PJN
ISSN 1680-5194

PAKISTAN JOURNAL OF NUTRITION

ANSInet
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Pakistan Journal of Nutrition 7 (6): 763-765, 2008
ISSN 1680-5194

Essential Trace Elements and Metal Binding Proteins in Nigerian Consumers of Alcoholic Beverages

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Abstract: Throughout the world 7% of individuals above 18 years of age are habitual consumers of alcoholic beverages, despite the fatal consequences of alcohol consumption on immune system and other organs. This study is designed to provide biochemical basis for the fatal consequences of alcohol consumption. The levels of metal binding proteins (transferrin, caeruloplasmin and alpha 2-macroglobulin) and essential trace elements (Zn, Cu, Mn, Fe and Se) were determined in male Nigerians that consume alcohol beverages compared with controls using immuno diffusion method and atomic absorption spectrophotometric method respectively. Transferrin and Zn were significantly reduced while Cu and Mn were significantly raised in alcohol consumers compared with the controls. No correlation was found between the levels of metal binding proteins and essential trace elements. Reduction of transferrin and Zn might explain susceptibility of alcohol consumers to infections and that Zn supplementation is recommended for alcohol consumers to boost their immunity.

Key words: Alcohol, immunity, Nigeria and micronutrients

Introduction

Alcohol is a very common chemical in today's society and has for a long time formed an intricate part of African social life (NIAAA, 2000). A moderate dose of alcohol beneficially increase plasma HLD, reduces blood pressure, reduces blood clotting and level of thromboxane A2 which decreases blood vessel constriction and platelet aggregation (Klatsky, 1999). Acute alcohol consumption reduces the pathogen-induced production of inflammatory cytokines such as TNF-alpha, IL-1 and IL-6 (Lippi *et al*., 1992). Acute alcohol exposure also increases the production of IL-10 and TGF-beta, which promotes humoral immunity (Lippi *et al*., 1992).

In heavy drinkers, alcohol has been associated with necrotic nerve degeneration, brain atropy, impaired cognitive and neurological impairment (NIAAA, 2000). Chronic alcohol consumption increases the expression of CD8 molecules on the surface of neutrophils, increases the infiltration/accumulation of neutrophils and macrophages to liver, thus leading to liver injury (Do-Carmo and Das, 1988). Chronic alcohol consumption causes significant serum increases of mucoprotein, alpha-1-acid glycoprotein, haptoglobin and fibrinogen (Limuro *et al.,* 2000). This previous study did not evaluate the levels of caeruloplasmin or transferrin in these alcoholic subjects. Nevertheless, numerous investigation have found that administering antioxidant, agents that reduces the levels of free Fe, or agents that replenish GSH levels can prevent or ameliorate the toxic actions of alcohol (Galan *et al*., 2005). It is therefore hypothesized that supplementation of diets consumed by alcoholics with essential trace elements may improve their immune functions.

The interrelation of micronutrients and immune functions in alcohol consumers has received little attention and such study was not carried out in Nigerian consumers of alcohol beverages. Based on the fact that alcohol consumption is known to reduce nutrient absorption and appetite (Galan *et al*., 2005), therefore alcohol consumption might be considered as a state, which depletes minerals and micronutrients. The present study determines the titers of metal binding proteins (transferrin, caeruloplasmin, alpha 2 - macroglobulin) and essential micronutrients (Se, Mn, Zn, Fe and Cu) in Nigerian alcohol users compared with non- alcohol users. Knowledge gained may help reduce morbidity and mortality associated with alcohol consumption.

Materials and Methods

Participants: The test subjects were male participants (26-48 yrs of age), that consume alcoholic beverages while the controls were male participants not consuming alcohol (26-48 yrs of age). The test subjects selected are daily consumers of alcohol beverages for at least 10 years (15.8 ± 11.8 yrs drinking history). The test subjects were recruited from customers of a hotel in Apata, Ibadan, Oyo state, Nigeria. The control subjects were recruited from staff of University College Hospital, Ibadan, Oyo State, Nigeria. The controls were selected based on their responses to questionnaire that they never drank any of the alcoholic beverages and gamma glutamyl transferase (GGT) values above 30 U/L. The

brand of beer commonly consumed are Star, Guilder, 33 export, Guinness stout and Heinekens. Cigarette smokers or those on locally brewed drinks were excluded. Others excluded were those with high parasite densities, abnormal liver functions, pathogenic infections (including HIV and pulmonary tuberculosis), and abnormal renal functions as presented by blood, urine, sputum and stool tests described in a standard text (Cheesbrough, 1991). They had no recent injuries or history of recent immunization or on any form of compulsory medication/special diet (nutrient supplement). Those that declined their consents were also excluded. These strict exclusion criteria lead to the low numbers of alcohol consumers (n = 15) and controls (n = 14). The serum titer of acute phase proteins were determined using immuno-diffusion method as previously described (Arinola *et al.,* 2006). The level of trace elements were determined using atomic absorption spectrophotometer (Arinola *et al.,* 2005).

Statistical analysis: The result was presented as mean and standard deviation. The significance of the differences between values were determined using Students (t) test. Pearson's correlation was used to correlate metal binding proteins trace elements.

Results

Table 1 shows that the level of transferrin was significantly reduced while the level of alpha 2-macroglobulin and caeruloplasmin were not significantly reduced in Nigerians that consume alcohol beverages compared with the controls. In Table 2, Zn was significantly reduced while Cu and Mn were significantly raised in the tests compared with control. There was no correlation between acute phase protein with trace elements (Table 3).

Table 1: Mean titer of metal binding proteins in Nigerians that consume alcohol beverages compared with the control

Test (n =15)	Control	(n = 14)	t	p
A2MG (g/L)	1.50±0.40	2.0±1.2	1.79	>0.500
CLP (g/L)	0.83±0.51	0.9±0.7	0.43	>0.200
TRF (g/L)	2.14±0.50	2.8±1.0	2.01	<0.50

A2MG = Alpha 2-macroglobulin. CLP = Caeruloplasmin.
TRF = Transferrin.

Table 2: Mean titer of Zn, Fe, Cu, Mg, Mn and Se in Nigerians that consume alcohol beverages compared with the controls

Tests (n = 15)	Controls	(n = 14)	t	p
Zn (Mmol/dl)	78.3±20	99.1±11.8	3.47	<0.01
Fe (mg/dL)	77.3±4.9	80.3±8.7	1.15	>0.50
Cu (ug/dL)	70.3±17.1	56.2±7.1	2.94	<0.01
Mn (mg/dL)	60.9±6.9	55.5±5.5	2.35	<0.01
Se (ug/dL)	75.5±5.4	79.3±7.1	0.75	>0.50

Discussion

The present study provides explanation for defective immunity in alcoholics by determining the levels of metal binding proteins and essential trace elements. This study shows that the level of Zn was significantly reduced in alcoholics compared with controls. Significantly reduced Zn level in consumers of alcohol may be due to increased demand since Zn dependent enzymes are involved macronutrient metabolism and cell replication. These two processes had been found to be on the increase in alcohol consumers (Szabo *et al.,* 1999). Moderate alcohol consumption leads to production of TGF-beta that promotes collagen formation (Szabo *et al.,* 1999). Excess collagen may be deposited in the liver leading to liver diseases. The implication of liver damage includes reduced synthesis of acute phase proteins and certain cytokines. Reduction in Zn level in alcoholics is of considerable concern because of the significant role it plays in the metabolism of other micronutrients, which are important to healthy living. Vitamins A and E metabolism and bioavailability are dependent on Zn status (Szabo *et al.,* 1999). The deficiency of these vitamins as a result of Zn deficiency in alcohol consumers may increase their risks of infections.

Cu is a component of SOD and it is transported by caeruloplasmin. Thus, both Cu and caeruloplasmin are parts of endogenous antioxidants that ameliorate alcohol induced oxidative stress. Cu was found to be significantly raised in consumers of alcoholic beverages. Significantly raised level of Cu may be one of the mechanisms to compensate for significantly reduced Zn, since both Cu and Zn are among the micronutrients needed for effective immune responses. This study observed that caeruloplasmin (CLP) is reduced (non-significantly) in the test subjects. CLP releases Fe from cells prior to uptake by transferrin (Limuro *et al.,* 2000). Therefore, reduced CLP in consumers of alcoholic beverages may be responsible for observed reduction (non-significantly) of Fe in the alcohol consumers. Purified CLP has been shown to remove reactive oxygen intermediates causing altered intracellular redox state of vascular cells (Limuro *et al.,* 2000). Thus reduced CLP in consumers of alcoholic beverages could be its removal by reactive oxygen species generated by alcohol.

The level of transferrin was found to be low in the alcoholics compared with the controls.

Significantly low level of transferrin in alcoholic subjects considered for this study might have been caused by reduced production by the liver because of gradual alcohol-induced liver damaged or loss through the kidney into the urine. The implication of low transferrin in the consumers of alcoholic beverages is impaired haemoglobin production since Fe is required for making haemoglobin. (Galan *et al.,* 2005).

Table 3: Correlation of trace elements with metal binding proteins in Nigerians that consume alcohol beverages

	Zn		Fe		Mn		Cu		Se	
	r	p	r	p	r	p	r	p	r	p
A2MG	-0.02	0.95	0.39	0.16	-0.21	0.45	0.05	0.86	0.42	0.14
CLP	- 0.19	0.51	0.19	0.51	-0.13	0.65	0.09	0.76	0.21	0.46
TRF	-0.14	0.63	-0.21	0.46	-0.03	0.91	0.21	0.47	-0.18	0.52

Alpha 2-macroglobulin is a proteinase inhibitor and also transport of Zn (Arinola *et al.,* 2006), thus its reduction may explain low level of Zn in alcohol consumers. Fe was reduced in alcoholic beverage consumers. Fe is a pro-oxidants which also needed by micro-organisms for proliferation (Galan *et al.,* 2005). Non-significant reduction of Fe in Nigerian alcohol consumers may be of benefit by reducing Fe induced pro-oxidant effect and non-availability of Fe for bacteria proliferation. Se deficiency was found to result in lower glutathione peroxidase activity of phagocytic cells, reduced microbicidal activity of NKC and T-cell mediated cytoxicity (Galan *et al.,* 2005). This study observed low level (non-significant) of Se in alcohol consumers, thus the likely basis of reduced immunity in chronic alcoholics.

In conclusion, reduction of transferrin and Zn might explain susceptibility of alcohol consumers to infections and that Zn supplementation is recommended for alcohol consumers to boost their immunity.

Acknowledgement

This study was supported by Senate Research Grant, University of Ibadan, Nigeria (SRG/COM/2006/38A).

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