fat diet

Onyebuchi Obia[1], Ledu Nda-ue[2] and Frank Nwabueze Nwokocha[2]
[1.]Department of Human Physiology, faculty of Basic Medical Sciences, College of Medical Sciences, Rivers State University, Nkpolu-Oroworukwo, Port Harcourt, Nigeria.
[2.]Department of Human Physiology, faculty of Basic Medical Sciences, College of Health Sciences, University of Port Harcourt, Nigeria.
Corresponding author's e-mail; *onyebuchi.obia@ust.com*
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Abstract

Background to the study*: Nicotine is the main active component of cigarettes. Smoking has been associated with higher prevalence of abnormalities in lipid metabolism. This study investigated the effects of nicotine withdrawal on the plasma lipid profile of wistar rats fed with high-fat diet (HFD).*

Methodology*: The experiment involved 24 male wistar rats separated into 3 groups of 8 rats each. All the animals were placed on high-fat diet in addition to their respective doses of nicotine as follows; Groups 1, 2 and 3 received 200µg/kg, 400µg/kg and 800µg/kg of nicotine oral solution respectively. The experiment was performed in two phases. In the first phase, the animal groups were placed on their respective doses of nicotine solution for 4 weeks. Thereafter, 4 animals in each group were sacrificed and blood samples collected to determine their nicotine exposed plasma lipid profile. In the second phase of the experiment, nicotine was discontinued in all the groups. The remaining 4 animals in each group continued without nicotine for the next four weeks after which they were sacrificed and blood samples collected to determine their nicotine withdrawal plasma lipid profile.*

Results*: The results showed that the levels of total cholesterol (TC), high-density lipoprotein (HDL) and low-density lipoprotein (LDL) increased significantly while there was no significant change in triglycerides (TG) concentration four weeks after withdrawal of 200µg of nicotine compared to the exposed groups. However, following cessation of 400µg and 800µg respectively of nicotine, the plasma levels of TC, TG, HDL and LDL increased significantly compared to their exposed groups suggestive of an initial suppression of the lipid profile parameters with nicotine exposure.*

Conclusion*: Conclusively, higher concentrations of nicotine caused significant suppression of TC, TG, HDL and LDL with significant reversal in the four weeks preceding exposure. Therefore, in quitting smoking, it is important to reduce or stop the consumption of high-fat diet in the immediate periods following cessation of nicotine. The study also recommends that nicotine cessation programs should be accompanied by improved physical activity to prevent possible post-cessation excessive weight gain.*

Key words: *Nicotine, withdrawal, Plasma lipid profile, high-fat diet, wistar rats.*

INTRODUCTION

The growing number of retail food outlets which prepare meals enriched with high levels of fats is a public health concern and may be contributory to the rising prevalence of obesity and dyslipidaemia (Smith et al., 2013; da Costa Peres et al., 2020; Li et al., 2020; de Albuquerque et al., 2022). Smoking and obesity are known risk factors for many cardio-metabolic diseases (Santos et al., 2005; Nwafor et al., 2015; Maddatu et al., 2017; Kondo et al., 2019; Parmar et al., 2023; Hu et al., 2024). Although, the smoke from combustible tobacco products contains several chemicals, nicotine is its main active component (Sansone et al., 2023). It is known to be highly addictive making it almost difficult for cigarette smokers to quit despite having knowledge of its deleterious effects. A higher prevalence of abnormalities in the lipid profile of smokers has been documented in human studies (Hasan et al., 2022; Momayyezi et al., 2024). Nicotine particularly increases the plasma triglyceride concentrations while reducing the high density lipoprotein levels. Previous studies have linked exposure to nicotine with a rise in insulin and reduction in blood glucose (Obia et al., 2024).

Cessation of nicotine is associated with uncomfortable withdrawal symptoms that may compel smokers who wish to quit resuming again. Quitting smoking at an earlier age or after a short period of exposure to cigarette smoke have been associated with lower risk of diseases (Cho et al., 2024). The mortality associated with continued smoking might be reduced by about 90% if cessation of smoking occurred before the age of 40 years (Jha et al., 2024). The aim of the present study was to investigate the effects of nicotine withdrawal on the plasma lipid profile [total cholesterol (TC), triglyceride (TG), high-density lipoprotein (HDL) and low-density lipoprotein (LDL)] of wistar rats fed with high-fat diet.

MATERIALS AND METHODS

This study was carried out in the department of Human Physiology, Faculty of Basic Medical Sciences, College of Health Sciences, University of Port Harcourt with ethical approval number: UPH/CEREMAD/REC/MM68/053. The experiment involved 24 male wistar rats separated into 3 groups of 8 rats each which were acclimatized for a period of two weeks being provided with standard animal chow and water *ad libitum*. After acclimatization, all the animals were placed on high-fat diet in addition to the different doses of nicotine in the experimental groups. Groups 1, 2 and 3 received 200µg/kg, 400µg/kg and 800µg/kg of nicotine oral solution respectively. The experiment was performed in two phases. In the first phase, the experimental groups were placed on their respective doses of nicotine solution for 4 weeks. Thereafter, 4 animals in each group were sacrificed and blood samples collected to determine their nicotine exposed plasma lipid profile. In the second phase of the experiment, nicotine was discontinued in all the groups. The remaining 4 animals in each group continued without nicotine for the next four weeks after which they were sacrificed and blood samples collected to determine their nicotine withdrawal plasma lipid profile. All the parameters were determined using standard methods and values recorded.

Data were analyzed using SPSS vs 23 and presented in Tables. Continuous variables were expressed as mean ± SEM. The differences between each group were analyzed using paired sample t-test and ANOVA. Values of $p< 0.05$ were considered significant with a confidence level of 95%.

RESULTS AND DISCUSSION

Table 1; Plasma lipid profile following nicotine exposure and withdrawal in high-fat diet fed wistar rats (mean values are in mmol/l).

Group	Total Cholesterol		Triglyceride		High-density lipoprotein		Low-density lipoprotein	
	Exposure	Withdrawal	Exposure	Withdrawal	Exposure	Withdrawal	Exposure	Withdrawal
200µg	1.80±0.26	4.30±0.08[c]	0.98±0.23	0.98±0.05	0.68±0.16	1.28±0.19[c]	0.88±0.10	2.68±0.13[c]
400µg	2.03±0.10	5.35±0.19[d]	0.50±0.00	1.10±0.07[d]	0.70±0.23	1.95±0.06[d]	0.98±0.14	2.93±0.22[d]
800µg	1.15±0.19	7.98±0.46[e]	0.63±0.22	2.10±0.08[e]	0.28±0.11	1.65±0.16[e]	0.60±0.06	5.43±0.50[e]

c; Significantly higher than exposure group in the 200µg nicotine group.

d; Significantly higher than exposure group in the 400µg nicotine group.

e; Significantly higher than exposure group in the 800µg nicotine group.

DISCUSSION

In the present study, the levels of total cholesterol (TC), high-density lipoprotein (HDL) and low-density lipoprotein (LDL) increased significantly four weeks after withdrawal of 200µg of nicotine compared to the exposed groups. There was no significant change in the triglycerides (TG) concentration. Following cessation of 400µg and 800µg respectively of nicotine, the plasma levels of TC, TG, HDL and LDL increased significantly compared to their exposed groups. High-fat diet feeding disrupts lipid metabolism increasing the plasma concentrations of TC, TG and LDL and decreased HDL (Binayi et al., 2020). In the first phase of the study, the levels of lipid profile parameters were probably suppressed by nicotine when administered concomitantly with high-fat diet (Wang et al., 2019). In previous studies involving plant extracts, lipid lowering potential is beneficial (Emmanuel et al., 2025; Obia et al., 2025). However, nicotine exposure in animal models have been associated with reduction in body weight, liver weight and blood glucose (Wang et al., 2019; Dangana et al., 2020; Obia et al., 2024). These effects could reverse four weeks after the nicotine exposure (Obia et al., 2024). Amongst other factors, nicotine suppresses body weight via increased fat metabolism (Rupprecht et al., 2018) and increased physical activity in animal models (Liu et al., 2018). Studies suggest a positive relationship between plasma lipids and blood glucose (Wang et al., 2022) such that a reduction in the blood glucose could be linked with reduction in the lipid profile parameters. Other studies suggest that nicotine exposure may influence leptin release and therefore cause reduction in food intake and alteration in energy expenditure amongst smokers (Bellinger et al., 2010; Suhaimi et al., 2016; Callarco & Picciotto, 2020). The results from our study in high-fat diet fed wistar rats did not agree with previous studies on human smokers where nicotine increased the levels of TC, TG and LDL but reduce the concentrations of HDL compared to non-smokers (Nath et al., 2022).

Cessation of nicotine is commonly associated with some unpleasant effects which are more pronounced within the first week post-exposure (Chellian et al., 2021). In our study, using high-fat diet fed wistar rats, the withdrawal of nicotine for a period of 4 weeks after initial 4-week exposure resulted in an increase in the lipid profile parameters (TC, TG, HDL and LDL) compared to the nicotine exposed groups. Cessation of nicotine improves food intake and reduces nicotine-induced increased metabolic rate (Liakoni et al., 2019) leading to weight gain (Gepner et al., 2011; Driva et al., 2022). The beneficial effects of smoking cessation may be obscured by weight gain in the periods following cessation. This underscores the need to add regimens such as improved physical activity and dietary modifications in smoking cessation program (Obia et al., 2015). In our study, the increase in LDL levels 4 weeks after nicotine cessation could suggest that in the preceding initial weeks after quitting smoking, the risk of cholesterol induced morbidity and mortality might still be unaltered. A similar study in human subjects showed that smoking cessation did not affect the concentration of LDL (Grepner et al., 2011). This result differs from our study in which high-fat diet (HFD) was continuously being administered after nicotine cessation. However, the post-nicotine rise in HDL may be part of reduced cardiovascular risk associated with nicotine cessation.

Conclusively, higher concentrations of nicotine caused significant suppression of TC, TG, HDL and LDL with a reversal in the four weeks preceding exposure. Therefore, in quitting smoking, it is important to reduce or stop the consumption of high-fat diet in the immediate periods following cessation of nicotine.

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