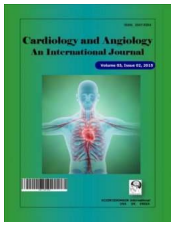

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Therapeutic Approach to Hypertension Using Thiazide Diuretic is Accompanied with Physiological Micro Nutrients and Vitamins Depletion

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Authors' contributions

This work was carried out in collaboration between all authors. Author MA designed the study. Author AO wrote the protocol and final draft of the manuscript, performed laboratory and statistical analysis. While author SA managed the literature searches and wrote the first draft of the manuscript. All authors read and approved the final manuscript.

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ABSTRACT

Aims: This study tends to investigate the effect of thiazide diuretic as an antihypertensive agent on some physiological micro nutrients and vitamins.

Study Design: One factor quasi-experimental design.

Place and Duration of Study: Department of Biochemistry, Ekiti State University, Ado- Ekiti, Ekiti State, Nigeria. December, 2014-November, 2015.

Methodology: Selected micro nutrients such as Cu^{2+} (copper ion), Fe^{2+} (iron ion), Ca^{2+} (Calcium ion), Zn^{2+} (Zinc ion), Co (Cobalt ion), Mn^{2+} (Manganese), Se (Selenium ion), Mg^{+}(Magnesium ion) and vitamins such as Vit C (Vitamin C), Vit E (Vitamin E), Vit A (Vitamin A) were analyzed in blood samples of normotensive, uncontrolled hypertensive subjects and controlled hypertensive subjects under thiazide diuretic administration using standard methods.

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Results: There were significant decreases (p=.0001) in all blood concentration of selected blood micro nutrients of uncontrolled and control hypertensive subjects under thiazide diuretic when compared with normotensive subjects with the exception of Fe^{2+} in both uncontrolled and controlled hypertensive subjects under thiazide diuretic which was found to be significantly increased when compared with normotensive subjects while similar picture was observed for Ca^{2+} but only in controlled hypertensive subjects in both male and female group (P=0.0001). Comparing blood vitamin profile of untreated hypertensive subjects and hypertensive subjects under thiazide diuretic therapy with normotensive showed significant decreases in blood vitamins in both condition irrespective of sex (P=.0001).

Conclusion: The above findings suggest that thiazide diuretic may further deplete the already depleted micronutrients and vitamins in hypertensive subjects. Also, iron and calcium rich diet or supplement may be moderately consumed due to its implication in the pathophysiology of hypertension and should be monitored when administering thiazide diuretic while consumption of micronutrients and vitamins rich diet or supplement may be encourage when administering thiazide diuretic antihypertensive agent to augment for depleted micronutrients and vitamins.

Keywords: Thiazide; vitamins; diuretic; macro nutrients; normotensive; subject.

1. INTRODUCTION

Diuretics have been discovered as one of the age long and most widely prescribed antihypertensive agents for the regulation of blood pressure especially thiazide diuretic [1]. Some of the reasons responsible for wide acceptance and usage of thiazide diuretic antihypertensive agents ranges from low cost and antihypertensive effectiveness apart from the fact that it has been a first line of antihypertensive prescription [2-3]. Antihypertensive mechanism of thiazide diuretic includes a mechanistic reduction in cardiac output via extracellular fluid and plasma volume reduction [4] leading to diminishing sodium reabsorbtion at different points in the nephron causing urinary sodium and water losses and increased urine volume [5-9]. Despite the general acceptability of thiazide diuretic as an hypertensive agent, it is not without metabolic side effect just like other antihypertensive agents that have been implicated in one way or the other [10-13]. This study tends to investigate the effect of thiazide diuretic as an antihypertensive agent on some physiological micro nutrients and vitamins profile considering its route of antihypertensive action on renal system and the physiological roles of vitamins and micro nutrients as cofactor, carrier protein and immunity among others for proper physiological function.

2. MATERIALS AND METHODS

2.1 Subjects

The research subjects were selected from people in Ilesa metropolis of Osun State of Nigeria both male and female with age range of 31-60 years. The research subjects were grouped into three. Group one consist 100 (male=50, female=50) essential hypertensive subjects that have be under a thiazide diuretic antihypertensive agent for more than six months, group two consist of 100 essential hypertensive subjects (male=50, female=50) that are not under any antihypertensive agent while group three consist of 100 subjects (male=50, female=50) that are not hypertensive and not under any anti hypertensive agent. Exclusion criteria include secondary hypertension, pregnancy and any other pathological case.

2.2 Clinical History and Blood Pressure Measurement

Informed consent was obtained from the subjects after the study guidelines had been explained to them before clinical history was obtained using structured questionnaire. Blood pressure was taken from dominant arm after ten minutes of rest using appropriate cut size and mercury sphygmomanometer. Systolic (SP) and diastolic blood (DP) pressures were measured at the first and the fifth keroktoff sound respectively. Three consecutive measurements were made at an interval of five minutes. The mean SP and DP from the 2^{nd} and 3^{rd} measurement were used.

2.3 Collection of Blood Sample

About ten (10) milliliters of venous blood was withdrawn from each subject into a lithium heparin bottle. The blood samples were centrifuged and the plasma separated and stored at -20℃ until analyzed.

2.4 Determination of Vitamin C Concentration

Plasma Vitamin C was determined by using the method of Briggs [14] where ascorbic acid in the plasma is oxidized by Cu (II) to form dehydroascorbic acid, which reacts with acidic 2, 4 – dinitrophenylydrazine to form a reddish – hydrazone, which is measured at 520 nm.

2.5 Determination of Vitamin E

Vitamin E was assayed using the method of Desai [15].

2.6 Determination of Vitamin A

The concentration of plasma vitamin A was determined using high pressure liquid chromatography as described by Bieri et al. [16].

2.7 Determination of Blood Micro Nutrients

Blood elements such as Cu^{2+} = copper ion, Fe^{2+} =Iron ion, Ca^{2+} =Calcium ion, Zn^{2+}= Zinc ion, Co=Cobalt ion, Mn^{2+}=Manganese, Se=Selenium ion, Mg^{+} = Magnesium ion were determined using atomic absorption spectrophotometer (AAS) as described by Kaneko et al. [17].

2.8 Statistical Analysis

Results are presented as mean± SEM. Statistical significance and difference from control and test values evaluated by Student's t-test. Statistical difference at probability of P= .05 were considered to be significant.

3. RESULTS AND DISCUSSION

Physiological micronutrients imbalance have reached an alarming stage with public health consequences contributing to global morbidity and mortality rate which may be as a result of dietary intake and drug interference. In this study, blood micro nutrients and vitamins were determined in uncontrolled hypertensive subjects, controlled hypertensive subjects under thiazide diuretic and compared with the normotensive subjects. There were significant decreases (p=.0001) in all blood concentration of selected blood micro nutrients of uncontrolled and control hypertensive subjects under thiazide diuretic when compared with normotensive subjects with the exception of Fe^{2+} (Tables 1 and 3). Similar picture was observed in both male and female group. Comparing blood vitamin profile of untreated hypertensive subjects and hypertensive subjects under thiazide diuretic therapy with normotensive showed a significant decreases in blood vitamins in both condition irrespective of sex (P=.0001) (Tables 2 and 4).

From the above results, it can be suggested that micronutrients and vitamins depletion with the exception of Fe^{2+} and may be some of the biochemical change implicated in the pathophysiology of hypertension which was in line with other research findings [18]. Non communicable disease such as hypertension has been linked with increase oxidative activity which might be responsible for non enzyme antioxidants (Vitamin C,E A) estimated to be significantly decrease in hypertension subject (P=.0001) when compound with normotensive subject. Similar picture was observed in

Table 1. Blood trace metals profile of untreated essential hypertensive subjects compared with normotensive subjects

Indices	Gender			
	Male		Female	
	Normo. (n=50)	Hyper. (n=50)	Normo. (n=50)	Hyper. (n=50)
Cu^{2+}(µmol/l)	27.56±0.75	19.27±0.73*	27.86±0.73	19.77±0.81*
Fe^{2+}(µmol/l)	19.12±1.27	27.13±2.03*	16.20±1.04	25.20±1.89*
Ca^{2+}(mmol/l)	2.21±0.05	1.39±0.05*	2.17±0.05	1.61±0.06*
Zn^{2+} (µmol/l)	26.80±0.73	15.61±0.69*	24.88±1.06	15.40±0.60*
Mg^{2+}(mmol/l)	1.41±0.02	1.25±0.161*	1.40±0.02	1.25±0.221*
CO (µg/dl)	52.70±0.32	29.93±0.38*	54.48±0.52	36.90±0.35*
Mn^{2+} (µg/dl)	61.56 ±0.73	52.18±0.28*	68.14±0.27	46.45±0.29*
Se (µg/dl)	50.00±0.14	35.65±0.24*	55.00±0.43	29.84±0.09*

Values are mean ± SEM. Significant difference between normotensive and hypertensive group by t-test
**p=.0001. Cu^{2+} = copper ion, Fe^{2+} =Iron ion, Ca^{2+} =Calcium ion, Zn^{2+}= Zinc ion, Co=Cobalt ion, Mn^{2+}=Manganese, Se=Selenium ion, Mg^{+} = Magnesium ion, Normo. = Normotensive, Hyper = Hypertensive, n = sample size*

controlled hypertensive subject under thiazide diuretic but it should be noted that the degree of significant decrease was more. This suggests that administration of thiazide diuretic as a hypertensive agent may further depletes physiological micronutrient and vitamins which may enhance the oxidative activity in hypertension and make the significant blood pressure control unachievable. Unlike other micronutrients, blood Fe^{2+} in both uncontrolled and controlled hypertensive subjects with thiazide diuretic were found to be significantly increased when compared with normotensive subjects while similar picture was observed for Ca^{2+} but only in controlled hypertensive subjects. This suggest an involvement of Fe^{2+} in the development of hypertension while elevated calcium suggests an enhanced calcium reabsorbing and diminished urinary calcium execratory effect of thiazide diuretic on physiological system irrespective of the sex.

Table 2. Blood vitamins profile of untreated essential hypertensive subjects compared with normotensive subjects

Indices	Gender			
	Male		Female	
	Normo. (n=50)	Hyper. (n=50)	Normo. (n=50)	Hyper. (n=50)
Vit. C(mg/dl)	31.29±0.12	11.51±0.26*	34.95±0.07	19.68±0.06*
Vit E (mg/dl)	19.34±0.16	11.29±0.14*	28.79±0.19	11.29±0.14*
Vit A (µg/dl)	56.72±0.34	39.95±0.29*	66.44±0.09	48.55±0.32*

*Values are mean ± SEM. Significant difference between normotensive and hypertensive group by t-test *p=.0001. Vit C=Vitamin C, Vit E=Vitamin E, Vit A= Vitamin A, Normo. = Normotensive, Hyper = Hypertensive, n = sample size*

Table 3. Trace metals profile of essential hypertensive subjects under thiazide diuretic therapy compared with normotensive subjects

Indices	Gender			
	Male		Female	
	Normo.(n=50)	Hyper. (n=50)	Normo.(n=50)	Hyper. (n=50)
Cu^{2+}(µmol/l)	27.56±0.75	18.80±0.75*	27.86±0.73	18.37±0.67*
Fe^{2+}(µmol/l)	19.12±1.27	23.64±1.76*	16.20±1.04	23.37±1.98*
Ca^{2+}(mmol/)	2.21±0.05	3.58±0.14*	2.168±0.05	3.47±0.15*
Zn^{2+}(µmol/l)	26.80±0.73	9.98±0.69*	24.88±1.06	10.76±1.84*
Mg^{2+}(mmol/)	1.41±0.02	1.17±0.028*	1.40±0.02	0.98±0.03*
CO(µg/dl)	52.70±0.32	29.93±0.38*	54.48±0.52	31.98±0.50*
Mn^{2+} (µg/dl)	61.56 ±0.73	42.18±0.28*	68.14±0.27	37.57±1.22*
Se (µg/dl)	50.00±0.14	28.04±0.68*	55.00±0.43	22.95±0.68*

*Values are mean±SEM. Significant difference between normotensive and hypertensive group by t-test *p=.0001. Cu^{2+} = copper ion, Fe^{2+} =Iron ion, Ca^{2+} =Calcium ion, Zn^{2+}= Zinc ion, Co=Cobalt ion, Mn^{2+}=Manganese, Se=Selenium ion, Mg^{+} = Magnesium ion, Normo. = Normotensive, Hyper = Hypertensive, n = sample size*

Table 4. Blood vitamins profile of essential hypertensive subjects under thiazide diuretic therapy compared with normotensive subjects

Indices	Gender			
	Male		Female	
	Normo.(n=50)	Hyper. (n=50)	Normo. (n=50)	Hyper. (n=50)
Vit C(mg/dl)	31.29±0.12	10.19±0.68*	34.95±0.07	14.96±0.61*
Vit E (mg/dl)	19.34±0.16	8.59±0.18*	28.79±0.19	9.22±0.27*
Vit A (µg/dl)	56.72±0.34	32.34±0.74*	66.44±0.09	37.10±1.18*

*Values are mean±SEM. Significant difference between normotensive and hypertensive group by t-test *p=.0001. Vit C=Vitamin C, Vit E=Vitamin E, Vit A= Vitamin A, Normo. = Normotensive, Hyper = Hypertensive, n = sample size*

4. CONCLUSION

Conclusively, findings from this research suggest that thiazide diuretic may further deplete the already depleted micronutrients and vitamin in hypertensive subjects. Also, iron and calcium rich diet and supplement may be moderately consumed due to its implication in the pathophysiology of hypertension and should be monitored while consumption of micronutrients and vitamin rich diet or supplement may be encourage when administering thiazide diuretic antihypertensive agent to augment for depleted micronutrients and vitamins.

ETHICAL APPROVAL

All authors hereby declare that all experiments have been examined and approved by the appropriate ethics committee and have therefore been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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