The effects of drugs on nutrition

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Introduction

Many interactions exist between drugs and nutrition. In many instances drugs and nutrients use similar sites for absorption, and are metabolised and excreted through the same organs.

Poor nutritional status can impair drug metabolism. People who are at higher risk for drug–nutrient interactions include those who:

- Have impaired hepatic, renal or gastro-intestinal function.
- Are nutritionally compromised due to chronic disease.
- Have recent weight loss or dehydration.
- Are on multiple and prolonged drug therapy.
- Are at the extremes of age with changes in lean body mass, total body fluids and plasma protein concentration.

Drug treatment can have a detrimental effect on nutritional status and drugs which are most likely to have nutritional implications are those that:

- Have a narrow therapeutic window.
- Need to be taken for prolonged periods.
- Have implications in terms of the timing of food intake.
- Necessitate dietary restrictions or regulation.
- Have side effects which impact on appetite and gastric function.
- Compete directly with nutrients.

The elderly are documented to consume most of the prescription and non-prescription medication dispensed due to chronic diseases such as, hypertension, diabetes and cardiovascular disease. They are also the more likely to receive drugs which may impact on nutritional status e.g. cytotoxics, anti-Parkinson's drugs. The reason(s) for the known increased susceptibility for drug-induced adverse events include diminished salivation, which can cause bulky drugs to stick to the oesophageal mucosa; failing hearing, vision, memory; and impaired mobility, which often leads to poor compliance or incorrect dosing.

Drug–nutrient interactions are broadly divided into drugs that i) adversely affect nutritional status by impairing the intake of food and/or, the absorption, metabolism and excretion of nutrients, and ii) conversely the adverse effect of nutritional status on drug metabolism, by impairing their absorption and therefore their efficacy.

Effects of drugs on nutrition

Many medications have specific recommendations regarding food intake (Table I) in order to maximise their absorption. Such recommendations can alter the usual pattern of food intake and may reduce overall food intake when meals are omitted, as is often the case in the elderly.

Anorexia is a common side effect of several medications resulting in weight loss and patients with pre-existing malnutrition should be closely monitored when initiating medicines associated with hypogeusia and/or dysgeusia (Table II).

Drugs are also associated with weight changes (Table III), nausea and vomiting (Table IV), decreased gastrointestinal motility (Table V), diarrhoea (Table VI), xerostomia (Table VII), and taste (Tables VIII and IX), as well as olfactory disturbances (Table X).

Table I: Examples of medication with specific dosing instructions

- Thirty minutes before food, or on an empty stomach: phenoxymethylpenicillin, itraconazole
- Not to be taken with indigestion medication: ketoconazole
- Not to be taken with iron, zinc or antacid preparations: ofloxacin, levofloxacin, doxycycline, penicillamine
- Not to be taken with milk, iron, zinc or antacid preparations: ciprofloxacin, norfloxacin, tetracycline

Table II: Drugs associated with anorexia or weight loss

Amantadine
Digoxin
Fluoxetin
Levodopa
Lithium
Metformin
Penicillamine
Topiramate
Nortriptyline

Table III: Drugs associated with weight gain

Tricyclic antidepressants, excluding nortryptiline
Valproate
Beta blockers
Oral contraceptives
Antipsychotics
Steroids
Anabolic steroids

Table IV: Drugs associated with nausea and vomiting

- Action on chemoreceptors in the GIT: cytotoxics, potassium, iron preparations, antibiotics
- Action at the chemoreceptor trigger zone: cytotoxics, anaesthetics, opiates, nicotine, levodopa, selective serotonin reuptake inhibitors (antidepressants)

Table V: Drugs associated with decreased gastrointestinal motility

- Anticholinergic effect: tricyclic antidepressants, oxybutynin, propantheline
- Opiates: morphine, codeine, ondansetron

Table VI: Drugs associated with diarrhoea

Erythromycin
Metoclopramide and domperidone
Broad-spectrum antibiotics
Misopristil
Proton-pump inhibitors
Antivirals and antiretrovirals
Magnesium salts
Iron
Lithium (toxicity)
Digoxin (toxicity)
Acarbose
Metformin
Colchicine (toxicity)

Table VII: Drugs associated with dry mouth

Anticholinergic drugs: atropine, oxybutynin, hyoscine, benztropine	Sedatives: diazepam, temasepam
Antidepressants and antipsychotic drugs	Muscle relaxants
SSRIs citalopram, fluoxetine, paroxitine, venlafaxine	Orphenadrine
Tricyclics: amitryptiline, imipramine	Analgesics: codeine, methadone, tramadol, buprofen
Diuretics furosemide, chlorothiazide	Antihistamines: astemisole, chlorphenamine
Antihypertensives: captopril, enalapril, lisinopril	Loratidine
Clonidine, methyldopa	Carbamazepine, carbidopa, levodopa, ipratropium

Table VIII: Drugs associated with ageusia and hypogeusia

ACEI	Azathioprin	Corticosteroids	Metochlopramide
Amphetamines	Baclofen	Diltiazem	Nifedipine
Amiloride	Benzodiasepines	Furosemide	Spironolactone
Amphoteracin	Cephalosporins	Levodopa	Sucralfate
Ampicillin	Claritromicin	Metformin	Tricyclic antidepressants
Asperin	Clopidogrel	Methotrexate	Venlafaxine

Table IX: Drugs associated with dysgeusia

Bitter taste	Metallic taste
Aspirin	Allopurinol
Carbamazepine	Captopril
Clarithromycin	Ethambutol
5 fluoro-uracil	Lithium
Isosorbide mononitrate	Metformin
Levodopa	Metronidazole
Risperdal	Sartan antihypertensives
	Sulphasalazine
	Nifedipine

Medications can also impair the absorption of nutrients by forming pharmacological compounds, changing gastric acidity, altering the rate of absorption, reducing bacterial flora and directly irritating or damaging the lining of the digestive tract (Table XI).

Effects of nutrition on drug metabolism

After oral intake the drug is transported from the gut lumen to the intestinal erythrocytes. Transported in the blood the drug is usually plasma protein bound. Deactivation occurs by a two-stage metabolic process oxidation by the microsomal enzymes involving NADPH and cytochrome P450 in the liver, lungs and small intestine and conjugation with glucuronic acid, sulphate or glycine. The conjugate is then excreted in the urine or bile.

The absorption of a drug can be reduced, delayed or increased by food consumption (Table XII). The presence of food in the stomach and proximal intestine may reduce drug absorption as a result of:

- Delayed gastric emptying.
- Altered gastrointestinal pH.
- Competition for binding sites with nutrients.
- Chelating of drugs by food cations, e.g. tetracycline with calcium ions in milk.
- Dietary fats impeding the absorption of hydrophilic drugs.

Table X: Drugs associated with olfactory disturbances

ACE inhibitors	Calcium-channel blockers	Gemfibrozil	Quinolones
Amikacin	Chlorhexidine	Gentamycin	Statins
Amiodarone	Cocaine	Isotretanoin	Streptomycin
Amphetamine	Corticosteroids	Levodopa	Sumatriptan
Amoxicillin	Decongestants	Methotrexate	Terbinafine
Beta blockers	Doxycycline	Pentamidine	Tobacco

Table XI: Impaired nutrient absorption

Drug	Mechanism	Duration of use	Adverse effect
Antacids, e.g. Maalox®	Bind to phosphate	Chronic	Weakness, fatigue, osteomalacia
Antibiotics, e.g tetracycline	Bind calcium and reduce calcium absorption, damage intestinal lining and reduce bacterial flora	Acute and/or chronic	Bone and tooth lesions in children, yellow-brown discolouration of nails, impair nutrient absorption, diarrhoea
Laxatives	Increase intestinal motility	Chronic	Reduce vitamin and nutrient absorption
Anti-inflammatories, e.g. aspirin	Damage intestinal lining and reduce enzymes needed for absorption	Chronic	Fatigue, weakness, bleeding ulcers
Hypoglycaemic drugs, e.g. sulphonylureas	ß sitotrophic: stimulate release of insulin, increase carbohydrate utilisation	Chronic	Decrease blood glucose, fatigue
Lipid-lowering drugs, e.g simvastatin	Reduce HMG-CoA reductase enzyme	Chronic	Muscle pain
Immunosupressants, e.g methotrexate	Inhibit the enzyme dihydrofolate reductase	Chronic	Folate deficiency with mouth and gut ulcers, decreased bone marrow activity
Anticonvulsants, e.g Epanutin®	Decrease calcium absorption, decrease vitamin D (dihydroxy-folic acid reductase inhibitor)	Chronic	Macrocytic anaemia, rickets, osteomalacia, delirium, depression
Anti-depressants, e.g MAOIs	Inhibit breakdown of endogenously produced amine neurotransmitters as well as dietary amines	Chronic	Interaction with thyramine in cheese and biltong causes hypertensive crisis.
Diuretics, e.g. Lasix®	Increase urinary loss of potassium, magnesium sodium and calcium with fluid loss	Acute and/or chronic	Muscle weakness, decreased mentation, fatigue, muscle cramps
Antihypertensive drugs, e.g ACE inhibitors (Coversyl®)	Inhibit R-A-A-system	Chronic	Elevated potassium levels with impaired renal function, increase sodium excretion

Table XII: Absorption of selected drugs that may be affected by food

Drugs with reduced absorption	
Antibiotics	Amoxicillin, penicillin
ACE inhibitors	Captopril
Ethanol	Alcoholic beverages
Anti-Parkinson's	Levodopa
Bronchodilators	Theophylline
Drugs with delayed absorption	
Anti-ulcer	Cimetidine
NSAIDS	Diclofenac
Antiarrythmics	Digoxin
Antidiabetics	Glipizide
Antibiotics	Metronidazole

Drugs with increased absorption	
Antibiotics	Nitrofurantoin
Anti-anxiety	Diazepam
Antihypertensives	Hydralazine
Anti-manic	Lithium
Diuretics	Chlorthiazide

Nutrients can also impair the absorption of drugs by forming compounds, deficiency in carrier and/or transport proteins, adverse effects on drug metabolism and /or excretion (Table XIII)

Table XIII: Impaired drug absorption

Nutrient	Mechanism	Adverse effect
Minerals, e.g. iron sulphate	Form compounds with antibiotics: tetracyclines, ciprofloxacin and reduce absorption	Reduced efficacy
Vitamins, e.g. vitamin K	Inhibit the effect of coumadin (warfarin), increasing production of Factor II, IIV, IX and X	Decrease clotting time
Indolic compounds, e.g. broccoli, cabbage, cauliflower	Increase rate of drug metabolism	Increased rate of drug metabolism
Flavones in citrus	Stimulate liver drug metabolism	Stimulated liver drug metabolism
Grapefruit	Inhibit cytochrome P450, affects the intestinal transporter protein	Altered bioavailability and pharmacokinetics of calcium-channel blockers and statins
Cranberry juice	Interact with coumadin	Increased INR , increased risk of bleeding
Vitamin C	Increase urinary acidity, decrease elimination of salicylates, e.g aspirin	Ulcerogenic

Table XIV: Examples of drugs not to be taken with grapefruit juice

Drug class	Examples
Anti-angina	Norvasc®, nifedipine
Anticonvulsants	Carbamazepime
Antihypertensives	Norvasc®, Plendil®
Anti-ulcer	Cisapride

Conclusion

There is a direct correlation between the number of medications taken by a patient and the incidence of side effects. This is compounded by the physical condition of the patient, nutritional status, age and underlying chronic diseases. Increasingly important is the fact that drug therapy may have an impact on the nutritional status of the patient both positive and negative and that a nutritional assessment should be part of the review of the patient's drug therapy.