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EFFECT OF ANTIOXIDANT VITAMINS AND MINERALS SUPPLEMENTATION ON THE RENAL FUNCTIONS AND HAEMATOLOGICAL INDICES OF ACUTE ISCHAEMIC STROKE SUBJECTS IN SOKOTO, NIGERIA

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ABSTRACT

Acute ischaemic stroke (AIS) is characterized by renal and haematological indices impairements, which might have conspired to the development of the disease and its attendant complications. The current work studied the effect of antioxidant vitamins and minerals supplementation on serum renal functions and haematological indices in AIS subjects. A total of fourty two ischaemic stroke subjects presented within 72 hour of symptom onset were treated with conventional drug and supplemented with daily oral dose of 10 mg vitamin E, 60 mg of vitamin C, 700 IU of vitamin A, 3 mg of copper, 15 mg of zinc, 5 mg of manganese, 200 µg of chromium and 200 µg of selenium for 2 weeks. The results suggested that supplementation significantly ($P<0.05$) reduced serum urea, creatinine, potassium, white blood cell count and platelet count. Supplementation also significantly ($P<0.05$) increased serum sodium, chloride, red blood cell count and haemoglobin. The beneficial effect is more pronounced in a group supplemented with RDA X 1.5 of the antioxidant vitamins and minerals. It is concluded that supplementation with RDA/RDA X 1.5 of antioxidant vitamins and minerals may reduce the risk of renal and haematological impairements associated with acute ischaemic stroke.

KEYWORDS: Antioxidant vitamins and minerals, acute ischaemic stroke.

INTRODUCTION

Stroke is a syndrome caused by disruption of the blood flow to part of the brain due to either occlusion of a blood vessel (ischaemic stroke, seen in approximately 87% of cases); or rupture of a blood vessel, resulting in injury to cells and causing sudden loss of focal brain functions.[1] Most people survive stroke but about half are disable, placing enormous burden on the survivors, their families and the community.[2] The prevalence of stroke varies greatly between communities. It accounted for over 56,000 deaths in England and Wales in 1999, which represent 11% of all deaths.[3] In United State of America (USA) and England approximately 795,000 and 900,000 respectively.[4] In Africa is about 19% with Ibadan, Nigeria having 17%.[5]

Acute ischaemic stroke (AIS) is the most common type of stroke.[4] AIS, intracerebral haemorrhage (ICH) and subarachnoid haemorrhage (SAH) accounts for 87%, 10% and 3% of cases respectively.[4] Stroke is the third common cause of death worldwide and over two-thirds of those deaths occur in developing regions of the world including sub-saharan Africa.[5]

The brain undergoes neurodegeneration when excess free radicals overwhelm the antioxidative defence system during senescence, head injury and neurotoxic conditions.[6,7] There are reports of rapid increase in oxidative stress-related markers immediately after ischaemic stroke which rapidly overwhelmed antioxidant defences, thus allowing further tissue damage.[8] At high concentrations, these free radicals react and damage the cellular macromolecules leading to cell injury and necrosis.[8]

Epidemiological evidence suggests that antioxidant vitamins such as vitamins A, C, and E, as well as antioxidant minerals copper, zinc, chromium, selenium and manganese play protective roles in the development of AIS and its attendant complications.[6,9] Antioxidants act by scavenging biological reactive oxygen species, preventing their formation or repairing the damage they induced.[10]

In this current study, serum urea, creatinine, sodium, potassium, bicarbonate, chloride, red blood cell count, haemoglobin, white blood cell count and platelets counts were determined in acute ischaemic stroke subjects

supplemented with antioxidant vitamins and minerals at RDA/RDA X 1.5 for 2 weeks. It is expected that this study will stimulate interests, discussion and further studies on the role of antioxidant vitamins and minerals supplementation on renal and haematological indices vis-à-vis complications of acute ischaemic stroke.

MATERIALS AND METHODS

Participants: A total of fourty two (42) acute ischaemic stroke subjects presented within 72 hour of symptoms onset of both sexes admitted at Neuro Medical Ward of Usmanu Danfodiyo University Teaching Hospital (UDUTH), Sokoto and 20 non-acute ischaemic stroke (NAIS) subjects of comparable socio-economic status. The consents of all the participants were sought for and obtained. Ethical committee approval was also obtained from UDUTH, Sokoto, Nigeria.

Sample collection: Blood samples were collected by venipuncture and delivered into clean dry tubes and allowed to clot at room temperature. The samples were centrifuged at 3000 rpm for 5 minutes using bench top centrifuge and the serum separated and kept in labeled sample bottles at (-20^{0}C) until required.

Chemical and reagents: All chemicals and reagents were of analytical grade. Vitamin A was obtained from Softgel healthcare private Ltd., Tanminadu, India. Vitamin C was obtained from Greenlife pharmaceuticals Ltd., Lagos, Nigeria, while vitamin E was obtained from Pharco pharmaceuticals Bolkely Alexandria, Egypt. Copper, zinc, chromium, manganese and selenium were obtained from Pharmedic in compliance with GMP-WHO norms Ho Chi Minh city, Vietnam. Chemicals for vitamins, trace elements, renal profile and haematological indices were obtained from Randox Laboratory Limited, Switzerland.

Experimental design: The AIS subjects presented within 72 hour of symtoms onset of both sexes were divided into groups as follows:

Group 1: Conventional treatment of AIS subjects only (n=14).
Group 2: Conventional treatment of AIS + Supplementation with RDA of antioxidant vitamins and minerals (n=14).
Group 3: Conventional treatment of AIS + Supplementation with RDA X 1.5 of antioxidant vitamins and minerals (n=14).
Group 4: Non acute ischaemic stroke (NAIS) subjects (n=20).

Daily oral dose of 10 mg of α-tocopherol (vit.E), 60 mg of vitamin C, and 700 IU of vitamin A, 3 mg of copper, 15 mg of zinc, 5 mg of manganese, 200 µg of chromium and 200 µg of selenium[11] were administered for 14 days. Blood samples were obtained for biochemical analyses before commencement of supplementation and after 7 and 14 days intervals.

Biochemical analysis: Urea was determined by method of[12], creatinine was determined by method of[13], sodium and potassium were determined by method of[14], bicarbonate was determined by method of[15a], chloride was determined by method of[15b] and full blood count was determined by method of.[16]

Statistical analysis: All data were presented as mean±SD. Data was analysed using analysis of variance (ANOVA) by Instat 3 Software. Significant difference was considered at 5% ($P<0.05$).

RESULTS

The result of the serum levels of urea, creatinine, sodium, potassium and biocarbonate of AIS subjects supplemented with antioxidant vitamins and minerals at RDA/RDA X 1.5 were presented in Table 1. The result shows a significantly ($P<0.05$) decreased levels of urea, creatinine and potassium and increased levels of sodium, chloride and bicarbonate when compared to AIS subjects neither treated non-supplemented.

Table 1: Serum renal functions of AIS subjects supplemented with antioxidant vitamins and minerals.

Parameter	AIS subjects non-supplemented (n=14)	AIS subjects supplemented with RDA of antioxidant vitamins and minerals (n=14)	AIS subjects supplemented with RDA X 1.5 of antioxidant vitamins and minerals (n=14)	Non-acute ischaemic stroke subjects (n=20)
Urea (mmol/l)	6.75±0.65^a	4.27±0.13^b	4.25±0.42^b	4.62±0.69^b
Creatinine (mg/dl)	1.24±0.45^a	1.00±0.16^a	0.88±0.26^b	0.85±0.18^b
Sodium (mmol/l)	134.75±8.11^a	141.27±4.76^b	143.77±2.55^b	142.55±4.05^b
Potassium (mmol/l)	4.92±0.94^a	3.92±0.58^b	3.88±0.15^b	3.88±0.34^b
Bicarbonate (mmol/l)	22.86±4.01^a	30.45±1.25^b	28.62±1.50^b	27.79±2.06^b
Chloride (mmol/l)	97.42±3.33^a	104.09±1.51^b	104.23±0.44^b	102.85±3.56^b

Values are mean±SD. Values bearing different superscripts on the same row differ significantly ($P<0.05$). n: number of participants.

Table 2 shows serum haematological indices levels in AIS subjects supplemented with antioxidant vitamins and minerals at RDA/RDA X 1.5. The results indicate significant (*P<0.05*) increase in red blood cell counts and haemoglobin and decrease white blood cell count and platelet counts when compared to AIS subjects neither treated non-supplemented.

Table 2: Effect of antioxidant vitamins and minerals supplementation on haematological indices of AIS subjects.

Parameter	AIS subjects non-supplemented (n=14)	AIS subjects supplemented with RDA of antioxidant vitamins and minerals (n=14)	AIS subjects supplemented with RDA X 1.5 of antioxidant vitamins and minerals (n=14)	Non-acute ischaemic stroke subjects (n=20)
RBC Count X 10^6/µl	3.06±1.13[a]	3.42±0.44[b]	3.05±0.32[b]	3.25±0.22[b]
Hb (g/dl)	11.69±2.33[a]	13.33±1.84[b]	15.01±1.29[c]	14.74±0.89[c]
WBC Count X 10^6/µl	10.27±2.10[a]	8.65±0.68[a]	5.95±1.21[b]	6.56±1.84[b]
Platelets Count X 10^6/µl	259.37±88.30[a]	246.73±15.41[b]	230.15±16.80[b]	224.02±48.02[b]

Values are mean±SD. Values bearing different superscripts on the same row differ significantly (*P<0.05*).RBC count: red blood cell count; Hb: haemoglobin; WBC count: white blood cell count; n: number of participants.

DISCUSSION

Acute ischaemic stroke (AIS) exacts a heavy toll in death and disability worldwide and results from the abrupt interruption of focal cerebral blood flow.[17,18] It is characterized by elevated level of oxidative stresss indices, renal and haematological impairements.[10] Thus, supplementation with antioxidant vitamins and minerals may delay or prevent AIS and its attendant complications. Supplementation with antioxidant vitamins and minerals are thought to be effective in increasing the activities of antioxidant defence enzymes, scavenging free radicals, preventing oxidative damage and thereby sparing renal and haematological indices against peroxidation.[19]

The current result indicated significant high levels in urea, creatinine and potassium and lowered sodium, chloride and bicarbonate at baseline AIS (AIS non-supplemented) compared to control (NAIS) subjects is consistent with previous studies of[20,21] who reported similar findings. Supplementation with antioxidant vitamins and minerals at RDA/RDA X 1.5 significantly decreased levels of urea, creatinine and potassium and increased sodium, chloride and bicarbonate compared to baseline AIS (AIS non-supplemented). The beneficial effect is more pronounced in group supplemented with antioxidant vitamins and minerals at RDA X 1.5. The improved renal functions profile by ameliorating the derangement in renal functions associated with AIS patients could probably through up-regulation of nuclear factor kappa B and activator protein-1 genes that boosted the activities of antioxidant enzymes which led to prevention and delay of AIS and its attendant complications including renal impairement.

It has been documented that elevated white blood cell count and platelet count have been associated with cerebrovascular disease in several epidemiological studies.[20,22] The values at baseline AIS subjects are in line with these report. The higher level could probably be adaptive response to oxidative stress in AIS subjects.[20] Supplementation with antioxidant vitamins and minerals at RDA/RDA X 1.5 significantly (*P<0.05*) increased red blood cell count and haemoglobin and decreased white blood cell count and platelets count compared to AIS non-supplemented. The beneficial effect is more pronounced in group supplemented at RDA X 1.5. The improvement could be due to antioxidant properties of micronutrients which are known to stimulate the up-regulation of nuclear factor kappa B (NKκB) and activator protein-1(AP-1) genes and consequently reflect the altered redox balance of affected fluids, tissues or organs in AIS subjects. Vitamin E is required for normal function of immune system and control of aggregation of platelets via activation of NFκB.[23] Vitamin C has been shown to be capable of decreasing haemolysis under *in vitro* conditions, apparently by strengthening the physical integrity of the erythrocytes.[24,25]

CONCLUSSION

Based on the current results it can be concluded that supplementation with antioxidant vitamins and minerals at RDA/RDA X 1.5 for 2 weeks may delay or prevent the onset of AIS complications including renal and haematological impairements.

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