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Should Potential Micronutrient Deficiencies be evaluated when designing Weight Loss Interventions for Obese Individuals?

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Abbreviations

BMI: Body Mass Index, NHANES: National Health and Nutrition Examination Survey

Introduction

The rising prevalence of people who are overweight (Body Mass Index or BMI >=25g/m^2) and obese (BMI >=30 kg/m^2) has been described as a global pandemic [1-3]. Concerns about the health risk associated with increased weight have medical ramifications that cross multiple sub-specialties. In 2010, overweight and obesity as health conditions were estimated to have resulted in 3.4 million deaths, 4% of life years lost, and 4% of disability-adjusted life years, internationally [4]. Worldwide, the combined prevalence of overweight and obesity rose by 27.5% for adults and 47.1% for children between 1980 and 2013. The worldwide number of overweight and obese individuals increased from 857 million in 1980, to 2.1 billion in 2013.

Data from studies in the United States have supported the concern that during the past 20 years, there has been a steady increase in the prevalence of obesity, and that the prevalence rates remain high. More than one-third of U.S. adults (34.9%) and approximately 17% (or 12.7 million) of children and adolescents aged 2 to 19 years-old are obese [5,6]. In 1998 the medical costs of obesity in the United States were estimated to be as high as $78.5 billion dollars, and this estimate increased to $147 billion dollars by 2008 [7].

Treatment protocols for obesity cover a broad spectrum and have combined the regulation of social factors, psychological traits and treatments, physical activity, dietary intake and its timing, nutritional supplementation, pharmacological therapies, endoscopic procedures, and surgical procedures. This mixture of treatments has a long history. It has been reported that a physician (Susruta) at the University in Benares, India advised diet and physical exercise for treatment of diabetes and obesity during 600 BCE [8]. Indeed, Susruta believed obesity was the result of overconsumption of food combined with a sleep disorder and sedentary living [8].

It is now well known that when multiple factors are involved in the patho physiology of a systemic disorder, such as obesity, the treatment of the disorder may be limited by difficulty in controlling all of these individual factors. While we have improved on the protocol developed by Susruta, we still must examine individual factors that could limit the results of our intervention for the treatment of obesity. We consider herein the potential for micronutrient deficiencies to lead to sub-clinical manifestations in obese individuals.

Types of and Prevalence of Micronutrient Deficiencies in the Obese

Malnutrition is considered to be a condition that develops when individuals do not receive adequate quantities of energy-providing nutrients, vitamins, minerals, and water. Inadequate intake does not permit the maintenance of physiologically normal tissue and organ function. Dietary intake could be an origin for obesity, as well as an origin for the development of micronutrient deficiencies. The National Research Council has reported that more than 80% of Americans consume a diet that is below the recommended daily allowance for vitamins and minerals. Obese individuals may have intake of calorie-dense foods containing large amounts of carbohydrates and fat, but lacking various micronutrients, a potential origin for deficiencies [9-13]. This dietary intake could be compounded by a substantial proportion of obese individuals exhibiting problematic eating behaviors, including loss of control eating, night eating syndrome, binge eating disorder, and bulimia nervosa [14]. Additionally, "high calorie malnutrition" (a state of excess intake of calories with concurrent nutrient deficiencies resulting in inadequate ability to utilize calories efficiently) in these individuals may alter bioavailability of micronutrients [10].

The international ramifications of the intake of grains are summarized in table 1. While Dr. Christian Eijkman was awarded the Nobel Prize in Physiology or Medicine in 1929 after declaring in 1896 that "white rice is poisonous" (e.g. it lacked the anti-beriberi factor present in the rice skin), one can see upon inspection of table 1 that there are low contents of thiamine, riboflavin, niacin, Vitamin B6, and iron in maize, a low content of riboflavin in white rice, and low contents of pantothenic acid, folic acid, zinc, and copper in sorghum [15-18].

The prevalence of potential micronutrient deficiencies in the obese have been estimated by national survey data as well as by retrospective studies of obese individuals considering bariatric surgery. In the

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Table 1: Nutrient Content of common grains

	Units	Brown rice	White rice	Processed wheat	Wheat germ	Maize	Sorghum	Rye
Thiamine (B1)	mg	0.401	0.576	0.502	1.882	0.155	0.332	0.316
Riboflavin (B2)	mg	0.093	0.049	0.165	0.499	0.055	0.096	0.251
Niacin (B3)	mg	5.091	4.192	4.957	6.813	1.770	3.688	4.270
Pantothenic acid (B5)	mg	0.392	1.01	1.2	2.6	0.717	0	1.456
Vitamin B6	mg	0.509	0.164	0.407	1.300	0.093	0.443	0.294
Folic acid	µg	20	387	44	281	42	20	38
Vitamin B12	µg	0.00	0.00	0.00	0.00	0.00	0.00	0.00
Vitamin D	IU	0	0	0	0	0	0	0
Iron	mg	1.47	4.31	3.60	6.26	0.52	4.4	2.63
Zinc	mg	2.02	1.09	2.60	12.29	0.46	0	2.65
Copper	mg	0.081	0.22	0.5	0.31	0.054	0	0.367

Table 2: Micronutrient deficiencies in the obese

Micronutrient deficiencies in the obese : (Nhanes Iii; N=3831) [15]	Women : Vitamin E , Alpha- & Beta- Carotene, Vitamin D & Folate, Vitamin C & Selenium	
	Men : Alpha- & Beta- Carotene, Vitamin C, Folate &Selenium	
Preoperative Biochemical Micronutrient Deficiencies :	Retrospective Study (N=379): Deficiencies of Thiamine (29%), Iron (44%) &25-Hydroxy Vitamin D (68%) [16]	
	Retrospective Study (N=437) Low Blood Thiamine Levels (15.5%) [17]	
Biochemical Deficiencies in Preoperative Morbidly Obese Women [18]	Biochemical Nutrients	% of Morbidly Obese Women with Deficiency (N =115)
	Ferritin	5 %
	Copper (Cu)	68 %
	Zinc (Zn)	74 %
	Folate	25 %
	Vitamin B 12	10 %
	Vitamin D	95 %

Table 3: Individual micronutrient deficiencies in the obese

Iron	44% [16]
Thiamine	29% [16] &15.5% [17]
Copper	68% [18]
Zinc	74% [18]
Folate	25% [18]
Vitamin D	68% [16] &97% [17]
Vitamin B12	9.5% [18]

Table 4: Potential mechanisms of micronutrient deficiencies in the obese

- Inadequate dietary intake
- Gastric *Helicobacter Pylori*
- Alcohol inhibition of intestinal (Jejunal) Vitamin B1 absorption
- Low circulating & tissue levels of Vitamin B1
- Consumption of micronutrients by small intestinal bacterial overgrowth

National Health and Nutrition Examination Survey (NHANES) III, micronutrient deficiencies were estimated by identification of low blood levels of multiple micronutrients including Vitamin A, folic acid, Vitamin C, Vitamin D, Vitamin E, selenium in women, and Vitamin A, folic acid, Vitamin C, and selenium in men (Table 2).

The results from several studies of obese individuals being seen for bariatric surgery support the presence of multiple micronutrient deficiencies, as defined by low blood levels of the micronutrients (Table 2). The relative prevalence of micronutrient deficiencies in obese individuals being seen for bariatric surgery is summarized in table 3. It is apparent that deficiencies of iron, copper, zinc, and Vitamin D are especially common in obese individuals who are being evaluated for bariatric surgery.

Potential Mechanisms of Micronutrient Deficiencies in the Obese

As described above, inadequate dietary intake may be a major origin for micronutrient deficiencies in obese individuals (Table 4). There are multiple other proposed mechanisms. It has been reported that individuals with gastric infection with the *Helicobacter pylori* bacterium have decreased absorption of both Vitamin C and Vitamin B12 [19]. In addition, it has been shown that alcohol can inhibit absorption of Vitamin B1 in the jejunum [20]. This is especially worrisome due to the large percentage of individuals who use alcohol products routinely. These problems could exacerbate the low circulating and tissue levels of Vitamin B1 that have been identified in a human study [21].

Based on old literature on the interference with B vitamin absorption, we have been especially interested in the potential relationship between small intestinal bacterial overgrowth and micronutrient deficiencies in the obese. Potential origins of small intestinal bacterial overgrowth include intestinal neuropathy, diabetes mellitus, motility disorders; prior gastrointestinal surgery, pancreatic insufficiency, achlorhydria, and small intestinal diverticulosis [22]. We have evaluated the high prevalence of Vitamin B1 deficiency in individuals with small intestinal bacterial overgrowth after Roux-en-Y gastric bypass surgery [23]. In our study, levels of whole blood thiamine were improved by treatment of small intestinal bacterial overgrowth with oral antibiotics but not by simply providing oral supplements of Vitamin B1. Proposed mechanisms of vitamin mal absorption in the presence of small intestinal bacterial overgrowth include de conjugation of bile salts, interference with micelle formation, consumption of micronutrients by bacteria, and interference with (vitamin) binding proteins.

Management of Obesity

Management options for the treatment of individuals with obesity presently include dietary and activity programs, pharmacological therapy, endoscopic procedures, and surgical procedures. Recent studies have showed that an increased focus on healthy eating and physical activity have led to a decrease in obesity rates in school children in a school based program [24]. Unfortunately, dietary and activity program and pharmacological therapy can result in poor weight loss or poor maintenance of weight loss, especially in

individuals with severe obesity [25,26]. Disappointing results raise the question about what other factors may be important for the treatment and management of obese individuals. There is presently minimal data available to support the hypothesis that concomitant treatment of micronutrient deficiencies could improve the outcomes in these treatment trials. If further studies are warranted to address the question of micronutrient deficiencies interfering with clinical trials, it would seem that the micronutrient deficiencies with high prevalence and severe patho physiological implications should be considered. In this group of micronutrient deficiencies, Vitamin B1 deficiency may be an important origin for subclinical symptoms and disorders in obese individuals.

Vitamin B1 Deficiency States

The prevalence of clinical and subclinical symptoms of Vitamin B1 deficiency in obese individuals is presently under study. Vitamin B1 or thiamine deficiency is one of the major nutritional complications that result from bariatric surgery. Vitamin B1 is one of the eight major water soluble vitamins, and it was the first vitamin to be discovered (thus it was named Vitamin B1). Vitamin B1 is involved in a wide variety of intricate biochemical pathways necessary for proper tissue and organ function, including decarboxylation of pyruvate and oxidation of alpha-keto-glutamic acid. In the Krebs cycle, Vitamin B1 functions as a link between the glycolytic and citric acid cycles. Among the major clinical manifestations of thiamine deficiency or beriberi, patients with neuropsychiatric beriberi may develop auditory or visual hallucinations or aggressive behavior, patients with cardiovascular disease (wet beriberi) may present with tachycardia, respiratory distress, or lower extremity edema, patients with dry beriberi may present with polyneuritis of the lower extremities and upper extremities, or muscle weakness and pain, and patients with gastrointestinal beriberi may present with symptoms of delayed gastrointestinal emptying, i.e. nausea and vomiting, or constipation [27].

Summary

Because of the established and well known health risks and rising prevalence, obesity has become a major health challenge. Urgent global action is required to help countries more effectively intervene to both control the rise in the prevalence of obesity and to offer effective therapy to obese individuals. However, no country has been a success story during the last few decades. It seems inevitable that co morbidities associated with obesity will continue to increase in epic proportions. There is a need for increased awareness among physicians regarding the prevalence of the various micronutrient deficiencies and their associated symptoms in obese individuals. It will be important to determine whether the presence of micronutrient deficiencies in part reduce the effectiveness of interventions for the treatment of obesity.

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