Helicobacter pylori infection and micronutrient deficiencies

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Abstract

It is known that deficiencies of micronutrients due to infections increase morbidity and mortality. This phenomenon depicts itself conspicuously in developing countries. Deficiencies of iron, vitamins A, E, C, B12, etc. are widely prevalent among populations living in the third world countries. Helicobacter pylori (H pylori) infection has a high prevalence throughout the world. Deficiencies of several micronutrients due to H pylori infection may be concomitantly present and vary from subtle sub-clinical states to severe clinical disorders. These essential trace elements/micronutrients are involved in host defense mechanisms, maintaining epithelial cell integrity, glycoprotein synthesis, transport mechanisms, myocardial contractility, brain development, microaerophilic human pathogen which colonizes the gastric mucosa. Infection with Helicobacter pylori (H pylori) infection has a high prevalence throughout the world. Deficiencies of several micronutrients due to H pylori infection may be concomitantly present and vary from subtle sub-clinical states to severe clinical disorders. These essential trace elements/micronutrients are involved in host defense mechanisms, maintaining epithelial cell integrity, glycoprotein synthesis, transport mechanisms, myocardial contractility, brain development, etc.

INTRODUCTION

Helicobacter pylori (H pylori) is a gram negative, microaerophilic human pathogen which colonizes the gastric mucosa. Infection with H pylori leads to gastritis and is associated with the development of peptic ulcer disease, gastric carcinoma and lymphoma[1]. H pylori may be acquired at any age, and the infection persists for years once acquired. The age specific prevalence of H pylori infection is higher in developing countries and particularly in lower socioeconomic group[2]. In developing countries H pylori infection occurs early in life, and hypochlorhydria commonly develops in the malnourished predisposes them to repeated gastrointestinal infection, persistent diarrhea and malnutrition[3]. H pylori infection usually causes both acute and chronic inflammatory cell infiltration, leading to an increase in reactive oxygen species (ROS) which have been shown to accumulate in H pylori gastritis[4]. Excessive production of reactive oxygen metabolites (ROMs) by phagocytic cells is thought to contribute to mucosal lesions produced by H pylori infection. These are highly reactive compounds capable of combining with DNA in a number of potentially genotoxic ways[5]. Reactive oxygen species can react with the lipid-bilayers releasing peroxidation products such as malondialdehyde. These processes could lead to alterations in the structure of DNA facilitating mutations and carcinogenesis.

Nutrition is a critical determinant of the outcome of host microbe interactions through a modulation of the immune response. “Micronutrient” or “trace elements” are generally defined as constituting less than 0.01 % of body mass and are needed in much smaller amounts. Trace minerals and vitamins are essential for life and include iron (Fe), zinc (Zn), copper (Cu), nickel (Ni), etc. They act as essential cofactors of enzymes and as organizers of the molecular structures of the cell, e.g. mitochondria and its membrane. Deficiencies of micronutrients influence immune homeostasis and thus affect infection-related morbidity and mortality. Micronutrients like β carotene, vitamin C, selenium, copper and others are powerful antioxidants and have a significant impact on infection-related morbidity in humans. Subclinical deficiencies are known to impair biological and immune functions in the host. Antioxidants play a part in gastric mucosal defense by protecting against damage caused by excessive oxygen derived free radicals. β-carotene and α-tocopherol are lipophilic and have been shown to suppress the oxidation induced by either lipophilic or hydrophilic radical species[6]. In addition, they could act as anti-carcinogens through their ability to prevent the formation of N-nitrosamines which are important in the development of gastric carcinoma[7]. These vitamins are the major oxidant scavengers in biomembranes in contrast to vitamin C, which is mainly responsible for scavenging free radicals in the aqueous phase. However, compensatory mechanisms may become defective while gastric inflammation develops from normal to chronic gastritis and finally to gastric atrophy/intestinal metaplasia, perhaps due to reduced infiltration of inflammatory cells, loss of gastric gland cells and increased ROM production.

IRON

Iron deficiency anemia affects all groups of the underprivileged population in most developing countries. Iron is an essential growth factor for H pylori, which contains Fe in their outer membrane protein and a system for intracellular storage of iron, consisting of ferritin like molecules pfr and napA[8]. Patients with H pylori associated iron deficiency anemia (IDA) would have involvement of both antral and corporal mucosa when compared with controls (90 % vs 42.7 %; P=0.0001)[9]. Iron deficiency anemia associated with H pylori gastritis is characterized by a concomitant increase in median intragastric pH value >3 and lowering of intragastric concentrations of ascorbic acid. A significant percentage (43 %) of H pylori positive IDA patients presented atrophic changes in the gastric body, and the remaining had a superficial gastritis extended to the fundic mucosa, in contrast with H pylori positive controls[10]. H pylori eradication has also been shown to improve the absorption of other nutrients besides iron, and produce more rapid and complete clinical responses in patients with iron deficiency anemia[11].

COPPER

Copper is involved in the function of several enzymes. It is required for infant growth, host defense mechanisms, bone strength, red and white cell maturation, iron transport, etc. Acquired deficiency is mainly seen in infants. However, it has been diagnosed also in malnourished children and adults[12]. A
VITAMIN B12

The mechanisms of vitamin B12 malabsorption caused by Helicobacter pylori infection are unclear but following are the possibilities:
a) The diminished acid secretion in Helicobacter pylori induced gastritis may lead to a failure of critical splitting of vitamin B12 from food binders and its subsequent transfer to R binder in the stomach.
b) A secretory dysfunction of the intrinsic factor. c) Decreased secretion of ascorbic acid from the gastric mucosa and increased gastric pH[15,16]. Annibale et al. studied the prevalence of Helicobacter pylori infection in pernicious anemia patients and have demonstrated that almost two thirds of pernicious anemia patients had evidence of Helicobacter pylori but only those with an active Helicobacter pylori infection had distinctively functional and histological features[17]. These findings support the hypothesis that Helicobacter pylori infection could play a triggering role in a subgroup of pernicious anemia patients, and suggest the possibility that Helicobacter pylori is involved in the early stages of PA that lead to severe corpus atrophy. The later progress of gastritis seems to be dependent on factors other than Helicobacter pylori, most likely “autoimmune” mechanisms[18]. Helicobacter pylori may also be involved in the pathogenesis of pernicious anemia via antigenic mimicry as antibodies directed against the H+, K+- adenosine-triphosphate adenosine-triphosphatase-derived protein that has been found in high numbers of patients with Helicobacter pylori infection[19]. Food cobalamin malabsorption may occur without gastric atrophy or achlorhydria. Malabsorption can respond to antibiotics, but only in some patients[20].

VITAMIN A

Vitamin A has effects on important determinants of immune function and epithelial cell integrity such as gene expression, cellular proliferation and differentiation and also glycoprotein synthesis. Loss of integrity of the epithelial lining of mucus membranes in a vitamin A deficient state could explain the close association with increased susceptibility to infections particularly of gastrointestinal, respiratory and genitourinary tracts especially in children and pregnant women[21,22]. Even mild or subclinical vitamin A deficiency could induce keratinizing metaplasia of the epithelium and depletes goblet cells from mucosal linings thus causing xerosis of the membrane[23]. The xerotic surfaces form potential sites for increased bacterial adherence thus leading to bacterial colonization. The antimicrobial enzyme lysozyme depends on vitamin A for its synthesis. A decrease in T cell number with no change in proliferative activity has been demonstrated in children suffering from mild xerophthalmia due to vitamin A deficiency. Helicobacter pylori infection and low β-carotene in plasma contribute to the increased risk of gastric atrophy, indicating that Helicobacter pylori infection might be associated with low plasma β-carotene[24].

VITAMIN E

Vitamin E is composed of a group of compounds termed tocopherols and tocotrienols. α-tocopherol is the major active form in the human body, accounting for 95% of vitamin E and is the most effective lipid soluble anti-oxidant in biomembranes. It acts as the major chain breaking antioxidant and is able to interfere with the propagation of lipid peroxidation. It plays an immune modulatory part and is capable of increasing natural killer cell activity. Concentrations of α-tocopherol in Helicobacter pylori negative subjects were higher in the corpus than in the antrum or duodenum[25]. This distribution of α-tocopherol is reversed in the presence of antral Helicobacter pylori infection. These findings may reflect a mobilization of antioxidant defenses to the sites of maximal inflammation in the stomach.

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