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 atrophy, 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 titer 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 the 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 Heineken. 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).

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
doensases are involved macronutrient metabolism and
cell replication. These two processes had been found to
be on the increase in alcohol consumers (Szaobo et al.,
1999). Moderate alcohol consumption leads to
production of TGF-beta that promotes collagen formation
(Szaobo 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

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

<table>
<thead>
<tr>
<th>Test</th>
<th>(n = 15)</th>
<th>(n = 14)</th>
<th>t</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>A2MG (g/L)</td>
<td>1.50±0.40</td>
<td>2.0±1.2</td>
<td>1.79</td>
<td>&gt;0.50</td>
</tr>
<tr>
<td>CLP (g/L)</td>
<td>0.83±0.51</td>
<td>0.9±0.7</td>
<td>0.43</td>
<td>&gt;0.20</td>
</tr>
<tr>
<td>TRF (g/L)</td>
<td>2.14±0.50</td>
<td>2.8±1.0</td>
<td>2.01</td>
<td>&lt;0.50</td>
</tr>
</tbody>
</table>

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

<table>
<thead>
<tr>
<th>Tests (n = 15)</th>
<th>(n = 14)</th>
<th>t</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Zn (Mmol/dl)</td>
<td>78.3±20</td>
<td>99.1±11.8</td>
<td>3.47</td>
</tr>
<tr>
<td>Fe (mg/dl)</td>
<td>77.3±4.9</td>
<td>80.3±8.7</td>
<td>1.15</td>
</tr>
<tr>
<td>Cu (ug/dl)</td>
<td>70.3±17.1</td>
<td>58.2±7.1</td>
<td>2.94</td>
</tr>
<tr>
<td>Mn (mg/dl)</td>
<td>60.9±6.8</td>
<td>55.5±5.5</td>
<td>2.35</td>
</tr>
<tr>
<td>Se (ug/dl)</td>
<td>75.5±5.4</td>
<td>79.3±7.1</td>
<td>0.75</td>
</tr>
</tbody>
</table>

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 (Szaobo 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
carreluplasmin. Thus, both Cu and carreluplasmin 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 carreluplasmin (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

<table>
<thead>
<tr>
<th></th>
<th>Zn</th>
<th>Fe</th>
<th>Mn</th>
<th>Cu</th>
<th>Se</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>r</td>
<td>p</td>
<td>r</td>
<td>p</td>
<td>r</td>
</tr>
<tr>
<td>A2MG</td>
<td>-0.02</td>
<td>0.65</td>
<td>0.39</td>
<td>0.16</td>
<td>0.21</td>
</tr>
<tr>
<td>CLP</td>
<td>-0.19</td>
<td>0.51</td>
<td>0.19</td>
<td>0.51</td>
<td>-0.13</td>
</tr>
<tr>
<td>TRF</td>
<td>-0.14</td>
<td>0.63</td>
<td>-0.21</td>
<td>0.46</td>
<td>-0.03</td>
</tr>
</tbody>
</table>

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 cytotoxicity (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
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