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The Effect of Blood Pressure Lowering Treatment on Serum Uric Acid Levels Among Nigerians with Uncomplicated Essential Hypertension

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Abstract

Elevated serum uric acid levels were observed among Nigerian patients with essential hypertension. The levels of serum uric acid may vary according to the type of antihypertensive drugs the individual is placed on. This study evaluates serum uric acid levels in subjects with uncomplicated hypertension on different type of antihypertensive agents. The serum uric acid, glucose, malondialdehyde, triglycerides, total cholesterol and high density lipoprotein cholesterol levels were assayed in 200 known adults with hypertension and 100 normotensive subjects by spectrophotometric method using reagents supplied by Randox Laboratories, UK. The observed mean values were compared between groups using Analysis of Variance (ANOVA). Serum uric acid level was significantly lower ($p < 0.001$) among hypertensive subjects who were on calcium channel blockers than in those on thiazide diuretics, combine therapy and other antihypertensive drugs. The observed serum uric acid levels were highest among those on thiazide diuretics (482±15.0µmol/L), followed β-blockers, angiotensin II receptor inhibitors and angiotensin II converting enzyme inhibitors (465±9.0µmol/L) and those on combine treatment (448±9.2µmol/L). Serum Uric was level was highest in subjects on thiazide diuretics and lowest in those on combine regimen. It is suggested that serum uric levels may be routinely assay in subjects with uncomplicated hypertension.

Keywords

Hypertension, Calcium Channel Blockers, Diuretics, Serum Uric Acid

1. Introduction

Serum uric acid has been reported to be associated with increased risk of cardiovascular morbidity and mortality in subjects with hypertension [1, 2]. Some authors have investigated the role of uric acid in blood pressure control in order to know whether hyperuricaemia is an independent risk factor in the development of cardiovascular events [3]. This was necessary in order to know if uric acid lowering treatments could be used to reduce cardiovascular risk. Others also reported that uric acid lowering drugs may have an antihypertensive effect [4]. However, uric acid has been observed to play a role in the early stages of vascular damage and contributes to the aetiology of hypertension. Elevated serum uric acid levels are commonly observed in adults with hypertension and were previously thought to reflect renal damage accompanying established hypertension [5]. Several studies have determined whether hyperuricaemia is a bystander of hypertension, associated with metabolic cardiovascular risk factors or a predictor and independent risk factor in hypertension. We previously reported elevated serum uric acid levels in subjects with essential hypertension [6]. Elevated serum uric acid level was reported to be a common feature among Nigerian patients with essential hypertension and an association between serum uric acid

level and blood pressure was observed [6].

An average adult male has a total body uric acid concentration of about 1200mg and 60% of the daily turnover is achieved by balanced production and elimination. Even though uric acid can be derived majorly from diet about two-thirds is generated endogenously by the liver [7]. The rate of endogenous generation and or elimination may be modified by hypertension and drugs that are used in the treatment of hypertension. Information on the effects of antihypertensive treatment on the serum uric acid levels have not been sufficiently documented among Nigerians. It is important to know whether hyperuricaemia play any role in blood pressure control and which of the antihypertensive drugs also act as uric acid lowering agent in order to prevent the complications associated with hyperuricaemia in hypertension. It was suggested that some antihypertensive drugs may increase the levels of serum uric acid thereby contributing to the risk of hyperuricaemia [8]. Several authors have reported that diuretic drugs induced hyperuricaemia and gout [9, 10], while β-blockers have been shown to increase serum uric acid levels in short-term trials [10, 11]. Others observed that calcium channel blockers and Losartan could lower serum uric acid levels [8, 12]. This study therefore seeks to evaluate serum uric acid levels in subjects with uncomplicated hypertension who were on different types of antihypertensive agents in Benin City, Nigeria.

2. Materials and Methods

Adult male and female known hypertensive subjects visiting the Outpatient Department of the University of Benin Teaching Hospital, Benin City that gave informed consent were enrolled into the study. This prospective case controlled study of 200 hypertensive subjects made up of 82 males aged 50.3±10.15 years; confidence interval (CI): 27–68 years and 118 females aged 49.7±9.2 years; CI: 28–65 years. The control subjects were 100 normotensive subjects made up of 50 males aged 49.7±2.7 years; CI: 27–64 years and 50 females aged 49.0±1.4 years; CI: 26–65 years. The mean systolic blood pressure (SBP) of the male hypertensive subjects was 158.02±3.20 mmHg; CI: 121–174 mmHg and for female hypertensive subjects was 152.16±2.13 mmHg; CI: 129–170 mmHg. The mean diastolic blood pressure (DBP) for the males was 94.32±1.60 mmHg; CI: 75–115 mmHg and for females was 96.23±1.12 mmHg; CI: 85–108 mmHg.

2.1. Inclusion and Exclusion Criteria

All previously diagnosed hypertensive patients above 18 years of age were included in the study. Those subjects below 18 years and/or diagnosed with hypertension, hypothyroidism, and trauma were excluded from this study. In addition, the subjects who were pregnant or lactating and those who recently donated blood or were vaccinated within the last three months were excluded.

2.2. Sample Collection

Five milliliters of fasting venous blood was aseptically collected from the ante cubital vein. The blood specimens were allowed to clot at room temperature for 30 minutes and sera were obtained after centrifugation at 1000g for 10minutes. The sera were used for the evaluation of uric acid, glucose, malondialdehyde, triglycerides, total cholesterol and HDL cholesterol using reagents supplied by Randox Laboratories, UK. The LDL cholesterol was calculated using Friedewald's formula [13].

2.3. Statistical Analysis

The data was analyzed using SPSS version 20.0. Unpaired Student's t test was used to compare the means of the study group with the control and level of significance set at $p < 0.05$. Serum uric acid levels were compared between the different groups on antihypertensive treatments using two ways Analysis of variance (ANOVA).

3. Results

Table 1 shows the characteristics of the study subjects. Two hundred known hypertensive subjects on different types of antihypertensive treatment were evaluated. They were 82 males and 118 females with mean age 51.6±10.59years. Their mean systolic blood pressure was 155±5.0mmHg while the diastolic blood pressure was 101±5.5mmHg. The control subjects were made up of 50 males and 50 females with a mean age of 50.9±6.2years. Their systolic blood pressure was 120±2.0mmHg and diastolic blood pressure of 80±5.0mmHg. The serum uric acid levels of the subjects who were on calcium channel blockers was significantly lower ($p < 0.001$) than those who were on thiazide diuretics, combine therapy and other antihypertensive drugs. The serum uric acid levels in subjects who were on thiazide diuretics were higher (482±15.0μmol/L), followed by those on other antihypertensive drugs (either β-blockers, angiotensin II receptor inhibitors and angiotensin II converting enzyme inhibitors) (465±9.0μmol/L) and those on combine treatment (448±9.2μmol/L) (table 2). Table 3 shows that the mean serum uric acid was significantly higher ($p < 0.001$) than controls (474±8.0 vs 308±3.9μmol/L).

Table 1. *Characteristics of study participants.*

Variables	Essential Hypertension	Normotensives (controls)
Number of subjects	200	100
Number of males	82	50
Number of females	118	50
Age (years)	51.6±10.5.9	50.9±6.2
Systolic blood pressure (mmHg)	155±5.0	120±2.0
Diastolic blood pressure (mmHg)	101±5.5	80±5.0

Table 2. *Comparison of the measured biochemical parameters in hypertensive subjects on different types of antihypertensive drugs.*

Measured variables	Calcium channels blockers (n = 67)	Thiazide diuretics (n = 51)	Other anti-hypertensive agents (n = 28)	Combine therapy (n = 54)
Serum Uric acid (µmol/L)	418±10.0	482±15.0[a]	465±9.0[a]	448±9.2[b]
Malondialdehyde (nmol/L)	4.02±0.05	4.08±0.06[d]	4.01±0.06[d]	3.91±0.04[c]
Total Cholesterol (mmol/L)	5.45±0.40	6.06±0.14[a]	5.61±0.12[d]	5.80±0.09[d]
Triglycerides (mmol/L)	1.49±0.05	1.52±0.06[d]	1.50±0.05[d]	1.46±0.05[d]
HDL-c (mmol/L)	1.14±0.04	1.16±0.05[d]	1.10±0.02[d]	1.09±0.03[d]
LDL-c (mmol/L)	3.10±0.02	3.24±0.02[d]	3.18±0.01[d]	3.20±0.02[d]

A = $p < 0.001$; b = $p = 0.002$; c = $p = 0.01$; $p > 0.05$; HDL-c = high density lipoprotein cholesterol; LDL-c = low density lipoprotein cholesterol.

Table 3. *Comparison of measured variables between hypertensive and normotensive subjects.*

Measured parameters	Hypertensive subjects	Control subjects	p-values
Serum Uric acid (µmol/L)	474±8.0	308±3.9	0.001
Malondialdehyde (nmol/L)	3.98±0.03	1.45±0.04	0.001
Total Cholesterol (mmol/L)	6.02±0.02	4.59±0.05	0.001
Triglycerides (mmol/L)	1.50±0.02	0.96±0.04	0.001
HDL-c (mmol/L)	1.14±0.02	1.17±0.03	0.41
LDL-c (mmol/L)	3.29±0.02	3.02±0.05	0.001

HDL-c = high density lipoprotein cholesterol; LDL-c = low density lipoprotein cholesterol.

4. Discussion

In this study it was observed that the serum uric acid was lower in subjects on calcium channel blockers antihypertensive agent and the levels were higher in those on thiazide diuretics, β-blockers, angiotensin II converting enzyme inhibitors and angiotensin II receptor blockers. This observation is consistent with previous studies elsewhere [1, 7, 8]. Choi et al [8] reported that the magnitude of relative risk of developing hyperuricaemia was strong with diuretics use and more moderate with the other antihypertensive drugs. It was observed that the associations were independent of the use of other antihypertensive and other risk factors and tend to become strong with a lower duration of use and a higher dose [8]. The data presented in our study do not include duration of use of antihypertensive drugs and the subjects have been using the antihypertensive drugs for over 6months duration. Some authors have suggested that hyperuricaemia in hypertension may be associated with inadequate blood pressure control in subjects treated with antihypertensive drugs [5]. It was difficult to access drug compliance of subjects in this study since the respondents reported to taking their drugs as prescribed.

The relatively lower levels of serum uric acid observed among subjects on calcium channel blockers may be attributed to its action on renal function. Some authors have demonstrated that there is an increased uric acid excretion following the use of calcium channel blockers [14, 15]. It was suggested that calcium channel blockers could increase the glomerular filtration rate and consequently the clearance rates of uric acid and creatinine. Particularly, amlodipine has been reported to increase the output of fluid from the proximal tubules as indicated by the significant decrease in the fractional proximal reabsorption of sodium and a correspondence increase in the reabsorption of sodium in the distal tubule [14]. In the same vein, nifedipine possesses renal vaso-dilatory effects and has been reported to reduce serum uric acid levels in the Coronary Disease Trial investigation Outcome with Nifedipine GITS (ACTION) trial [12].

The probable mechanism by which diuretics increase serum uric acid levels may its ability to increase the net reabsorption of uric acid in the proximal tubule of the nephron, thereby reduce urinary excretion and increase uric acid concentrations in the blood [9, 10]. The increased uric acid levels following diuretics use may be observed within a few days of the start of therapy [16, 17]. Although the β-blockers such as propranolol have hyperuricaemic property as diuretics, they all have been observed to increase uric acid levels [10, 11]. It was reported that the administration of 50-100mg daily of atenolol (β-blocker) for 12weeks increased uric acid levels by 0.5mg/dL but when combined with propranolol, uric acid levels was increased by 0.3mh/dL [18]. The mechanism by which β blockers increase uric acid levels is not clear as authors have suggested that uric acid increasing effects of β-blockers have not indicated increased renal uric acid excretion or changes in renal clearance [18].

A large cohort study of 2191 subjects in the Brisghella Heart Study indicated that elevated serum uric acid levels could be associated with inadequate blood pressure control in patients treated with antihypertensive drugs [19]. The hypertensive subjects with both uncontrolled blood pressure and hyperuricaemia were reported to have increased arterial stiffness. Therefore, arterial stiffness may be a factor inhibiting blood pressure during antihypertensive treatment.

It has been reported that most drugs commonly administered in the treatment of illnesses in clinical practice could either increase or lower serum uric acid levels [7]. Some increase uric acid production or decrease its excretion rates while others increase uric acid excretion or decrease its absorption from the intestine. Interestingly, salicylate which is commonly prescribed as an adjunct to antihypertensive drugs was observed to have a biphasic effects. When administered in low doses, it raises serum uric acid levels but

at higher doses it lowers uric acid levels.

5. Conclusion

This study suggests that serum uric acid level was lower in subjects on calcium channel blockers than other types of antihypertensive drugs and a cautious use of these drugs in the management of hypertension is advocated.

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None.

Conflicts of Interest

None declared.

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References

[1] Jones DP, Richey PA, Alpert BS, Li R. Serum uric acid and ambulatory blood pressure in children with primary hypertension. Pediatr Res 2008; 64: 556-61.

[2] Verdecchia P, Schillaci G, Reboldi GP, Santeusanio F, Porcellati C, Brunetti P. Relation between serum uric acid and risk of cardiovascular disease in essential hypertension. The PIUMA study. Hypertension 2000; 36: 1072-78.

[3] Borghi C, Rosei EA, Bardin T, Dawson J, Dominiczak A, Kielstein JT, Manolis AJ, Perez-Ruiz F, Mancia G. Serum uric acid and the risk of cardiovascular and renal disease. J Hypertens 2015; 33: 1729-41.

[4] Johnson RJ, Kang DH, Feig D, Kivlighn S, Kanellis J, Watanabe S, Tuttle KR, Rodriguez-Iturbe B, Herrera-Acosta J, Mazzali M. Is there a pathogenetic role for uric acid in hypertension and cardiovascular and renal disease? Hypertension 2003; 41: 1183-90.

[5] Grassi G. Effects of serum uric acid on blood pressure lowering treatment. Curr Med Res Opinion 2017; 33 (53): 15-9.

[6] Emokpae MA, Abdu A. Serum Uric levels among Nigerians with essential hypertension. Niger J Physiol Sci 2013 (28): 041 –4.

[7] Moriwaki Y. Effects on uric acid metabolism of the drugs except the antihyperuricemics. J Bioequiv Availab 2014; 6: 1.

[8] Choi HK, Soriano LC, Zhang Y, Rodriguez LAG. Antihypertensive drugs and risk of incident gout among patients with hypertension: Population base case-control study. BMJ 2012; 344: d8190.

[9] Choi HK, Atkinson K, Karlson EW, Curhan G. Obesity, weight change, hypertension, diuretic use, and risk of gout in men: the health professionals follow-up study. Arch Intern Med 2005; 165: 742-8.

[10] Reyes AJ. Cardiovascular drugs and serum uric acid. Cardiovasc Drugs Ther 2003; 17: 397-14.

[11] Adverse reactions to bendrofluazide and propranolol for the treatment of mild hypertension. Report of Medical Research Council Working Party on Mild to Moderate Hypertension. Lancet 1981; 2: 539-43.

[12] Ruilope LM, Kirwan BA, de Brouwer S, Danchin N, Fox KA, Wagener G, et al. Uric acid and other renal function parameters in patients with stable angina pectoris participating in the ACTION trial: impact of nifedipine GITS (gastro-intestinal therapeutic system) and relation to outcome. J Hypertens 2007; 25: 1711-8.

[13] Friedewald WT, Levy RL, Fredrickson DS. Estimation of concentration of low density lipoprotein cholesterol in plasma without use of preparative ultracentrifuge. Clin Chem 1972; 10: 499-502.

[14] Chanard J, Toupance O, Lavaud S, Hurault de Ligny B, Bernaud C, Moulin B. Amlodipine reduces cyclosporin-induced hyperuricaemia in hypertensive renal transplant recipients. Nephrol Dial Transplant 2003; 18: 2147-2153.

[15] Burnier M, Roch-Ramel F, Brunner HR. Renal effects of angiotensin II receptor blockade in normotensive subjects. Kidney Int 1996; 49: 1787-90.

[16] Leary WP, Reyes AJ, Wynne RD, van der Byl K. Renal excretory actions of furosemide, of hydrochlorothiazide and of the vasodilator flosequinan in healthy subjects. J Int Med Res 1990; 18: 120-41.

[17] Hunter DJ, York M, Chaisson CE, Woods R, Niu J, Zhang Y. Recent diuretic use and the risk of recurrent gout attacks: the online case-crossover gout study. J Rheumatol 2006; 33: 1341-5.

[18] Pedersen OL, Jacobsen FK, Stengaard-Pedersen K. Renal uric acid handling is not affected by beta-adrenoceptor blockade in normotensive subjects. Eur J Clin Pharmacol 1985; 28: 223-4.

[19] Cicero AF, Rosticci M, Fogacci F, et al. High serum uric acid is associated to poorly controlled blood pressure and higher arterial stiffness in hypertensive subjects. Eur J Intern Med 2017; 37: 38-42.