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Reduction in nitric oxide bioavailability shifts serum lipid content towards atherogenic lipoprotein in rats

Esther Oluwasola Aluko[a,*], Temidayo Olutayo Omobowale[b], Ademola Adetokunbo Oyagbemi[c], Olumuyiwa Abiola Adejumobi[b], Temitayo Olabisi Ajibade[c], Adesoji Adedipe Fasanmade[d]

[a] Department of Physiology, Faculty of Basic Medical Sciences, University of Uyo, Uyo, Akwa-Ibom State, Nigeria
[b] Department of Veterinary Medicine, Faculty of Veterinary Medicine, University of Ibadan, Nigeria
[c] Department of Veterinary Physiology, Biochemistry and Pharmacology, Faculty of Veterinary Medicine, University of Ibadan, Nigeria
[d] Department of Physiology, Faculty of Basic Medical Sciences, University of Ibadan, Nigeria

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ABSTRACT

Nitric oxide (NO) is major endothelial relaxing factor and reduction in its bioavailability has been linked to hypertension. Furthermore, high lipid content is a strong risk factor predisposing to cardiovascular diseases. The principal focus of this study was to investigate the effect of blockade of nitric oxide synthase (NOS) on serum lipid content in rats. Male Wistar rats (150–170 g, n = 15) were randomly divided into two groups designated control (n = 5), and L-Name group (n = 10) and were gavage with distilled water and 60 mg/kg of L-NAME respectively daily for three weeks. After 3 weeks, the L-NAME group was sub-divided into two sub-groups (n = 5 each): L-NAME (60 mg/kg of L-NAME), and L-NAME plus ramipril (LR) (60 mg/kg of L-NAME plus 20 mg/kg of ramipril) and were treated daily for another three weeks. The blood pressure (BP) of the conscious rats was measured by tail-cuff method at the onset, at the third and at the sixth weeks of the experiment; while serum lipid contents and NO were measured at the third and sixth weeks. At the end of the experiment blood sample was drawn by ocular puncture for evaluation of lipid profile and NO, and the animals were later euthanized by overdose of anaesthesia. Data were analyzed using ANOVA at $p < 0.05$. There was a significant increase in BP, triglyceride, total cholesterol, low density lipoprotein-cholesterol, and atherogenic indices in L-NAME group compared to the control and LR group ($p < 0.05$); NO and high density lipoprotein-cholesterol was significant lower in the L-NAME group compared to control and LR ($p < 0.05$). In conclusion, reduction in NO bioavailability alters lipid metabolism, which was rectified by ramipril.

1. Introduction

Hypertension and hyperlipidemia are major risk factors for cardiovascular diseases. In addition, the combined occurrence of these two risk factors such as seen in metabolic syndrome augments greatly the risk for cardiovascular complications [1].

Nitric oxide (NO) is a main local mediator released by the endothelium and serves as a key signaling molecule in various physiological processes. It is a major endothelial relaxing factor essential for dilating the blood vessels to facilitate blood flow. Reduction in nitric oxide (NO) bioavailability plays an important role in blood pressure elevation [2] and several diseases associated with vascular dysfunction such as atherosclerosis, diabetes mellitus, hypertension, or preeclampsia are associated with altered NO signaling [3]. Nitric oxide has been documented to be a principal factor involved in the anti-atherosclerotic properties of the endothelium [4] and inhibition of NO synthase causes accelerated atherosclerosis in experimental models [5].

Studies have suggested the role of nitric oxide in the regulation of lipid metabolism and endothelial and inducible nitric oxide synthase (NOS) have been shown to be present in adipose tissue of the rat [6], suggesting that adipose tissue may be a potential source of NO production. NO exerts beneficial effects on lipid metabolism through activation of hepatic sterol regulatory element-binding protein (SREBP)-2 [7].

On the contrary, the renin angiotensin aldosterone system (RAAS) plays major role in blood pressure regulation, and excessive activation of this system, is implicated in the pathogenesis of hypertension and end-organ damage associated with hypertension [8]. Furthermore, angiotensin II has been reported to inhibit the endothelium-dependent relaxation by decreasing nitric oxide bioavailability. Angiotensin converting enzyme has also been shown to inhibit kallikrein–kinin-bradykinin system, which is an important system involved in nitric oxide production [9].

The adipose tissue has been shown to express renin-angiotensin

* Corresponding author at: Physiology Department, Faculty of Basic Medical Sciences, University of Ibadan, Ibadan, Nigeria.
E-mail address: [illegible] (E.O. Aluko).

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