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Joseph Eberendu Ahaneku* Olu Emmanuel Agbedana†

Oladunni Grace Taylor‡

*Nnamdi Azikiwe University, Nigeria,

†University of Ibadan, Nigeria,

‡University of Ibadan, Nigeria,

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Joseph Eberendu Ahaneku, Olu Emmanuel Agbedana, and Oladunni Grace Taylor

Abstract

Eighty-one adult Nigerians with essential hypertension were randomly allocated to receive doxazosin, hydrochlorothiazide/amloride, or amlodipine. In each group, the patients were further classified as obese and non-obese, and total cholesterol as well as high density lipoprotein (HDL) cholesterol was determined before and after the 3-month treatment period. The total cholesterol level was significantly reduced in the non-obese patients, but did not show any significant change in the obese patients after doxazosin therapy, indicating the beneficial effects of doxazosin therapy in non-obese patients. The levels of total cholesterol increased and HDL cholesterol decreased in both the obese and the non-obese patients after hydrochlorothiazide/amloride therapy. Amlodipine treatment did not cause any significant change in the total and HDL cholesterol levels in both the obese and non-obese patients. These findings are worthy of consideration by clinicians and researchers when selecting the most appropriate drug for antihypertensive pharmacotherapy.

KEYWORDS: body mass index, cholesterol, hypertension, African patients

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Relationship Between Body Mass Index (BMI) and Changes in Plasma Total and HDL-Cholesterol Levels During Treatment of Hypertension in African Patients

Joseph Eberendu AHANEKU*, Olu Emmanuel AGBEDANA[a] and Oladunni Grace TAYLOR[a]

Department of Chemical Pathology, College of Health Sciences, Nnamdi Azikiwe University Teaching Hospital Nnewi, P. M. B. 5025 Nnewi, Anambra State, Nigeria and [a]Department of Chemical Pathology, College of Medicine, University of Ibadan, Ibadan, Oyo State, Nigeria

Eighty-one adult Nigerians with essential hypertension were randomly allocated to receive doxazosin, hydrochlorothiazide/amloride, or amlodipine. In each group, the patients were further classified as obese and non-obese, and total cholesterol as well as high density lipoprotein (HDL) cholesterol was determined before and after the 3-month treatment period. The total cholesterol level was significantly reduced in the non-obese patients, but did not show any significant change in the obese patients after doxazosin therapy, indicating the beneficial effects of doxazosin therapy in non-obese patients. The levels of total cholesterol increased and HDL cholesterol decreased in both the obese and the non-obese patients after hydrochlorothiazide/amloride therapy. Amlodipine treatment did not cause any significant change in the total and HDL cholesterol levels in both the obese and non-obese patients. These findings are worthy of consideration by clinicians and researchers when selecting the most appropriate drug for antihypertensive pharmacotherapy.

Key words: body mass index, cholesterol, hypertension, African patients

Plasma cholesterol levels during antihypertensive therapy have been studied extensively (1-2). Although favorable changes have been reported during treatment with alpha adrenergic and calcium channel blockers in some of the previous studies (3-5), the results are not always consistent (6). Treatment with thiazide diuretics was found to adversely affect blood levels of lipids and lipoproteins in caucasian patients (7-8), but similar lipid studies with African patients are lacking. Only recently, we were able to present a comprehensive report of lipid and lipoprotein changes in our African patients during amlodipine (9), hydrochlorothiazide/amloride (Moduretic) (10) or doxazosin therapy (11). Meanwhile, the underlying mechanism responsible for the lipid and lipoprotein changes in different racial populations during antihypertensive treatment is not yet understood. However, obesity has been suggested to be a risk factor that may influence the lipid response differently during treatment in different races (1).

In the present work, we allocated our patients to three treatment groups and then classified them as obese or non-obese based on their body mass index (BMI) (12). We present here the results of total and high-density lipoprotein (HDL) cholesterol changes and their relation with BMI during doxazosin, hydrohlorothiazide/amloride or amlodipine treatment. This would elucidate the influence of obesity on lipid and lipoprotein responses during the treatment of hypertension with the above antihypertensive drugs in African patients.

* To whom correspondence should be addressed.
Present address: Department of Biochemisty, Saga Medical School, Nabeshima, Saga 849, Japan.

Subjects and Methods

Patients Selection

A total of 81 Nigerian patients of both sexes, aged 39–65 years with essential hypertension, were studied at the hypertension clinic of the University College Hospital, Ibadan, Nigeria. The protocol for this study was approved by the ethical committee of the University College Hospital/College of Medicine University of Ibadan, and the patients gave oral and written consent prior to their entry into the study. The diagnosis of essential hypertension was confirmed by two separate blood pressure readings taken a minimum of 2 weeks apart and by laboratory examinations such as renal function tests, liver function tests, urine microscopy, plasma proteins and electrolytes. Some of the patients were newly diagnosed while those that were previously on antihypertensive agents had their drugs withdrawn for a washout period of 2 weeks. During the washout period, their blood pressure was carefully monitored.

The patients were arbitrarily allocated into the three treatment groups based on the World Health Organisation (WHO) criteria for mild to moderate hypertension. A diastolic blood pressure in the range of 95–115 mmHg either in the sitting or supine position, and a systolic blood pressure of more than 160 mmHg at the end of the washout period were regarded as the baseline values. After the washout period, 27 patients were started on doxazosin at a daily dose of 2 mg and this dose was adjusted stepwise up to 4 mg, 8 mg or 16 mg daily until the desired average diastolic blood pressure (< 90 mmHg) was achieved in the sitting or supine position. Similarly, 34 patients were placed on hydrochlorothiazide 50 mg and amloride 5 mg once daily. Another 20 patients were placed on 5 or 10 mg amlodipine once daily.

The patients in each treatment group were further subdivided into the obese and non-obese (Table 1), as defined by the body mass index (BMI) values. BMI was determined as weight/height^2 (kg/m^2). Patients with BMI above 25 were regarded as obese, while those with BMI below 25 were regarded as non-obese (Table 1). All participants were seen every 2 weeks at the clinic by the same physician, between the hours of 8:00 and 12:00 on the appointment date, throughout the study. Drugs were dispensed in the clinic by a co-investigator in amounts sufficient to last until the next visit, and pill counts were checked at each visit in order to ensure compliance with the dosage schedule. Uncomplicated essential hypertension was confirmed in all of the patients by thorough clinical and laboratory assessments at each clinic visit. The patients maintained their usual diets which was mainly a high-carbohydrate, low-fat, low-protein and high-vegetable diet. No female patients were pregnant, lactating, or on oral contraceptives. Other risk factors such as smoking and alcohol intake were eliminated through interview assessments before inclusion in the study (Table 1).

Table 1 Demographic profile of the patients

	Patients with doxazosin treatment	Patients with moduretic treatment	Patients with amlodipine treatment
Sex (M/F)	10/17	15/19	10/10
Age (years)	39–65	39–65	39–65
Number of patients			
Obese	7	12	6
Non-obese	20	22	14
Mean BMI (kg/m^2)			
Obese	30 ± 1.1	29 ± 0.58	28 ± 1.02
Non-obese	22 ± 0.62	23 ± 0.62	21 ± 0.79
Mean weight (kg)			
Obese	76.8 ± 1.1	74.2 ± 1.0	72.5 ± 1.2
Non-obese	56.3 ± 0.6	58.9 ± 1.2	54.4 ± 0.8
Mean height (m)			
Obese	1.6 ± 0.01	1.6 ± 0.01	1.61 ± 0.06
Non-obese	1.6 ± 0.02	1.6 ± 0.03	1.61 ± 0.02

M: male; F: Female; BMI: Body mass index. Values are expressed as the mean ± standard error.

Sample Collection and Lipid Determination

At the beginning and after 3 months of doxazosin, hydrochlorothiazide/amloride or amlodipine treatment, 8 ml of venous blood was withdrawn from each patient after an overnight fasting (10–14 h) into a bottle containing dry sodium EDTA (1 mg/dl), mixed gently and placed on ice. Blood was centrifuged at 4 °C within 1 h of collection, and plasma was separated and stored at − 20 °C until analysis. HDL was isolated from the other lipoproteins with heparin-manganese reagent by the method of Burstein and Samaille (13). After HDL isolation, the levels of HDL cholesterol and total cholesterol were determined by the method of Libermann-Burchard reaction as described by Searcy and Berquist (14).

Data Analysis

Analysis of variance was used to assess the variability between and within the obese and non-obese patients in all the treatment groups; and the mean total and HDL cholesterol levels before and after 3 months of treament in the different groups were compared by the paired t-test.

Results

As shown in Fig. 1, the mean value of the total cholesterol in the non-obese patients was significantly reduced ($P < 0.01$) after doxazosin treatment ($P < 0.01$). The reduction in the mean total cholesterol in the obese patients was not significant, while the mean values of HDL cholesterol in the obese and non-obese patients were unchanged after 3 months of doxazosin therapy.

In Fig. 2, the increases in the mean values of total cholesterol in the obese and non-obese patients after hydrochlorothiazide/amloride treatment were significant after 3 months ($P < 0.01$). The reductions in the mean values of HDL cholesterol in the obese and non-obese patients after hydrochlorothiazde/amloride therapy were also significant ($P < 0.01$). In the patients on amlodipine treatment (Fig. 3), whether obese or non-obese, the mean values of the total and HDL cholesterol before and after treatment were not significantly different.

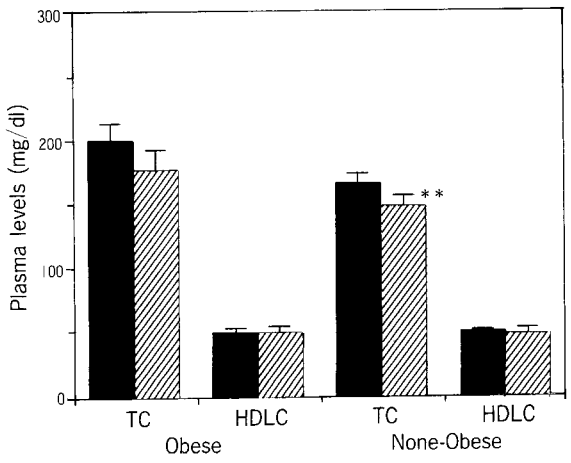

Fig. 1 Total and HDL cholesterol levels in the obese and non-obese patients before and after doxazosin treatment. (■): Before treatment; (▨): After treatment. TC: Total cholesterol; HDLC: High density lipoprotein cholesterol.
** $P < 0.01$ Data are expressed as the mean ± standard error.

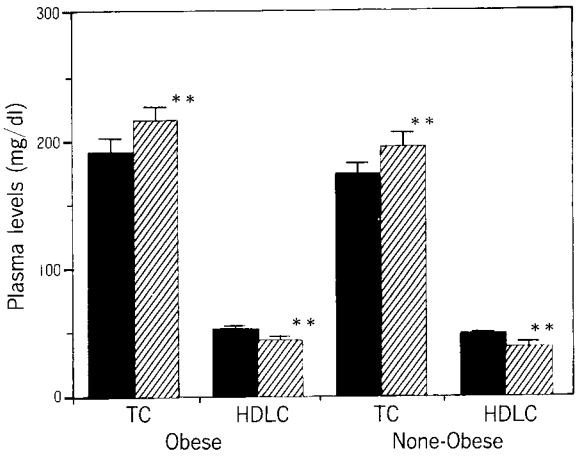

Fig. 2 Total and HDL cholesterol levels in the obese and non-obese patients before and after Moduretic[a] treatment. (■): Before treatment; (▨): After treatment. TC: Total cholesterol; HDLC: High density lipoprotein cholesterol.
[a]Moduretic = Hydrochlorothiazide/amloride. ** $P < 0.01$ Data are expressed as the mean ± standard error.

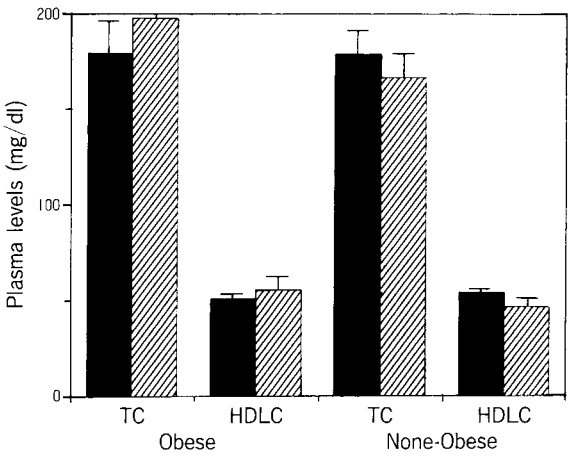

Fig. 3 Total and HDL cholesterol levels in the obese and non-obese patients before and after amlodipine treatment. (■): Before treament; (▨): After treatment. TC: Total cholesterol; HDLC: High density lipoprotein cholesterol. Data are expressed as the mean ± standard error.

Discussion

The decrease in total cholesterol levels observed after

doxazosin treatment is consistent with an earlier report of decreased cholesterol levels after α-adrenergic blocker therapy in caucasian patients (15). In recent study from our laboratory, a similar beneficial effect on lipid and lipoprotein changes was observed during doxazosin treatment (11). Although the total cholesterol (TC) level tended to decrease in both obese and non-obese patients, this study seems to confirm that the beneficial cholesterol-lowering effect of doxazosin therapy is more pronounced in non-obese patients. However, the significance of these results should be interpreted with caution since the number of obese patients receiving doxazosin was small. Meanwhile, the HDL cholesterol level after doxazosin treatment remained unchanged in both obese and non-obese patients. There were significant increases in total cholesterol and decreases in the HDL cholesterol in both the obese and non-obese patients treated with hydrochlorothiazide/amloride. This observation agrees with the previous reports of adverse changes in total and HDL cholesterol during thiazide therapy (7-8).

A recent report from our laboratory also indicated that hydrochlorothiazide/amloride treatment induced short-term adverse lipid and lipoprotein changes (10). The present study has further demonstrated that the short-term adverse effects of hydrochlorothiazide/amloride treatment is independent of the BMI of the patients. The slight increases in total and HDL cholesterol in the obese patients and the decreases in the non-obese patients after amlodipine therapy were not statistically significant. This demonstrates that total and HDL cholesterol were maintained after amlodipine treatment irrespective of the BMI of the patients. A previous report from our laboratory also documented that amlodipine therapy had no remarkable effect on lipid and lipoprotein levels (9).

In conclusion, these studies have confirmed that beneficial effects of doxazosin therapy are more remarkable in non-obese patients, and that amlodipine therapy does not alter cholesterol levels in either obese or non-obese patients. Hydrochlorothiazide/amloride therapy showed adverse cholesterol changes in all the patients. These findings should be considered by clinicians and researchers when selecting the most appropriate agent for the treatment of hypertension in African patients.

References

1. Ames RP: The effects of antihypertensive drugs on serum lipids and lipoproteins: I. Diuretics. Drugs (1986) **32**, 260-278.
2. Schoenfeld MR and Goldberger E: Hypercholesterolemia induced by thiazides: A pilot study. Curr Ther Res (1964) **6**, 180-184.
3. Ohman KP, Heiner L and Karlberg B. E: Antihypertensive and metabolic effects of nifedipine and labetolol alone and in combination in primary hypertension. Eur J Clin Pharmacol (1985) **29**, 149-154.
4. Vessby B, Abelin J, Finnson M and Hellsing K: Effects of nifedipine treatment on carbohydrate and lipoprotein metabolism. Curr Ther Res (1983) **33**, 1075-1081.
5. Pool PE, Seagren SC and Scilel AF: Effects of diltiazem on serum lipids, exercise performance and blood pressure: Randomized double-blind placebo-controlled evaluation for systemic hypertension. Am J Cardiol (1985) **56**, 86H-91H.
6. Nechwatal W, Berger J, Blurnrich W and Bouzo H: A double-blind comparative study of doxazosin and nitrendipine in patients with mild-to-moderate essential hypertension. Am Heart J (1980) **116**, 1806 1813.
7. Gluck Z, Weidmann P, Mordasini R, Bachmann C and Riesen W: Increased serum low density lipoprotein cholesterol in men treated short-term with the diuretic chlorthalidone. Metabolism (1980) **29**, 240-245.
8. Johnson B, Bye C and Larooy J: The relation of antihypertensive treatment to plasma lipids and other vascular risk factors in hypertension. Clin Sci Mol Med (1974) **47**, 9-10.
9. Ahaneku JE, Taylor GO, Agbedana EO, Walker O, Sowunmi A and Salako LA: Effects of amlodipine on plasma lipid and lipoprotein levels in hypertensive patients. J Intern Med (1992) **232**, 489-491.
10. Ahaneku JE, Taylor GO, Agbedana EO, Walker O and Salako LA: Effects of moduretic on plasma lipid and lipoprotein levels in hypertensive African patients. Tokai J Exp Clin Med (1993) **18**, 155-160.
11. Ahaneku JE, Taylor GO, Agbedana EO, Walker O and Salako LA: The Effects of doxazosin on plasma lipids and lipoprotein levels in hypertensive patients. Pharmacol Res (1994) **30**, 263-272.
12. Andres RD, Elahi JD, Tobin DC and Muller LB: Impact of age on weight goals. Ann Intern Med (1985) **103**, 1030-1033.
13. Burstein M and Samaille J: A rapid determination of the cholesterol bound to the serum alpha and beta lipoproteins. Clin Chim Acta (1960) **5**, 609.
14. Searcy RL, and Berquist LM: A new colour reaction for the quantitation of serum cholesterol. Clin Chim Acta (1960) **5**, 192-199.
15. Leren P: Comparison of effects on lipid metabolism of antihypertensive drugs with alpha and beta-adrenergic antagonist properties. Am J Med (1987) **82** (Suppl. 1A), 31-35.

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