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Review Article

# Antibiotics and Nutritional Implications- The Drugs-Nutrients Interactions

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## Abstract

A drug-nutrient interaction is a state in which either a drug or a nutrient affects the clinical functional or metabolic effect, that pose potential harm to the patient, cause changes in pharmaceutical, pharmacokinetic, or pharmacodynamic properties of the drug or nutritional benefit to the patient.

The nutritional effects of antibiotic are different than expected than that food -drug interactions. The patient who is on antibiotics should be carefully assessed for antibiotics- nutrients interactions and depletions, the current nutritional deficiencies, risk of further deficiency, the hypercatabolic status, aged, surgical concerns, polypharmacy, gut microbiota and food/ feed delivery route, beverages, dietary supplements the person is consuming that can risk for micronutrients deficiency or promote drug induced nutrients depletion.

Therefore it is advisable for patients to follow the physician and clinical dietitian's instructions to obtain maximum benefits with least antibiotics - nutrients induced interactions.

**Keywords:** Vitamins; Minerals; Nutrient Depletions; Nutrients-Drug Interactions; Xenobiotic Metabolism

## Introduction

Many medicines are used to treat, prevent or control health related problems. But some of these medicines provide the benefit at the cost of health, as these medicines cause complications, side effects, food-nutrients interactions, adverse reactions, etc.

One of the preventable side effects of the medications is the nutritional status of the patients, i.e. the drug-nutrients interactions and drug-nutrients depletions.

Among the various drugs prescribed antibiotics are the most common in hospital scenarios.

Antibiotics are drugs prescribed to fight against infections. They are called as anti-infective agents. Antibiotics are produced synthetically or from various species of living microorganisms.

### Classification

Antibiotics are generally classified based on

- Mode of action
- Spectrum of action
- Category and composition

Action of the antibiotics involves one of the following mechanisms

- Inhibition of protein synthesis
- Inhibition of nucleic acid synthesis
- Inhibition of cell wall synthesis
- Disruption of cell membrane functions
- Block pathways and inhibit metabolism

### Gut microbes and antibiotics

The antibiotics have shown to affect negatively on gut microbiota composition, distribution and functionality. As most of the antibiotics available in the market have a broad spectrum action, they impact not only on harmful bacteria, but also on healthy microbes. The antibiotics not only cause impairment of gut microbiota in the intestine, but also alter the mechanisms of action of the drugs on gastrointestinal epithelia and the spread of antibiotic-resistant microorganisms. Both the drug related factors and host-related factors affect the impact of antibiotics on human gut microbiota.

Common class of antibiotics prescribed are

1. Beta-lactams, e.g: Penicillins, Cephalosporins, etc.
2. Macrolides, e.g.

3. Tetracyclines
4. Fluoroquinolones
5. Aminoglycsides

## Antibiotics and nutrients interactions

Beta-lactams are used in treatment of a wide variety of infections. Among Beta-lactams, *penicillin* and *cephalosporins* are widely prescribed. Penicillins are broad spectrum antibiotics and as an excellent safety profile with few exception to allergy. Food effects on penicillin includes a high fat meal can decrease absorption of penicillin upto 36%, a high fiber and guar gum also reduced penicillin absorption. Intralipids and propofol used in clinical settings might also decrease penicillin effects, as lipids can become source microbes and thus reduce drug effects. Bromelain, an enzyme found in pineapple might increase the effect of Penicillin.

The gut flora is disturbed due to elimination of healthy gut bacteria. And thus can hinder the production of Vitamin K and B-complex vitamin by the gut friendly bacteria. High and long term dose of penicillin might disturb digestion and elimination. Supplementation of Vitamin K, B-complex vitamin, restoration of gut flora, consider serving curd, buttermilk, lassi and other fermented foods with each dose of the antibiotic. Antibiotics should be taken 1-2 hrs before or after meals Cephalosporins contribute to the malabsorption of vitamin B and K with long term use as these antibiotics kill bacteria, including beneficial flora in the gut. Supplementation with acidophilus or bifidus may aid in restoring the flora balance. Avoid alcohol, antacids, feverfew, ginkgo, garlic and other sulphur containing foods with cephalosporins.

## Aminoglycosides

Aminoglycosides act against gram negative bacteria by inhibiting protein synthesis. These antibiotics are neurotoxic and ototoxic. These include amikacin, neomycin, gentamicin, streptomycin, etc.

Amikacin and Supplements like citric acid, biotin, calcium, Vitamin $B_{12}$, choline, Magnesium, pantothenic acid, thiamin supplements. Thiamine ($B_1$) and pyridoxine ($B_6$) also decreases the level of vitamin by altering intestinal absorption, especially when taken orally. Amikacin decreases renal clearance levels of magnesium present in any supplement form. (Mg sulfate, citrate and hydroxide). Amikacin decreases the level of cyanocobalamin ($B_{12}$) by inhibition of gastrointestinal synthesis and absorption. Amikacin also reduces calcium absorption and reabsorption by renal tubular process.

Monitoring and supplementing of magnesium, potassium, calcium, vitamin $B_{12}$, vitamin K, etc. is advised in critically ill patients who require long term antibiotics prescription. It is also important to restore healthy intestinal ecology and stabilize the mucosal lining of gut and achieve the critical mass of bacterial restoration. Provide probiotics through feeds or one billion organisms per day for 5 days.

Gentamicin is used to treat serious bacterial infections. The side effects include stomach pain, diarrhea, oral ulcers, trouble swallowing, electrolyte imbalances, vomiting nausea, wt loss and dehydration. Gentamicin can cause calciuria (0.02 mmol per kg can increase 6-8 fold urine calcium excretion), by reducing renal tubular reabsorption of calcium. Patient may also develop hypomagnesemia, hypocalcaemia, hypokalemia, following gentamicin therapy due to inappropriate urinary excretion. Monitoring for hypercalciuria, hypomagnesemia, menopause, geriatric, morbid obese, GI and renal surgeries, etc. antacids, other drugs is advised.

Supplementation through serving a high calcium, magnesium and potassium rich diets is necessary as they prevent and protect against gentamicin induced nephrotoxicity. It is important to be cautious with Coronary Artery Bypass Graft patients when feeding high calcium diet and gentamicin, as it increases the risk of Acute Renal Failure.

The aminoglycoside, Neomycin is used to suppress intestinal bacteria (normal flora of intestine) The side effects nausea, vomiting, diarrhea, malabsorption syndrome - characterized by increased fecal fat and decreased serum carotene levels. Neoomycin dosage > 12gms/day can produce fatty stools, increase nitrogen excretion, cause malabsorption of cholesterol, xylose, glucose, lactose, sodium, calcium, vitamin $B_{12}$ and iron. It can also increases fecal bile excretion and reduces intestinal lactase activity, resulting in temporary lactose intolerance. Monitoring blood urea nitrogen, serum creatinine, urea and urinalysis for protein excretion, stools for fat, bile, etc. is required.

Streptomycin is used in moderate - severe infections like mycobacterium tuberculosis, respiratory, endocardial infections, etc. Side effects include nausea, vomiting, azotemia, hemolytic anemia, leucopenia, pancytopenia, thrombocytopenia, muscular weakness, etc. The antibiotic may affect the taste of food. Hence increase fluid intake. Streptomycin can interact with calcium, magnesium, sodium and biotin.

## Fluroquinolones

This class includes antibiotics like ciprofloxacin, levofloxacin, etc. These are used as broad spectrum antibiotics and some of these antibiotics members are removed from market due to adverse effects reports. The side effects of quinolones include, decrease in caffeine clearance and reduced caffeine metabolism. Nutrients like calcium, magnesium, aluminum, zinc may reduce absorption and effectiveness of the antibiotic and also antacids.

Advice patients to consume adequate fluids and avoid dairy products or supplements containing calcium, aluminum, magnesium and zinc at least 1-2 hours before or after drugs administration. Limiting caffeine products like coffee, tea, soft drinks, health beverages, etc. is also necessary.

Levofloxacin can cause side effects such as antibiotic-induced diarrhea. Magnesium rich foods, supplements, antacids, rich in magnesium can reduce the intestinal absorption of levofloxacin. Iron supplements, foods, also reduce absorption and effectiveness of the drug. Vitamin K may get depleted resulting in bleeding/ clotting disorders. Caffeine may show intensified effects in people taking levofloxacin. Levofloxacin should be taken 1-2 hrs before or after foods and drink. Supplements, foods, drugs, etc. containing magnesium, iron and caffeine should be used in caution.

Macrolides, these antibiotics can induce diarrhea. Long term use can result in overgrowth of pathogenic bacterium causing diseases like pseudomembranous colitis, vaginitis, dysbiosis, etc. Vitamin K and vitamin $B_{12}$ deficiency disorders can occur.

Azithromycin can interact with magnesium, calcium supplements, antacids, foods rich in magnesium, aluminum and calcium these interfere with drug absorption. Erythromycin apart from interactions common to macrolides, erythromycin also interferes with absorption and activity of calcium, folate, vitamin $B_6$, vitamin $B_{12}$, can cause deficiency diseases if administered for long. Erythromycin is best absorbed on empty stomach. It is advised to avoid taking with beverages, tea, coffee, juices, as these can affect degradation of drugs before they reach the intestine. Lactobacillus acidophilus can prevent these infections.

## Tetracyclines

Tetracyclines are used for a wide range of infections coverage. The side effects include serious difficulty in swallowing, breathing, loss of appetite, vomiting and stomach pain. Tetracyclines can interaction with iron. Calcium, magnesium, zinc, aluminum, interferes with absorption and chelates with tetracycline hydrochloride, also interferes with the activity of these nutrients like vitamin K, folate, $B_{12}$, vitamin C, etc.

Avoid tetracyclines with laxatives, antacids, food containing magnesium, calcium, iron, etc. Avoid giving 1-2 hours before or after foods, have with plenty of oral fluids. Supplementations can be done, if assessed for potassium, folic acid, vitamin K depletion.

Doxycyclines are affected by the dietary minerals, these can reduce the absorption and effectiveness of the drug especially calcium, magnesium, iron, zinc, etc [1-19].

## Conclusion

Antibiotics can influence gut flora activities and xenobiotic metabolism. They can deplete nutrients- especially micronutrients - minerals, vitamin k and $B_{12}$. Antibiotic also affects affect gut motility, transit time and colon processes. Food components like fat, fiber and carbohydrates digestion, absorption can be affected. Drug-meal spacing is important and fluid allowance for antibiotics should be adequately managed. Long duration antibiotic therapy can have negative impact on nutritional status and gut health, hence should be managed with probiotics. Geriatrics, pediatrics, patients with hepatic, gastrointestinal diseases and surgeries needs to be protected by preventive nutrition therapies.

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