Micronutrients in Critically Ill Surgical Patients

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ABSTRACT
Vitamins and trace elements are known as micronutrients. Vitamins are organic substances not synthesized by the body, and some are cofactors for various enzymes; therefore, they are required for normal metabolism. Trace elements are metals present in very small quantities in the body. Micronutrient deficiencies are often present in critically ill surgical patients and may occur as a result of the underlying disease, inadequate or inappropriate administration during therapy, or increased losses or increased requirements due to severe illness. This short review aimed to evaluate the requirements of micronutrients in critically ill surgical patients.

Key words: Micronutrients, Vitamins, Trace elements, Nutrition, Surgery

ÖZET
Kritik Cerrahi Hastada Mikrobesin Ögeleri

Anahtar kelimeler: Mikrobesinler, Vitaminler, Eser elementler, Beslenme, Cerrahi
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thesized by the body, and some are cofactors for vari-
ous enzymes; therefore, they are required for normal 
metabolism. Trace elements are metals present in 
very small quantities in the body. They are either 
cofactors of enzymes or form an integral part of the 
specific enzymes; therefore, they are also essential for 
normal functions\cite{1,2}. Trace elements including sele-
nium (Se), zinc (Zn), iron (Fe), manganese (Mn), cop-
per (Cu), and chromium (Cr) and vitamins including 
four fat-soluble (A, D, E, K) and nine water-soluble 
vitamins (ascorbic acid, folate, niacin, riboflavin, thia-
mine, pyridoxine, cobalamin, pantothenic acid, bio-
tin) are essential for homeostasis in the body\cite{1-3}.

Micronutrient deficiencies are often present in 
critically ill surgical patients and may occur as a result 
of the underlying disease, inadequate or inappropriate 
administration during therapy, or increased losses or 
increased requirements due to the severe illness. 
Whatever the reason, when the deficiencies occur, 
they affect various biochemical processes and enzy-
matic functions, resulting in organ dysfunction, mus-
cle weakness, poor wound healing, and altered 
immune functions, all of which carry deleterious 
patient outcomes\cite{4,5}.

Micronutrient requirements in critically ill patients 
are unknown. Decreased serum levels may not indi-
cate actual deficiencies but rather just their redistri-
bution\cite{4}. The decrease in serum levels may actually 
be an adaptive, beneficial response, as some vitamins 
at high doses act as pro-oxidants\cite{5}. Benefits of sup-
plementation, which may not result in increased 
serum levels, are also unclear. However, a multivita-
min preparation and a multi-trace element admixture 
are added to the parenteral nutrition formulations in 
clinical practice, and most standard enteral nutrition 
formulas also contain the recommended dietary 
allowance (RDA) of vitamins\cite{2,4}.

Most water-soluble vitamins are absorbed from 
the proximal gastrointestinal tract. Fat-soluble vita-
mins are absorbed in the mid- and distal part of the 
ileum as digestion of fat by bile and pancreatic lipase 
is required. Therefore, absorption of fat-soluble vita-
mins is affected by any condition causing fat malab-
sorption such as pancreatic insufficiency, high-output 
 fistulas, excessive diarrhea, and inflammatory bowel 
disease. Interactions between various vitamins are 
very complex. Vitamins C and E are synergistic, vita-
min A function is antagonized by an excess of vitamin 
E, and requirement for niacin is increased in pyridox-
one and riboflavin deficiencies. Thus, single vitamin 
supplementation may counteract the action of other 
vitamins\cite{6-9}.

Absorption of trace elements is difficult to study 
and the information available is limited. Food needs to 
be digested first before trace elements become bioa-
vailable. Zn and Se are absorbed mainly in the duode-
um and jejunum. Fe is absorbed in the duodenum 
and proximal jejunum. Cr and Cu are absorbed in the 
ileum. It is also known that numerous interactions 
exist between the different trace elements affecting 
absorption via the gastrointestinal tract\cite{1,2}.

Although the clinical significance is unclear, serum 
levels of some vitamins (A, C and E) decrease with the 
inflammatory response. On the other hand, B1, B2, 
B12, and folate levels are not affected by inflamma-
tion, and decreased levels may therefore represent a 
true deficiency\cite{10}.

Serum levels of trace elements also decrease in 
critically ill surgical patients. Se, Cu, Fe, and Zn levels 
are decreased due to sequestration, possibly in the 
 liver and reticuloendothelial system, increased uri-
nary or other losses or increased protein catabo-
lism\cite{11-13}.

Critically ill surgical patients are prone to various 
levels of stress. The acute phase of a critical illness is 
typified by a systemic inflammatory response syn-
drome (SIRS), which might be the cause, comorbid 
condition or consequence of critical illness. The 
inflammatory response to critical illness results in 
release of both pro-inflammatory and anti-inflamma-
tory cytokines, which in turn causes the release of 
oxigen free radicals (OFRs) from the inflammatory 
cells including neutrophils and macrophages. OFRs 
interact with cellular molecules and cellular enzyme 
systems, which prolongs the inflammatory response, 
leading to organ dysfunction and failure\cite{1,2,5,10}.

In critical illness, oxidative stress arises when the 
balance between protective antioxidant mechanisms 
and the generation of OFRs is disturbed. This imbal-
ance may be caused by excess generation of OFRs by 
means of ischemia/reperfusion injury, inflammation, 
infection, and toxic agents (chemotherapy or drugs), 
or by low antioxidant capacity (secondary to comor-
bid illnesses, malnutrition, and excessive losses, such 
as in the case of burns)\cite{10,14}.

To protect tissues from OFR-induced injury, the 
body maintains a complex endogenous defense sys-
system that consists of a variety of extra- and intracellular antioxidant defense mechanisms. The first line of intracellular defense is comprised of a group of antioxidant enzymes such as superoxide dismutase, catalase, glutathione peroxidase, and glutathione reductase, including their metal cofactors Se, Cu and Zn\textsuperscript{14}. When these enzymatic antioxidants are overwhelmed, OFRs are free to react with susceptible target molecules within the cell (i.e., unsaturated fatty acids of the cell membrane). Thus, there is a need for a second line of defense, scavenging OFRs by means of nonenzymatic antioxidants that are either water-soluble, such as glutathione and vitamin C, or lipid-soluble, such as vitamin E and beta-carotene. When vitamin E is oxidized, vitamin C and glutathione reduce it back to its active form. The enzymatic system, which is inducible and dependent on minerals such as Se, Cu, Zn and Mn, then acts to detoxify\textsuperscript{9-15}.

Endogenous antioxidant activity is found to be decreased in critically ill patients, and the clinical consequences of these low endogenous stores of antioxidant levels are increased morbidity and mortality. Therefore, it is vital to replenish the endogenous antioxidants at appropriate levels to counteract the toxic effects of OFRs. Though some studies have indicated the beneficial effects of prophylactic supplementation of antioxidant vitamins and some micronutrients (Se, Fe, Zn), the exact timing of micronutrient supplementation in critically ill surgical patients is still not clear \textsuperscript{11,14,16}.

Most of the immune formulas are fortified with vitamins and minerals that have increased antioxidant capabilities. Vitamins A, E and C and the trace mineral Se have antioxidant capabilities and are added in different amounts to the various formulas. The exact doses of these components have not been standardized\textsuperscript{17}.

The question of who needs micronutrient supplementation needs to be answered. Based on the available data, we could say that all critically ill patients need micronutrient supplementation as soon as nutritional support is initiated, either enterally or parenterally. Micronutrients might also be given directly to patients in intravenous (IV) fluids\textsuperscript{17,18}. As the largest increase in OFRs and decrease in serum levels of micronutrients occur early in the course of acute illness, it is logical to say that supplementation should begin early in the course. In clinical practice, antioxidants are given during the first five to seven days, which is followed by routine micronutrient supplementation \textsuperscript{7,19}.

Though the gut is the ideal route of administering vitamins and minerals, as absorption is regulated according to the body’s requirements, the most reliable route of administration is IV in critically ill patients, as the quantity of nutrients absorbed by the gastrointestinal tract is unpredictable due to bowel ischemia, edema or ileus. Serum levels must be monitored only if higher amounts are administered to avoid toxicity, especially in renal and hepatic insufficiencies, burns, gastrointestinal fistulas, and in long-term support\textsuperscript{19}.

Though there are some studies using Se alone or Zn alone in critically ill patients, many randomized controlled trials have chosen to administer a combina-

<table>
<thead>
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<th>Table 1. Micronutrient requirements in critically ill surgical patients</th>
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<td><strong>Micronutrient</strong></td>
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<tr>
<td>Vitamin A</td>
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<td>Vitamin C</td>
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<td>Vitamin E</td>
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<td>(\alpha-tocopherol)</td>
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<td>Zinc</td>
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<td>Iron</td>
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EN: Enteral nutrition, PN: Parenteral nutrition 1 IU of vitamin A = 0.344 µg. Standard PN dose is per day.
tion of antioxidants via various routes of administration, thereby making it impossible to attribute the outcomes to a specific nutrient. When 11 trials of single and combined antioxidants were aggregated, overall, antioxidants were associated with a trend towards a reduction in mortality and no effect on infectious complications[7]. Thus, for critically ill patients, Se supplementation in combination with other antioxidants (vitamin E/alpha tocopherol, vitamin C, N-acetylcysteine, and Zn) may be beneficial, but insufficient data currently exist to support clinical recommendations[16-18].

Daily recommendations of micronutrients in the critically ill are shown in the Table; however, clinicians should always check the package insert for detailed information for the commercially available formulations.

REFERENCES

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