Serum Zinc Deficiency Increases Susceptibility to Infection in Older Patients Who Have Long-term Hospitalizations

Toshiyuki Ukita\(^1\), Batgerel Oidov\(^1\), Etsuo Kawada\(^{1,2}\), Yoshio Ohyama\(^1\), Toyohoh Morita\(^2\) and Jun‘ichi Tamura\(^{1,2}\)

\(^{1}\) Department of General Medicine, Graduate School of Medicine, Gunma University, Gunma 371-8511, Japan
\(^{2}\) Department of Medicine, Ninosawa Hospital, Gunma 370-3531, Japan.

Abstract

A relation between serum zinc level and susceptibility to infection in older inpatients has not been studied well. A relation between serum zinc level and susceptibility to infection in older adults with long-term hospitalizations was studied. Forty-four (13 men, 31 women) hospitalized patients aged 45 years and older (mean, 81.4 years; range, 45-98 years with 38 patients (86%) aged 65 years and older) were divided into two groups. Retrospectively, 22 were assigned to the “no-infection group,” with 22 assigned to the “infection group.” Patients in the “no-infection group” did not receive any intravenous antibiotic treatment for bacterial infection for six months, whereas the others received at least one such treatment in the past six months. Serum concentrations of zinc, copper, albumin, total cholesterol, glucose, hemoglobin, and c-reactive protein were measured by general methods after six months observation. Mean serum Zn level was 56.9 µg/dL (SD, 14.4) in the “no-infection group” and 47.7 µg/dl (SD,14.9) in the “infection group.” Difference in levels was significant (\(P = .043\)). Serum levels of albumin, total cholesterol, and hemoglobin in the “no-infection group” were also significantly higher than those in the “infection group.” Deficiency in serum zinc appears to be associated with susceptibility to infection among older patients with long-term hospitalizations.

Keywords: Zinc, geriatrics, nosocomial infection, deficiency

INTRODUCTION

Knowledge of the functions of zinc in humans has accumulated for the past fifty years, revealing that zinc is an essential and multipurpose trace element\(^1\). Zinc is a component of various enzymes such as RNA polymerase, alcohol dehydrogenase, alkaline phosphatase, aminopeptidase, aldolase, and superoxide dismutase. Zinc plays an important role in and is necessary for cell proliferation, differentiation, maturation, function, and apoptosis\(^{1-3}\).

Zinc also affects immune function through its roles in T-cell division, differentiation and proliferation\(^{4-8}\). Relations between zinc concentration in either serum or plasma and immune function have been reported, and zinc supplementation decreases the incidence of infection\(^{9-12}\).

In the field of pediatrics, zinc depletion due to malnutrition is an important problem\(^{11,13}\). Moreover, zinc deficiency caused by aging leads to altered immune function. Many studies indicate that zinc supplementation can improve mortality and susceptibility to infection\(^{9-12}\). However, as far as we know, there are few reports on any relation between zinc status and susceptibility to infection in patients who have long-term hospitalizations.

We noticed that patients with long-term hospitalizations can be divided into two groups. One group of pa-
patients appears to be susceptible to infection, whereas pa-
tients in the other group seldom contract nosocomial in-
fec tion. We hypothesized that this difference in suscepti-
bility to infection may relate to zinc status; we have al-
ready confirmed this tendency with preliminary data[14].
Here we present new data and its analyses on this prob-
lem.

METHODS
Patients who had hospitalizations at least six months in
Ninosawa Hospital in Takasaki, Japan, were retrospec-
tively divided into two groups in the following manner:
The “infection group” consisted of patients who needed
intravenous administration of antibiotics to treat bacterial
infection at least one time in the past six months. Patients
who did not need intravenous antibiotics for the same
length of time were assigned to the “no-infection group.”
All patients were fed standard nourishment following na-
tional Japanese nutritional guidelines. Complete blood
cell counts and blood chemistry studies including zinc
and copper were obtained after six-month observation.
To avoid an effect on serum zinc level due to circadian
rhythm, all sampling was performed around 11 a.m.
Body temperature was taken around 12 a.m. on the same
day of blood collection. All statistical analyses were car-
rried out with use of R software (version 2.3.1 or later, R
Development Core Team, 2006. R : A language and en-
vironment for statistical computing, R Foundation for
Statistical Computing, Vienna, Austria. ISBN 3-900051-
07-0, URL http://www.R-project.org). The male-to-
female ratio and the proportion of patients who had oral
intake of nutrition in both groups were analyzed by
Fisher’s exact test; differences were not significant.
Mean age of patients in the “infection group” was 83.9±
13.0 years (range, 54-97 years) and 78.9±12.6 years
(range 45-98 years) in the “no-infection group.” The male-to-female ratio and the pro-
portion of patients with oral intake were analyzed by
Fisher’s exact test; differences were not significant.

RESULTS
The total number of subjects was 44, with each group
containing 22 patients. Characteristics of the two groups
are summarized in Table 1. There were six men in the
“infection group,” whereas there were seven in the “no-
infection group.” Four patients took nourishment orally
in the “infection group” compared with seven in the “no-
infection group.” The male-to-female ratio and the pro-
portion of patients with oral intake were analyzed by
Fisher’s exact test; differences were not significant.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Infection group</th>
<th>No-infection group</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of subjects</td>
<td>22</td>
<td>22</td>
<td></td>
</tr>
<tr>
<td>Number of men</td>
<td>6</td>
<td>7</td>
<td>1</td>
</tr>
<tr>
<td>Age (years)</td>
<td>83.9±13.0*1</td>
<td>78.9±12.6</td>
<td>.202</td>
</tr>
<tr>
<td>Number with oral intake</td>
<td>4</td>
<td>7</td>
<td>.488</td>
</tr>
</tbody>
</table>

*1mean ± SD (all such values)
of nutritional indicators such as hemoglobin, albumin and total cholesterol in the “no-infection group” compared with the “infection group” : $P$-values were 0.029, <0.001, and 0.028, respectively, showing significance for albumin and total cholesterol. Contrary to these results, serum glucose levels of the “infection group” and “no-infection group” were almost identical (154±41.7 mg/dL versus 155±50.9, $P=.959$). Serum c-reactive protein (CRP) levels of the “no-infection group” and “infection group” were also statistically equal (1.43±3.13 mg/dL versus 2.12±2.56, $P=.427$). White blood cell count of the “infection group” was significantly higher (9.08±4.26 x 10^9/L) than that of the “no-infection group” (6.59±2.54 x 10^9/L ; $P=.024$).

We further analyzed the relation between nutrient state and zinc concentration. As shown in Table 3, zinc concentration strongly correlated with nutritional parameters such as hemoglobin, albumin, and total cholesterol: Correlation coefficients were 0.5626, 0.5864 and 0.5675, respectively, with $P$<0.01 for all analyses. On the other hand, copper concentration had no relation to nutritional parameters except for total cholesterol. The correlation coefficient between copper and total cholesterol was 0.3184 ($P=.037$).

**DISCUSSION**

Serum zinc level in the “no-infection group” was significantly higher than in the “infection group.” Competition with copper in the absorption process could be the cause of the difference, but serum copper levels were statistically equal for both groups. Therefore it does not seem that copper significantly interfered with zinc ab-

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**Table 2** Clinical variables for the “no-infection group” and the “infection group.”

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Infection group (n = 22)</th>
<th>No-infection group (n = 22)</th>
<th>$P$ value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Zinc µg/dL</td>
<td>47.7±14.9 ±1</td>
<td>56.9±14.4</td>
<td>.043</td>
</tr>
<tr>
<td>Copper µg/dL</td>
<td>97.1±42.0</td>
<td>105±31.0</td>
<td>.481</td>
</tr>
<tr>
<td>Copper/Zinc</td>
<td>2.22±1.19</td>
<td>1.99±0.83</td>
<td>.457</td>
</tr>
<tr>
<td>Hemoglobin g/dL</td>
<td>10.8±1.86</td>
<td>12.1±2.15</td>
<td>.029</td>
</tr>
<tr>
<td>White blood cell count  10^9/L</td>
<td>9.08±4.26</td>
<td>6.59±2.54</td>
<td>.024</td>
</tr>
<tr>
<td>Albumin g/dL</td>
<td>2.7±0.5</td>
<td>3.4±0.5</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Total cholesterol mg/dL</td>
<td>132±30.7</td>
<td>153±29.7</td>
<td>.028</td>
</tr>
<tr>
<td>Glucose mg/dL</td>
<td>154±41.7</td>
<td>155±50.9</td>
<td>.959</td>
</tr>
<tr>
<td>C-reactive protein mg/dL</td>
<td>2.12±2.56</td>
<td>1.43±3.13</td>
<td>.427</td>
</tr>
<tr>
<td>Body temperature °C</td>
<td>37.3±0.78</td>
<td>36.5±0.61</td>
<td>&lt;.001</td>
</tr>
</tbody>
</table>

*mean ± SD (all such values)

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**Table 3** Correlation between trace metals and nutritional parameters.

<table>
<thead>
<tr>
<th>Zinc vs.</th>
<th>Hemoglobin</th>
<th>0.5626</th>
<th>&lt;.001</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Albumin</td>
<td>0.5864</td>
<td>&lt;.001</td>
</tr>
<tr>
<td></td>
<td>Total Cholesterol</td>
<td>0.5675</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Copper vs.</td>
<td>Hemoglobin</td>
<td>0.1113</td>
<td>.472</td>
</tr>
<tr>
<td></td>
<td>Albumin</td>
<td>0.2451</td>
<td>.109</td>
</tr>
<tr>
<td></td>
<td>Total Cholesterol</td>
<td>0.3184</td>
<td>.037</td>
</tr>
</tbody>
</table>
sorption. Moreover, copper/zinc ratios and their variances between groups were also statistically equal, another indication that the balance between serum copper and zinc affected the difference in zinc status between groups. Concentrations of nutritional parameters such as hemoglobin, albumin and total cholesterol were higher for the “no-infection group” than the “infection group.” This result raises the question of an absolute lack of nourishment intake in the “infection group.” This possibility can be excluded because all patients in the hospital were served standard nourishment. This is supported partially by the finding that serum glucose levels were not different. As shown in Table 1, body temperature of the “infection group” was higher than that of the “no-infection group,” a difference that may affect zinc status. If the object whose serum CRP level is less than 0.5mg/dL is selected from both groups, body temperature of the “infection group” would still be higher than that of the “no-infection group,” even though serum zinc levels were equal (data not shown). These results suggest that there is no relationship between body temperature and serum zinc level.

Zinc may be considered a candidate nutritional parameter based on our results. As shown in Table 3, serum zinc concentration correlated with other nutritional markers such as hemoglobin, albumin, and total cholesterol. Serum zinc level correlated inversely with age; the same tendency was also seen for hemoglobin, albumin, and total cholesterol (data not shown). This correlation between serum zinc and age matches results of studies on healthy subjects, with the exception that Abiaka et al. found no correlation between parameters in healthy older subjects[15]. The discordance may be due to differences in subjects: Our subjects all had long-term hospitalizations, whereas the subjects in Abiaka’s study were healthy.

Serum copper levels, as well as serum zinc levels, were obtained from the patients in this study. Our data show no correlation with age, although many studies have shown that serum copper level has a positive correlation with age[15-18]. Conflicting results have been published on correlations between serum concentrations of copper and lipids [15,19-20]. We found no correlation between serum copper and total cholesterol levels.

Due to limitations in study design, we cannot clarify whether infection lowers serum zinc level or low serum zinc level makes a patient susceptible to infection. To clarify this argument the subjects in this study have been followed after hospital discharge. The results will be reported in the near future.

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REFERENCES


