Addictive Disorders in Nutritional Diseases - From a Nutritional Viewpoint

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Addictive disorders in nutritional diseases – from a nutritional viewpoint

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20.1 INTRODUCTION

20.1.1 Definition of nutritional disorders

Nutritional disorders can be defined from a number of perspectives. One method of classification is based on the use of nutrients as therapeutic modalities in situations of disordered organ function. In this regard the Center for Medicare Services defines reimbursable medical nutrition therapy for diabetes, renal disease, and comorbid hypertension and hyperlipidemia. Another classification system is based on the effect of nutrient excess or deficiency on the functioning of organ systems. In this regard, illnesses such as osteoporosis, anemia, thyroiditis, obesity, marasmus, and kwashiorkor would be considered nutritional disorders. A third method of classification involves the behavioral relationship between nutrients and the regulation of their intake. In this regard, eating disorders such as anorexia nervosa, bulimia nervosa, binge eating disorder, night eating syndrome, and obesity could be considered nutritional disorders.

This chapter addresses the interaction of substance addiction and nutritional disorders classified by all three methods described above. It provides an overview of currently accepted nutrition therapy methods and discusses the pathophysiology of aberrant intake regulation.

20.1.2 Interaction of addictive disorders with medical nutritional therapy

Substance addictions involve the use of various classes of drugs that affect a range of bodily organ systems. Since all classes of misused drugs – alcohol, tobacco, stimulants, pain killers, tranquilizers – are believed to usurp the naturally occurring reward pathways meant to help control food (and thus nutrient/energy) intake [1], substance addiction has the potential to induce clinical and subclinical malnutrition states. In addition, psychological desire for food is altered in individuals misusing substances. This can be especially dangerous in diseases such as diabetes and renal disease in which acute nutrient intake plays a major role in treating the organ dysfunction.
20.1.3 Interaction of addictive disorders and food intake regulation

Food intake regulation involves interactions between peripheral sensory signals, intestinal hormonal signals, and central neurotransmitter signals. Oral stimulation with food through taste and smell as well as drugs of addiction directly causes release of brain dopamine that promotes pleasure and continued motivation to acquire more food or drug. Volkow et al. [1] reviewed the similarities in neural circuitries underlying motivation to acquire and ingest food and drugs. Common neurotransmitters involved in these processes include mesolimbic dopamine and opioid circuits. These neurotransmitter circuits are modulated by peptide hormones [2] which originate in the gastrointestinal tract, such as ghrelin, insulin, leptin, cholecystokinin (CCK), and glucagon-like-peptide-1 (GLP-1), as well as centrally derived peptides, such as neuropeptide Y (NPY), melanin concentrating hormone (MCH), and cocaine-amphetamine-related transcript (CART). Some data exist suggesting that overeating and obesity are protective against drug addiction [3,4] and Carr [5] reports that, in animals, chronic food restriction increases the sensitivity to addictive drugs.

20.1.4 Prevalence of nutritional disorders in chronic alcohol and drug use

Chronic alcoholics and drug addicts have distorted eating behavior that predisposes them to eating disorders [6], malnutrition disorders, and hematological disorders. There are high rates of co-occurrence of eating disorders and substance addiction [7]. Jonas et al. [8] found 32% of 259 surveyed cocaine users met the DSM-III criteria for anorexia, bulimia or both. Santolaria-Fernández et al. [9] found 66.4% of hospitalized drug addicts exhibited anorexia at the time of admission. When compared to the general population, those with eating disorders have higher frequencies of positive family history for substance addiction [10]. The development of de novo alcohol addiction and dependence after bariatric surgery for severe obesity is a topic of recent concern. Estimated incidence rates range from a low of less than 3% to a high of 30% [11]. Possible hypotheses explaining these findings are (1) the presence of a common mechanism for over-use of rewarding substances that is expressed differentially in different individuals, and (2) an interaction between food and substance addiction that increases the susceptibility to the other [10].

Drug addicts tend to lose interest in everything other than drugs, including food. Santolaria-Fernández et al. [9] reported that 92.4% of drug addicts without organic pathology were under the mean weight for the population. Of the 140 studied, 54 (39%) met the criteria for marasmus and/or Kwashiorkor-like malnutrition. Himmelgreen et al. [12] found significantly lower measures of body weight and anthropometric measures in drug users when compared to nondrug users.

In several studies of hospitalization due to diabetic ketoacidosis (DKA), a considerable percentage of patients admitted with DKA were found to have either alcohol or drugs in their system. Pedersen-Bjergaard et al. [13] found that 31% of diabetics admitted with severe hypoglycemia had a psychoactive substance in their blood sample, and 17% had alcohol in their system. Warner et al. [14] found that 14% of admissions of DKA were cocaine users. Hart and Frier [15] found 19% of diabetics were admitted with severe hypoglycemia due to alcohol intake.

Substance addiction and dependence can exacerbate the consequences of reduced nutrient intake and its concomitant diseases. It seems prudent then to screen for substance addiction/dependence in those with eating disorders, diabetes, malnutrition and those who have undergone bariatric surgery. Criteria for eating disorders and substance addiction/dependence can be found in the DSM-IV of the American Psychiatric Association. Simple anthropometric measurements of weight, waist circumference, and percentage body fat, as well as blood test indicating nutritional status (albumin, prealbumin, liver function tests, fasting glucose, hematocrit, hemoglobin, red and white blood cell counts, and platelet counts), can suggest the presence of malnutrition that can then be probed further for substance use.
20.2 INTERACTION OF ADDICTIVE DISORDERS WITH DISEASE-SPECIFIC MEDICAL NUTRITION THERAPY

20.2.1 Diabetes, metabolic syndrome and addictive disorders

Drug and alcohol use are major risk factors for complications in diabetic patients, whether due to changes in behavioral patterns, decreased awareness of symptoms, interference with self-care, or direct effects on carbohydrate metabolism. In addition, at least two separate studies have documented increased risk of developing metabolic syndrome, itself a risk factor for cardiovascular disease, with increasing over-consumption of alcohol. Freiberg et al. [16] and Fan et al. [17] both analyzed National Health and Nutrition Examination Survey (NHANES) data from 1990s and concluded that alcohol consumption in excess of daily recommend guidelines (one drink for women, two drinks for men) causes a significant increase in waist circumference, blood pressure, glucose intolerance, insulin resistance, and serum triglycerides.

20.2.1.1 Alcohol and carbohydrate metabolism

Alcohol is metabolized in preference to other energy sources in the body, thus reducing glucose disposal and causing insulin resistance. Higher levels may reduce insulin binding and inhibit intracellular signaling related to insulin. Alcohol also inhibits gluconeogenesis and, when used in moderation, may be related to enhanced insulin sensitivity, resulting in glycemic control [18]. In chronic alcoholics, whose liver stores of glycogen are often depleted, this inhibition of gluconeogenesis may lead to hypoglycemia [19].

20.2.1.2 Stimulant drugs and carbohydrate metabolism

Use of dopamine-related stimulants (cocaine and amphetamine, etc.) can interfere with certain aspects of glucose metabolism. Amphetamines have been found to have a counter-regulatory effect to insulin. In a study by Baudrie and Chaouloff [20] in rats, administration of amphetamine elicited a rapid rise in plasma glucose that was associated with a decreased insulin response to a glucose bolus. They found that the hyperglycemic effect was mediated by centrally located 5-HT2 receptors and, in turn, adrenal epinephrine release. Cocaine addicts are at high risk for DKA, mainly due to the omission of insulin therapy. Another possible reason is the effect of cocaine on counter-regulatory hormones. Cocaine increases the levels of catecholamines, which greatly affects carbohydrate metabolism in the following ways: inhibiting pancreatic insulin secretion, increasing glucagon production, stimulating glycogenolysis and gluconeogenesis in the liver, activating lipolysis in the skeletal muscle, impairing the peripheral use of glucose, as well as stimulating ketogenesis. This increased production of ketoacids combined with omission of insulin therapy greatly increases the chance of DKA [14].

20.2.1.3 Cannabis and nicotine and carbohydrate metabolism

Cannabis has been found to have little or no effect on diabetics, although it is known to cause food cravings, which could in effect cause hyperglycemia. A survey on young adult diabetics by Ng et al. [21] found that several subjects were admitted to the hospital for DKA after using cannabis. A study by Pedersen-Bjergaard et al. [13] found 5% of patients admitted with severe hyperglycemia had marijuana in their system.

Some people believe that smoking opium can reduce serum glucose and lipids in diabetes. To test this theory, Azod et al. [22] compared blood glucose and lipids in opium addicts and nonaddicts with individuals with Type 2 diabetes. They found a significant difference between the fasting blood glucose and two-hour post prandial glucose between the two groups, but no difference in hemoglobin A1C.
(HbA1C) levels. This indicates that opium decreases blood glucose levels temporarily, but has no long-lasting effects on blood glucose [22].

Studies on the relationship of nicotine and diabetes have reported mixed results. Nicotine use has been shown to cause insulin resistance, increase the risk of developing Type 2 diabetes, and increase the risks of micro- and macrovascular complications in both Type 1 and Type 2 diabetics [23]. Smoking increases the circulating levels of insulin-antagonistic hormones such as epinephrine and norepinephrine [24]. A study by Facchini et al. [25] reported chronic cigarette smokers to be insulin resistant, hyperinsulinemic, and dyslipidemic when compared with nonsmokers. Chiolero et al. [26] analyzed the tolerability of a nicotine lozenge or gum and found that the conditions in a majority of the diabetic patients were unaffected. A large cross-sectional study by Henkin et al. [27] found that smoking status did not influence insulin sensitivity. However, since smoking and diabetes are independent risk factors for cardiovascular disease, there is wide support for recommending smoking cessation in those with diabetes.

20.2.1.4 Diabetes control and substance addiction

There is a definite lack of awareness about the effects of drug and alcohol use on diabetes in chronic drug users. A survey done by Ng in London of young adults with Type 1 diabetes found that 72% of street drug users were unaware of the adverse effects of diabetes. Diabetic patients with either a drug or alcohol addiction are at high risk for poor diabetes control [21]. Physicians are encouraged to assess for substance addiction in diabetics, and counsel their patients about the adverse effects of drug and alcohol use on diabetes course and outcome.

20.2.2 Renal disease and addictive disorders

Drug and alcohol addictions have been associated with causing and exacerbating renal disorders. Chronic exposure to inhalants has been associated with various kidney abnormalities including acute and chronic renal failure [28]. Ecstasy and cocaine have both been associated with acute renal failure [29,30]. Several forms of renal disease and progression of chronic renal failure to end-stage renal disease have been associated with cocaine addiction. The mechanisms include the hemodynamics of cocaine and its effect on matrix synthesis, glomerular inflammation, and glomerulosclerosis [28]. Heroin has been associated with renal damage, though the current reduced incidence suggests that earlier impure heroin contained nephrotoxic substances [31].

Smoking has been found to hasten the progression of renal disease. It has been associated with decreased filtration rate, though the underlying mechanisms are not yet understood. Smoking is one of the most important remediable risk factors – cessation of smoking has been shown to improve both renal and cardiovascular prognosis and should be recommended to all renal patients [32].

Medical nutrition therapy for renal disease typically involves a high carbohydrate, low protein diet, with restrictions in sodium and potassium depending on the particular type of renal disease present [33]. As discussed previously, chronic alcoholics and drug addicts typically have poor diets with low carbohydrate intake, and little interest in eating or self-care processes. Consequently, diet therapy compliance is often difficult and needs to be carefully monitored. The kidney is involved in maintenance of calcium–phosphorus homeostasis through production of the active form of Vitamin D and elimination of calcium and phosphorus [33]. Activated Vitamin D regulates absorption of calcium and phosphorus from the gut [34]. This is complicated further in chronic alcoholics, as alcoholism commonly leads to hypocalcemia and hypophosphatemia, and Vitamin D deficiency is not uncommon [35]. Calcium and phosphorus control is crucial in maintaining bone composition, and should be closely regulated [34].

Some water soluble vitamins have been found to be in increased demand in those with chronic kidney disease [34]. This should be taken into consideration for chronic alcoholics and drug addicts who are
already prone to vitamin deficiencies as well as smokers, who have been found to be deficient in Vitamin C as well as carotenoids [36].

A higher body mass index (BMI) of 25–28 is correlated with increased survival rates compared to lower BMI in normal kidney function [34]. Chronic alcoholics and drug users typically have lower anthropometric measures when compared to the general population [9]. This is secondary to protein deficiencies, which are common in chronic alcoholics [9,12]. A heart healthy diet of limited saturated fat and increased “good” fats is recommended, as cardiovascular disease is accelerated in patients with chronic kidney disease [34].

20.2.3 Obesity and malnutrition

20.2.3.1 Caloric excess

Obesity is a multifactorial disease caused by an interaction of genetics, caloric over-consumption, and a sedentary lifestyle. Incidence of obesity has risen sharply since the 1990s and currently stands at ~30% of the adult United States population [37]. By definition, people are classified as obese if they have a body mass index of 30 or greater, with those who have a body mass index of 40 or greater considered severely obese. Although behavior therapy coupled with a low calorie diet can promote weight loss in obese individuals, those who are severely obese tend not to benefit very much from this intervention [38]. Currently, the most effective treatment for severe obesity is bariatric surgery.

Two types of bariatric surgery are common – the vertical gastric banding (VGB) and the Rouen Y gastric bypass. Both these procedures physically reduce stomach capacity, thereby creating a de facto state of caloric restriction. Since those individuals who qualify for surgery (those with BMI of 40 or greater) also have problems controlling food intake, the reduction in stomach capacity can present a major obstacle to successful weight loss if the individual has not learned to adjust food intake prior to surgery. Bariatric surgery reduces mortality rates due to diabetes, cardiovascular disease, hypertension, and stroke [39] in severely obese individuals. Although the benefits of bariatric surgery are impressive with respect to reductions in mortality, a new “concern” with respect to substance addiction in post-bariatric surgery patients has developed, specifically alcohol addiction. [11,40] reports that 28.4% of post-bariatric surgery patients have a difficult time controlling alcohol consumption, resulting in post-surgery alcohol consumption greater than that seen before surgery, while also reporting that in their own study (of post-surgery patients queried 6–10 years post surgery) incidence of alcohol addiction and dependence was less than 3%. There have been articles in the popular press [41] and stories on magazine news shows such as ABC’s Good Morning America that suggest that occurrence of de novo addictions following bariatric surgery may partly be due to “addiction transfer,” since there is overlap in reward circuitry between food and drugs. Another possible mechanism for de novo addiction post bariatric surgery may be related to the enhancement of drug reinforcement through food restriction that results as a consequence of bariatric surgery. No prospective study has addressed this hypothesis; however, animal studies on the effect of food restriction on substance use show increased substance use with caloric restriction and weight loss; and increased substance use is reversed after weight regain [5,42].

The increase in alcohol consumption also has an effect on weight loss and maintenance after bariatric surgery, as alcohol contributes calories as well as modulation of the reward circuitry [39]. Alcohol consumption also causes a shift in macronutrient preference, as those who consume more alcohol after bariatric surgery also tend to increase intake of lipids and proteins, and decrease intake of carbohydrates [39]. In addition, alcohol metabolism is altered in bariatric patients with intoxication occurring at lower levels of alcohol intake than before surgery [40,43]. It seems prudent to monitor alcohol consumption after bariatric surgery both to prevent negating of the positive effects of bariatric surgery and to intervene early in the potential development of de novo alcohol addiction and dependence.
20.2.3.2 Alcoholism and macronutrient deficiency

Malnutrition in alcoholics can be primary or secondary – alcohol can replace other nutrients in the diet or it can interfere with the absorption and use of nutrients [44]. Alcohol intake up to 23% of total kilocalories is typically associated with slightly increased total energy intake, while intake greater than 30% is associated with a decrease in total kilocalorie and, thus, nutrient intake [44]. Patients with chronic liver failure experience deficits in protein metabolism, possibly leading to ascites, internal bleeding, or hepatic encephalopathy [44]. Acute and chronic alcohol intake impairs amino acid uptake and synthesis into proteins, reduced protein synthesis and secretion from the liver, and increased catabolism in the gut [45].

20.2.3.3 Alcoholism and micronutrient deficiency

There is limited research on the nutritional effects of recreational drug use. Most research comes from patients who are beginning drug treatment programs. Malnutrition in drug users results from drug induced anorexia, poor self-care, and irregular eating behavior [12]. Drug users tend to lose interest in everything except drugs [46]. They are more likely to be food insecure and to consume lesser amounts of fruits and vegetables [12].

Heavy alcohol consumption can lead to reduced Vitamin A levels in the liver. The primary reason may be inadequate intake, but decreased hepatic storage may also play a role [47]. Normal levels of beta-carotene suggest an impaired ability of the liver to take up beta-carotene and/or convert it to Vitamin A [44]. The enzymes involved in the conversion of retinol to its active form are the same as those used to metabolize ethanol, suggesting a possible disruption in Vitamin A metabolism with chronic alcoholics. Deficiency can result in eye disorders, such as night blindness, and impaired immune function [48]. Excess Vitamin A can also have harmful consequences for chronic alcoholics. When taken with alcohol, excess Vitamin A causes a significant leakage of the mitochondrial enzyme glutamine dehydrogenase into the bloodstream, which may promote hepatic fibrosis. Both Vitamin A deficiency and excess have been associated with promoting carcinogenesis [49]. Due to the hepatotoxic effects of Vitamin A in conjunction with alcohol use, supplementation with Vitamin A should be carried out with caution and only used in those who are capable of modifying their alcohol intake [44].

Thiamin deficiency is the most common vitamin deficiency seen in chronic alcoholics, and may be the most important cause of tissue damage [48]. It occurs as a result of decreased intake, reduced absorption, and malutilization [50] and affects the cardiovascular (wet beriberi) and nervous (dry beriberi and Wernicke–Korsakoff syndrome) systems.

Deficiencies of Vitamin B6 and riboflavin may be seen in alcoholics due to a general low intake of B vitamins or the adverse effects of alcohol on hepatic storage of these vitamins. Vitamin B6 deficiency can be partly responsible for neurologic, hematologic, and dermatologic disorders in alcoholics. Alcoholics may be deficient in Vitamin B6 but not exhibit hematological or abnormal liver function [48].

Niacin deficiency is frequently seen among chronic alcoholics. It may result in pellagra, which presents with various mental, neurological, and gastrointestinal symptoms, with or without skin lesions. Pellagra can lead to death by bronchopneumonia if not recognized and treated [51].

Folate and Vitamin B12 deficiencies can lead to megaloblastic anemia. Levels of Vitamin B12 are often normal in chronic alcoholics until development of pancreatic insufficiency and/or liver disease due to the large body stores of the vitamin [48]. Folate deficiency usually appears first, as a result of poor intake, impaired absorption, accelerated excretion and altered storage and metabolism [45]. Folate deficiency can usually be treated with proper diet, but supplementation may be necessary due to poor diet compliance in active alcoholics [44]. Folate deficiency can result in megaloblastic anemia. Levels of Vitamin B12 are often normal in chronic alcoholics until development of pancreatic insufficiency and/or liver disease due to the large body stores of the vitamin [48]. Folate deficiency usually appears first, as a result of poor intake, impaired absorption, accelerated excretion and altered storage and metabolism [45]. 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intake usually falls below the recommended daily allowance (RDA [52]).

Depressed Vitamin E levels have been seen in patients with alcoholic liver cirrhosis [48] and with chronic alcohol induced pancreatitis [53]. Pancreatic insufficiency may cause Vitamin K deficiency due to a disruption of fat absorption [49].

Vitamin D deficiency may result from insufficient intake, malabsorption due to cholestasis, inadequate sunlight exposure, as well as pancreatic insufficiency [48]. Low Vitamin D status may contribute significantly to calcium and phosphorus deficiencies [35]. Hypocalcemia may also be caused by hypoalbuminemia, insufficient intake, hypomagnesemia, or excessive renal loss. Hypomagnesemia is very common among hospitalized alcoholics, along with hypophosphatemia, and results from deficient intake, malabsorption, excessive renal losses, and cellular uptake [35].

Chronic alcoholics occasionally present with zinc deficiency, most often in those with alcoholic cirrhosis, due to decreased intake and absorption as well as increased urinary excretion [49]. Iron may either be in excess or deficient in chronic alcoholics. Deficiency may result from gastrointestinal lesions [48]. Elevated hepatic stores of iron have been found in chronic alcoholics with liver disease. The mechanisms of iron accumulation and the source of excess iron remain unclear. These increased iron levels may contribute to liver injury, as both alcohol and iron cause oxidative stress and lipid peroxidation [54].

20.2.3.4 Smoking and malnutrition

Cigarette smoking has been found to be associated with poorer eating habits. Smokers tend to eat more white bread, meat, sugar, and potatoes and less fruits, vegetables, and whole grain and high fiber products [36,55]. They are more likely to have an imbalance between metabolic demand for antioxidants and dietary intake of antioxidant nutrients. For similar levels of nutrient intake, smokers were found to have lower circulating levels of beta-carotene, alpha-carotene, cryptoxanthin, and lycopene than nonsmokers [56]. Smoking is known to cause decreases in serum levels of Vitamin C. Marangon et al. [55] found an inverse association between serum Vitamin C levels and smoking, independent of dietary intake, suggesting that smoking may have a direct influence on Vitamin C metabolism.

20.2.4 Hematological disorders

20.2.4.1 Alcoholism and folate deficiency anemia

Chronic alcoholism is often associated with anemia, resulting from nutritional deficiencies, chronic gastrointestinal bleeding, hepatic dysfunction, or direct toxic effects of alcohol on erythropoiesis [57]. Macrocytosis is commonly seen among chronic alcoholics, particularly those with poor eating habits, and is associated with megaloblastic anemia due to folate deficiency [57,58].

Studies in folate-deficient alcoholics suggest that ethanol interferes with the recovery of folate status and the hematopoietic response to folate. Halsted et al. [59] reviewed the interactions of folate with alcohol intake and reported decreased intestinal folate absorption, increased renal excretion, and decreased expression of the reduced folate carrier in hepatic tissue. These disruptions in folate metabolism result in the development of megaloblastic anemia, a condition marked by elevated mean corpuscular volume of erythrocytes in the presence of reduced erythrocyte number. Since megaloblastic anemia is common to both folate and Vitamin B 12 deficiencies, it is important to determine the exact deficiency before providing supplement treatment. Supplementation with folate will correct the morphological symptoms but can mask Vitamin B12 deficiency which is associated with irreversible neurological damage [33]. Vitamin B12 deficiency is not common in chronic alcoholism as alcohol induced liver damage usually results is release of Vitamin B12 and concomitant increase blood Vitamin B12 levels.
20.3 FUTURE DIRECTIONS

The presence of common neurocircuits underpinning both over-eating and substance addiction, coupled with the current obesity epidemic suggests that greater attention must be directed at determining the interactions between substance addiction, food over-consumption, weight gain and loss. What are the common risk factors? Why is it that some individuals misuse drugs, while others abuse food? Recent data suggests the possibility that bariatric surgery can potentiate de novo additions in susceptible individuals. While the risk factors for this phenomenon have not been identified, it is possible that there is a common neuro substrate that links the two behaviors.

More information is needed on the effects of nutrients as they interact with genetic risk factors for choice of addicted substance, promotion of relapse and “transfer of addiction”. The field of epigenetics is relatively new but holds promise for determining the effects of nutrients on human disease [60]. Recent work (in rats) has demonstrated a role for nutrient exposure in the prenatal period to shape offspring preferences not only for food but also for alcohol [61], and Gomez-Pinilla [62] reviews data suggesting a role for nutrients in modulating brain cognitive functions. He states that, “Understanding the molecular basis of the effects of food on cognition will help us to determine how best to manipulate diet in order to increase the resistance of neurons to insults and promote mental fitness”. Since it is known that substance addiction can damage neurons as well as affect neuro-plasticity, the ability to identify those at genetic risk for these events (through their response to various nutrients) may provide additional options for treatment and prevention interventions.

REFERENCES


