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Adiponectin Levels in Essential Hypertensive patients: a predisposition for development of hypertension

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Abstract

Low plasma levels of adiponectin have been associated with essential hypertension. We carried out a study to ascertain whether adiponectin levels were reduced in essential hypertension. A case-control study was carried out at the University Teaching Hospital in Lusaka, Zambia involving indigenous black participants. Adiponectin was assessed in essential hypertensive and normotensive participants. Our results showed that essential hypertensive participants had higher mean adiponectin levels (11.5 ± 1.9 ng/ml) than normotensive participants (11.0 ± 1.2 ng/ml) p=0.291. The present study showed that the mean levels of adiponectin were higher in the essential hypertensive participants than in normotensive participants. In general, adiponectin was lower in our Zambian black patients than in the white population which might explain why hypertension may be more common in the black population.

Key words: Adiponectin, Essential Hypertension

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Introduction

Adiponectin is the most abundant gene product in adipose tissue and accounts for 0.01% of total plasma protein [1]. This is a 30-kDa molecule that has been identified independently by four groups in 1995 and 1996 with different experimental methods [2]. Adiponectin is produced abundantly by adipose tissue and circulates at relatively high concentrations (micrograms per millilitre) [3]. In contrast to other adipokines (leptin, tumour necrosis factor alpha and interleukin-6), adiponectin is paradoxically lower in obese subjects than in non-obese subjects [3]. In addition to its role in glucose metabolism, adiponectin has anti-atherogenic, anti-inflammatory and angiogenic properties [3]. Since its discovery in the mid-1990, the adipocyte secreted peptide adiponectin has attracted the interest of many researchers as a tool for investigating the function of the adipose tissue and its clinical implications [4]. On the epidemiological point of view, many studies suggest that abdominal adiposity is more closely associated with blood pressure, and, or the presence of hypertension than total adiposity [5]. Hypoadiponectinaemia has been associated with increased plasma free-fatty acids and hepatic fat content and have been linked to the development of insulin resistance, which might, in turn, represent a fertile ground for the development of hypertension [4]. Also association between obesity and hypertension has been recognized for many decades, and an almost linear relation appears between body mass index and systolic and diastolic blood pressure, at least over a body mass index range from 16 to 31 kilograms per meter square [6,7]. Despite Chow *et al*, [8] suggesting for the first time the hypothesis that low adiponectin levels may play an important role in the pathogenesis of human hypertension, the challenge now would be to establish the

pathophysiological mechanisms that demonstrate that the expansion of adipose tissue is associated hypoadiponectinaemia which induces hypertension [4, 8].

Materials and Methods

Selection of Participants and Specimen Collection
Blood was collected with informed consent from essential hypertensive black indigenous individuals reporting to the medical clinic 5 at the University Teaching Hospital, Lusaka, Zambia. Participants (study controls) were recruited from healthy individuals who came for medical checkups at high cost clinic in the University Teaching Hospital during normal clinic hours from 07:00 AM to 12:00 PM, from Monday to Friday. The study controls were required to give informed consent. Blood samples were collected from the research participants via veno-puncture in a 5ml syringe using 21G bore size needles. This study was cleared by University of Zambia Biomedical Research Ethics Committee reference 012-05-14.

Specimen Preparation and Storage- In the laboratory, each specimen serial number was recorded onto a compilation summary sheet. Thereafter the blood specimen was centrifuged at 3000 revolutions per minute (3000 rpm) in order to separate the plasma (supernatant) from the blood cellular components (sediment). Only supernatant (plasma) was then meticulously collected from the lithium heparin vacutainers using pipettes and transferred to 2ml plastic cryovial containers with sealable screw caps which was stored in a freezer at -80℃ until the specimens were analysed in a batch.

Adiponectin Estimation- Plasma adiponectin concentration was determined using the Novus® Human Adiponectin ELISA Kit (manufactured and supplied by biotechne® R&D Systems Europe Ltd, United Kingdom); an enzyme-linked immunosorbent assay for the quantitative detection of human Adiponectin in cell culture supernatant, serum and plasma (citrate, heparin) according to the manufacturer's protocol. This assay employed an antibody specific for human Adiponectin coated on a 96-well plate. ELISA plates were read using the VersaMaxPLUS Rom v1.23 ELISA plate reader.

Results

This study found that hypertensive participants had higher adiponectin concentration (11.5 ± 1.9 ng/mL) than the non-hypertensive participants (11.0 ± 1.2 ng/mL), p=0.291 although this was not statistically significant.

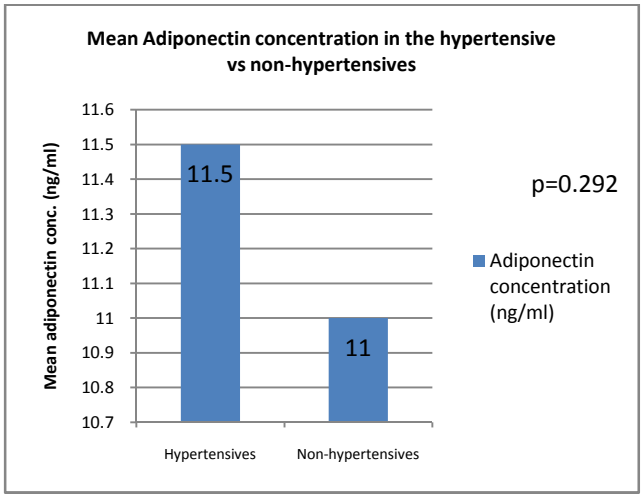

Figure-1: The figure showed that the mean adiponectin concentration in the hypertensive group (11.5 ± 1.9 ng/mL) was higher than in the non-hypertensive group (11.0 ± 1.2 ng/mL).

Discussion

Adiponectin differs from all other adipocytokines except leptin in being secreted exclusively by adipocytes, the details of all the factors regulating its synthesis, secretion and clearance remain incomplete [9]. Adiponectin is a 244 amino acid protein [10]. Adiponectin stimulates nitric oxide production in endothelial cells through Adenosine MonoPhosphate protein kinase (AMPK)-dependent and AMPK-independent phosphorylation of endothelial nitric oxide synthase [11]. Thus, hypoadiponectinaemia can result in decreased levels of endothelial nitric oxide synthase which produces the endothelium-derived vascular relaxing factor nitric oxide. This results in endothelial dysfunction by promoting vasoconstriction and therefore hypertension [4, 12, 13]. Our study found that the mean adiponectin levels were higher in the hypertensive group (11.5 ± 1.9 ng/ml) than the non-hypertensive group (11.0 ± 1.2 ng/ml) which was not statistically significant, p=0.291. However, these results are in contrast to what most studies found. A study by Adamczak *et al.*, [14] reported that essential hypertensive patients had significantly lower concentrations of plasma adiponectin compared with normotensive healthy subjects (9.1 ± 4.5 ug/ml compared with 13.7 ± 5.2 ug/ml; n=33 each; p<0.001) respectively. Yoshio *et al.*, [15] also reported a significantly lower concentrations of plasma adiponectin in patients with essential hypertension compared with normotensive healthy subjects (5.2 ± 0.2 ug/ml compared with 6.1 ± 0.2 ug/ml; p<0.001). A study supporting our findings was done by Jung *et al.*, [16], who reported a non-

significant difference in the adiponectin concentrations between the essential hypertensive group and the normotensive healthy group. The adiponectin concentrations were slightly higher in the essential hypertensive group (5.3 ± 2.8 ug/ml) than the normotensive group (5.1 ± 1.3 ug/ml). A number of reasons might have led to increased levels of adiponectin in the hypertensive group. This study was conducted in essential hypertensive patients on anti-hypertensive treatment. Anti-hypertensive drugs could lead to an increase in adiponectin levels. Thus, anti-hypertensive therapy might have confounded these study findings. A modest but significant increase in plasma adiponectin levels has been observed after treatment with angiotensin converting enzyme (ACE) inhibitors and angiotensin receptor blockers (ARBs) in patients with hypertension [17, 18]. Japanese adults with essential hypertension had significant increases in plasma adiponectin concentrations following three (3) months of losartan treatment [19]. Blocking the renin-angiotensin system (RAS) was associated with an increase in plasma adiponectin levels. Furthermore, angiotensin II (AngII) infusion decreased plasma adiponectin concentrations and adipose tissue adiponectin expression [20]. Olmesartan, an angiotensin II type-1 receptor blocker, reversed obesity-induced hypoadiponectinaemia [21]. There is a wide use of ACE inhibitors and ARBs for treatment of hypertension at the University teaching hospital in Lusaka. However, the precise molecular mechanisms by which renin-angiotensin system inhibition stimulated adiponectin production remained unclear. The other mechanism which could have affected the study findings was renal impairment. Essential hypertension is an important cause of renal dysfunction which impairs renal excretion of adiponectin in essential hypertensive [22]. And since renal disease was only identified by written questionnaires, participants with renal dysfunction which was not medically confirmed might have confounded the study findings. Other life style interventions like exercise, controlled diet including salt intake also affect adiponectin concentration levels. Exercise was another way that elevated adiponectin levels, possibly by improving oxidative capacity. Overweight males exhibited higher level of adiponectin after 10 week aerobic training programme [23]. Some dietary factors, such as soy protein [24], fish oils [25], and linoleic acid [26] also tended to increase adiponectin levels in blood. The mean adiponectin in our Zambian hypertensive patients was 11.5 ± 1.9 ng/ml which was lower than those reported in other places mainly the western countries for example 9.1 ± 4.5 ug/ml [14] and 5.2 ± 0.2 ug/ml [15]. The mean adiponectin in our Zambian normotensive subjects was 11.0 ± 1.2 ng/ml which was lower than the range of adiponectin reported in literature carried out in white subjects 3-30 ug/ml [27]. This difference in mean adiponectin might explain why hypertension was more common in blacks than in whites.

Conclusion

The study showed that essential hypertensive participants had higher mean adiponectin concentration than non-hypertensive participants although this was not statistically significant and therefore cannot be generalized to the whole black population. However, our adiponectin levels were much lower than those reported in the western studies and this might support the assertion that blacks are more prone to hypertension than whites with low adiponectin as a predisposing factor for the development of hypertension in black populations.

Conflict of interest: The authors declare no conflict of interest.

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