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Full Length Article

Niacin improves adiponectin secretion, glucose tolerance and insulin sensitivity in diet-induced obese rats

Ayodele Olufemi Morakinyo [a,*], *Titilola Aderonke Samuel* [b], *Daniel Abiodun Adekunbi* [c], *Olufeyi Adefunke Adegoke* [a]

[a] *Department of Physiology, College of Medicine of the University of Lagos, Idi-Araba 100254, Lagos, Nigeria*
[b] *Department of Biochemistry, College of Medicine of the University of Lagos, Idi-Araba 100254, Lagos, Nigeria*
[c] *Department of Physiology, Benjamin S. Carson (Snr.) School of Medicine, Babcock University, Ilishan-Remo, Nigeria*

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ABSTRACT

The present study examined the effect of dietary niacin supplementation on fat mass, glucose control, insulin sensitivity, lipid profile, and adiponectin level in diet-induced obese rats. Male Sprague-Dawley rats (n = 21) were initially divided into 2 groups of seven and fourteen rats; the group of 14 rats was fed with a high-fat diet (HFD) and the other group of 7 rats consumed the control diet. Eight weeks after the diet regimen started, half of the rats from the HFD group were shifted to the niacin-supplemented diet (HFND; 1 mg niacin/kg diet) while the remaining rats continued on the HFD for another 6 weeks. Results obtained showed that HFD-fed obese rats exhibited significant increase in body weight gain, reduced glucose tolerance, insulin sensitivity and increased adiposity, as well as altered lipid profile after 8 weeks of feeding compared with the controls. However, niacin-supplemented rats showed reduced weight gain and body weight compared with HFD-induced obese rats even in the absence of a significant difference in the food intake among the groups in the experiment. In addition, the rats showed an improved time-course glucose control and insulin sensitivity as demonstrated by a significantly lower area under curve (AUC) values for the glucose curves. The plasma levels of cholesterol, triglycerides and low density lipoprotein (LDL) returned towards control values in rats supplemented with niacin compared with obese rats. The findings suggest that niacin exerts beneficial effect on adiposity, glucose tolerance and insulin sensitivity, and plasma lipids, and that it specifically modulates the level of serum adiponectin under obese condition.

* *Corresponding author.* Tel.: +234 8055947623.
E-mail addresses: morakinyofemi@yahoo.com; aomorakinyo@cmul.edu.ng (A.O. Morakinyo).
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1. Introduction

Obesity is characterized by excessive accumulation or increase in adipose tissue mass [1]. The adipose tissue secretes numerous bioactive substances [2] collectively known as adipocytokines. Adiponectin is the most abundant of these adipocytokines and is known to have anti-inflammatory, antiatherogenic and insulin-sensitizing properties [3,4]. It modulates a number of metabolic processes, including glucose regulation and fatty acid oxidation [5], and plays an important role in the suppression of metabolic derangements that cause insulin resistance and type 2 diabetes mellitus (T2DM) [6].

Interestingly, although adiponectin is secreted by adipose tissue, the plasma level of adiponectin correlates inversely with adiposity and directly with insulin sensitivity [7–10]. It has been found that the plasma level of adiponectin in obese individuals was lower than in non-obese ones [7]; furthermore, low adiponectin concentrations in the plasma correlate with T2DM [11]. However, weight loss and some lipid-modifying drugs, such as omega-3 fatty acids, statins and niacin, are known to increase adiponectin concentration [4,12].

Niacin (also called nicotinic acid) is an old lipid-modifying drug that has favourable effects on all traditionally measured lipid parameters [13,14]. Niacin increases high density lipoprotein (HDL), but reduces low density lipoprotein (LDL), cholesterol (CHOL), and triglycerides (TRIG). Animal studies have shown that niacin stimulates adiponectin secretion in adipocytes [15,16]. A single dose of niacin given orally or through intra-peritoneal injection acutely increases serum adiponectin concentrations in rats and mice within minutes, and this effect is dependent upon activation of the niacin receptor [15]. Others have also demonstrated that niacin treatment results in increased adiponectin mRNA [16,17]. Additionally, niacin enhanced PPARγin rabbit adipocytes [18]; PPAR$\gamma$is a transcription factor that plays a central role in adipocyte biology, and it regulates adiponectin gene expression, processing, and secretion [19].

Given that niacin increases adiponectin level, it is conceivable that niacin could improve insulin sensitivity; however, previous studies reported otherwise [20–23]. For instance, Grundy et al. [20] suggested niacin may cause some negative effects on glucose and insulin metabolism by exacerbating glucose control and insulin sensitivity leading to hyperglycaemia. Other studies have also demonstrated that treatment with niacin produced hyperglycaemia and insulin resistance [24]. Meanwhile, past reports on the adverse effect of niacin on glucose and insulin sensitivity are limited with hyperlipidaemic or non-obese subjects. The present study was therefore carried out to investigate the effect of niacin on adiposity, glucose tolerance, insulin sensitivity and adiponectin level in HFD-induced obese rats.

2. Materials and methods

2.1. Animals, diet and experimental design

The experiment was carried out with male Sprague-Dawley rats (n = 21) obtained from the Animal House of the College of Medicine, University of Lagos, Lagos, Nigeria. They were divided into 2 groups of seven and fourteen rats, housed in transparent plastic cages, in environmentally controlled room under standard temperature (24 ± 2 ^{0}C) and humidity (45–64%), with alternating 12-h light–dark cycles. Generally, the study was conducted in accordance with the internationally accepted guidelines for laboratory animal use and care [19] and approved by the Experimentation Ethics Committee on Animal Use of the College of Medicine of the University of Lagos (2014/08). The group of 14 rats was fed with a high-fat diet (HFD) and the group of 7 rats consumed the control diet. Eight weeks after the diet regimen started, half of the rats from the HFD group were shifted to the niacin-supplemented diet (NSD; 1 mg niacin/kg diet) while the remaining rats continued on the HFD for another 6 weeks. Water and food were available *ad libitum* to the rats throughout the experimental period, and their diet intake and body weights were recorded weekly. The composition of the experimental diets employed in this study is shown in Table 1.

Table 1 – Composition of experimental diets (unit: g/Kg).

Components	Control	HFD	NSD
Corn flour	529.5	330.5	329.5
Casein	200	200	200
Sucrose	100	100	100
Soybean oil	70	40	40
Cellulose	50	50	50
Mineral mix	35	35	35
Vitamin mix	10	10	10
L-cystine	3	3	3
Choline	2.5	2.5	2.5
Butter	0	229	229
Niacin	0	0	1
Total	1000	1000	1000

2.2. Oral glucose tolerance test

Oral glucose tolerance test (OGTT) was performed at the end of the 14-week experimental period. For this purpose, the animals were fasted for about 16 h prior to the time the test commenced. Subsequently, a zero time (baseline) blood sample was drawn and designated 0 min glucose level. Thereafter, each rat was given an oral glucose load of 2g/kg BW [20] of glucose solution (D-Glucose: Sigma Cat. No. G-7528). Blood sample was drawn from tail vein after the glucose load at intervals of 30, 60, 120 and 180 min for measurement of glucose level. The glucose level was measured with a portable Acu-Chek glucose meter (Roche Diagnostics, Germany).

2.3. Insulin tolerance test

Rats that were used for insulin tolerance test (ITT) were fasted for 4 h. Basal blood glucose levels (0 min) were measured followed by injection of insulin (0.5 U/kg BW; Human Insulatard, Novo Nordisk) into the peritoneum, and blood glucose levels were measured at 15, 30, 60, 120 and 180 min by portable glucose meter using tail vein blood. Total area under the curves (AUC) in response to glucose or insulin administration was calculated using GraphPad Prism version 5.00 for Windows, GraphPad Software, San Diego, California USA.