Nutrient Depletion and Prescription Drugs

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According to the Centers for Disease Control, the number of adults aged 55-64 taking at least one pharmaceutical in the last month rose from 62 percent in 1988-1994 to 73 percent in 1999-2002.1 The large number of individuals taking pharmaceutics suggests that the potential for drug-nutrient interaction is substantial. The following discussion looks at common medications and the nutrient depletion considerations.

Common Pharmaceuticals that Deplete Nutrients

Hormone Replacement

In the U.S. from 1999 to 2002, approximately 15 million women were taking HRT annually accounting for 90 million prescriptions per year.2 Oral contraceptive pills (OCP) also contain estrogen/progestin combinations. Research suggests that estrogens significantly deplete several B vitamins. Oral estradiol decreases pyridoxines (vitamin B6) as well as albumin in postmenopausal women.3 This vitamin B6 deficiency is believed to be associated with a disruption in tryptophan metabolism.4 Proper tryptophan metabolism is essential for serotonin production, which is essential for proper mood stabilization and contentment in life.

Additional research indicated that oral contraceptives deplete riboflavin (vitamin B2), folic acid, cobalamin (vitamin B12), ascorbic acid (vitamin C), and zinc.5 Studies indicate a decrease by 40 percent of both folic acid and serum B12 levels with oral contraceptive use.6 Additionally, studies have shown that estrogen supplementation increases magnesium uptake into bone and soft tissue, causing lowered blood magnesium levels. This change leads to calcium and magnesium changes and can lead to an increase in coagulation and thrombosis seen with estrogen supplementation.7

Acid Blockers

Proton pump inhibitors (PPI) and histamine-2 receptor antagonists (H2 blockers) are commonly prescribed for treatment of ulcers and gastroesophageal reflux disease (GERD). Lansoprazole, or Prevacid, is a PPI ranking third in top pharmaceutical sales in the U.S. in 2004.8 Acid blockers have been linked to significant increases in the risk of vitamin B12 deficiency.9 One small study showed a 53 percent decrease in protein-bound B12 absorption in individuals taking an H2 blocker.10 Research also indicated that folic acid absorption is decreased with supplementation of H2 blockers and other antacids.11 Studies have also linked H2 blockers, which decrease gastric acid secretion, with decreased absorption of iron and zinc.12-13 One study showed a direct correlation between increasing dosage of cimetidine, an H2 blocker, and decreasing dietary non-heme iron absorption ranging from 28-65 percent.14 Animal studies also have demonstrated that cimetidine significantly decreases intestinal calcium transport.15 In addition, it also alters vitamin D metabolism by altering the enzyme vitamin D 25-hydroxylase activity.16 A small study performed with the PPI omeprazole demonstrated that serum levels of beta carotene were decreased with increased gastric pH.17
Corticosteroids

Corticosteroids are frequently prescribed for anti-inflammatory and immunosuppressant activity. Prednisone and hydrocortisone are often prescribed for various medical conditions such as autoimmune diseases and inflammatory conditions. Corticosteroid treatment has been associated with increased loss of bone mineral density. Studies show that these drugs decrease calcium absorption and increase calcium excretion. Also, a study with individuals with chronic airway obstruction showed long term oral steroid therapy is associated with decreased serum magnesium levels. Steroid medication has also been associated with low potassium in both animal and human studies.

Studies in individuals with rheumatoid arthritis (RA) showed serum levels of zinc and copper are two other nutrients that suffer declines after corticosteroid treatment, and urinary excretion of zinc and copper is elevated. Additional studies on patients with RA receiving corticosteroid therapy also demonstrated a decrease in plasma selenium levels. Although the evidence appears incomplete or conflicting, some studies suggest that vitamin C and vitamin D may be affected by corticosteroid therapy.

Aspirin

Aspirin is used for antipyretic, analgesic, and anti-inflammatory activity. Recent promotion of aspirin as prophylactic treatment to decrease platelet aggregation to prevent transient ischemic attacks, stroke and thromboembolism has increased the use of this over-the-counter medication. Treatment with aspirin, or acetyl salicylic acid, affects several nutrients. Multiple studies have shown that aspirin therapy decreases vitamin C absorption. Some studies also indicate that increasing aspirin dosage directly correlates to increasing ascorbic acid excretion in the urine. Research also suggests that aspirin therapy causes an increase in gastric blood loss leading to a decrease in total body iron. Evidence also supports that supplementation with aspirin significantly decreases both total and bound serum folate and slightly increases folic acid excretion.

Anti-Diabetic Drugs

According to the American Diabetes Association 2005 statistics, approximately 7 percent of the U.S. population is diabetic. They estimate that 57 percent of adult diabetics take oral medication only and an additional 12 percent take insulin plus oral medication to manage the condition. Metformin, a frequently prescribed biguanide, has been shown to deplete vitamin B12 and folic acid. Studies indicate that long term metformin therapy significantly decreases serum vitamin B12 levels. Additional studies suggest that short term treatment with metformin increases homocysteine levels, and supplementation
with B vitamins or folic acid can moderate this response. More specifically, serum folic acid levels have been shown to decrease 7 percent and vitamin B12 levels decrease by 14 percent with metformin therapy in type 2 diabetic individuals. Although limited, research also suggests that treatment with sulfonylureas (e.g., Glipizide Gliclazide glyburide, Glimpiride, etc.) increase the risk of CoQ10 deficiency.

**Statin Drugs**

The statin drug Lipitor® is one of the top selling pharmaceuticals worldwide and brought in an estimated 12.2 billion dollars in sales to Pfizer in 2005. Statins inhibit the enzyme 3-hydroxy-3-methylglutaryl-coenzyme A (HMGCoA reductase), which decreases cholesterol synthesis by inhibiting the conversion of acetyl CoA to mevalonate. Mevalonate is also necessary in the production of ubiquinone, or coenzyme Q10 (CoQ10). Numerous studies have demonstrated that statin drug therapy significantly decreases plasma levels of CoQ10. CoQ10 is necessary for mitochondrial energy production as well as exhibits potent antioxidant activity. Some researchers suggest that the depletion of COQ10 could account for some side effects associated with statin drugs such as myotoxicity and hepatotoxicity.

**Antihypertensives**

Common antihypertensive medications include beta-adrenergic blockers, calcium channel blockers, angiotensin-converting enzyme (ACE) inhibitors, diuretics, and vasodilators. According to the American Heart Association, an estimated 65 million Americans, almost one in three adults, has high blood pressure. Vasodilators such as hydralazine deplete vitamin B6. Captopril, an ACE inhibitor, has been shown to cause hyponatremia by increasing sodium excretion and may cause hyperkalemia. Also, studies with the beta blocker propranolol have shown that the drug inhibits the CoQ10 enzymes in myocardium.

**Diuretics**

Diuretics are known for altering certain nutrient levels such as potassium. However, many other nutrients are affected. Thiazide diuretics have been shown to deplete magnesium, sodium, potassium and zinc. One study found hyponatremia in 13.7 percent and hypokamemia in 8.5 percent with individuals treated with thiazide diuretics. Thiazide diuretics also decrease magnesium in approximately 20 percent of patients. Additionally, research indicates that thiazide diuretics cause significantly decreased serum zinc.

Loop diuretics have been shown to deplete potassium, magnesium, calcium, zinc, pyridoxine, thiamine and ascorbic acid. One study found that thiamine deficiency was found in 98 percent of congestive heart failure patients receiving 80 mg of furosemide per day and in 57 percent of those
receiving 40 mg per day. Ascorbic acid and pyridoxine excretion are also increased with furosemide treatment. Additionally, several studies demonstrate that loop diuretics increase the excretion of sodium, potassium, calcium, magnesium, and chloride.

Conclusion

Drug-induced nutrient depletion can lead to potential further health challenges. Visiting with your health care provider and pharmacist about how to minimize these potential nutritional-deficit side effects is essential. When managing drug therapy, keeping your doctor or other medical professional in the “loop” is critical.

References: