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Nutritional Status and Drug Therapy in Older Adults

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Abstract

The aging process is characterized by a high level of complexity with a progressive decline in several physiological systems coexisting with multiple chronic diseases (comorbidity), presence of cognitive and functional impairment and geriatric syndromes. Use of multiple drugs and problems in nutritional status are relevant components of this complex spectrum. Nutritional status may influence the pharmacokinetic and pharmacodynamic of many drugs, conversely drugs can impair nutrition by causing adverse drug reactions such as nausea and loss of appetite. The present article describes potential interactions between nutritional status and drug use in the elderly. The role of nutritional status in the pharmacokinetic of drugs (including absorption, distribution, metabolism and elimination) is reviewed and most relevant food drugs interactions are assessed.

Malnutrition and nutritional problems are common conditions in older adults. Multiple chronic disease, inflammation, cognitive and functional impairment, geriatric syndromes (including delirium, falls or chronic pain) and drug use (i.e. polypharmacy, adverse drug reactions) may play a role in the onset of malnutrition and nutritional problems. In particular, drugs and nutrition are closely connected. Nutritional status may influence the pharmacokinetic and pharmacodynamic of many drugs, conversely, drugs can impair nutrition by causing adverse drug reactions such as nausea and loss of appetite. The present article will assess potential interactions between nutritional status and drug use in the elderly.

Keywords: Pharmacokinetic; Pharmacodynamic; Nutritional status

Changes in Nutritional Status in Advanced Age and Drug Pharmacokinetic

Changes occurring in advanced age can impact on nutritional status, including modifications in secretion and action of hormones that regulate appetite, changes in gastrointestinal motility, taste loss and functional decline of multiple systems, including organs that directly affect drug disposition.

Several publications have shown that pharmacokinetic of drugs (including absorption, distribution, metabolism and elimination) may be modified by nutritional status, determining therapeutic or toxic response [1].

Drug absorption can be impaired by different factors commonly observed in the elderly: decreased intestinal blood flow, altered gastrointestinal motility, increased gastric pH [2], diminished gastro-intestinal absorption. For example, absorption of drugs normally soluble at low pH (i.e. ketoconazole, itraconazole and dipyridamole), could be reduced when gastric pH increases [3].

Also *drug distribution* might be influenced by nutritional changes occurring in advanced age. Aging is characterized by changes in body composition, characterized by gain of fat mass and loss of lean mass. These changes lead to reduction of drug's volume of distribution and might result in changes in drug concentration. *Water-soluble drugs, such as lithium, ACE (angiotensin-converting enzyme) inhibitors and digoxin, have a reduced distribution volume because of reduction of muscle mass and total body water in the elderly. This circumstance increases the risk for higher drug concentrations. In addition, water volume in elderly often fluctuates between extremes of over and underhydration and so it is difficult to regulate therapeutic levels for water soluble medications.* Fat soluble drugs (i.e. diazepam, antiarrhythmics) may have longer half lives because of a slower release from fatty tissues. In addition, aging decreases drug-binding capacity: elderly with protein energy malnutrition show a reduced synthesis of the hepatic protein and enzymes, with reduced levels of plasma protein concentration, particularly albumin (up to a 20%). Hypo-albuminemia is accompanied by a diminished protein-binding capacity, an increase in free drug concentration and the risk of developing toxic drug concentrations, especially for those with a narrow therapeutic index (anticoagulants, hypoglycemic, sulfamides, digitalis).

Metabolism of many drugs might be impaired by physiological changes observed during aging, including decreased intestinal blood flow, reduced perfusion of the liver and kidneys. *Particularly, a reduction in hepatic blood flow might result in a decrease in hepatic cleareance of drugs with a high hepatic extraction ratio (labetalol, levodopa, propranolol, verapamil)* [4]. *Presystemic cleareance, also known as first pass effect, occurring primarily in the intestine and in the liver, is often reduced and drugs bioavailability is impaired.* Phase I function (oxidation, reduction and hydrolysis) is predominantly reduced in advanced age, while phase II (conjugation) does not appear to be markedly modified. These alterations are enhanced by reduction in cytocrome P450 isoenzymes activity. Guengerich [5] investigated the CYP450 content in liver biopsy sample in 226 people and found that CYP content declines at rate of approximately 0.07 nmol/g of liver after 40 years of age.

Concerning drug *elimination*, *renal function progressively decreases with increasing age and latent renal insufficiency is a relevant problem in the elderly.* The lack of correlation between lean body weight and muscle mass may determine overestimation of creatinine clearance. In addition, dehydration or diuretic therapy, common concerns among older adults, may precipitate acute renal insufficiency leading to

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altered excretion of many drugs and increased half-life and risk of late toxicity.

Food-Drug Interactions

Nutrients and drugs might share the same receptors for absorption, metabolism and excretion. Elderly patient are particularly at risk of food-drug interactions because of the elevated number of drugs used. It has been estimated that more than 30% of all prescribed drugs are taken by this population [6].

Food drug interactions are defined as alteration of pharmacokinetics or pharmacodynamics of a drug or nutritional element, or a problem in nutritional status as a consequence of the use of a drug (Table 1). It results in a reduction or an increment in bioavailability of a drug which may lead to greater risk of treatment failure or increased toxicities, respectively. Four types of drug-nutrient interactions are known.

Type I - Direct interaction of food and drugs

It refers to interactions between drug and nutritional element through biochemical (hydrolysis, oxidation) or physical reactions. These are common when drugs and nutritional formulation are co-administered intravenously or by enteral feeding and result in a reduction in the amount of drug or nutrient absorbed. Several recommendations exist to minimize type I drug-nutrient interactions: preformulated oral solution or suspensions are preferred instead of crushing tablets when administering drugs through enteral feeding tubes, drugs should not be mixed directly with feeding enteral or parenteral formulas and tubes should be flushed with water before and after drug administration.

Type II - Interactions with absorption

The presence of food in the stomach and proximal intestine may reduce drug absorption through delayed gastric emptying, competition for binding sites with nutrients, chelating of drug by food cations. In addition, meals rich in fat, stimulating the release of bile salts, increase the dispersion of highly lipophilic drugs. Concomitant release of cholecystokinin slows gastro-intestinal motility and increases the contact time between drug and intestine wall. It is well known that to optimize absorption, certain drugs should be taken with food while other drugs between meals. For example, blood concentration of tetracycline can be reduced by over 50% if consumed with milk and dairy products because it is chelated by calcium.

Type III - Interaction with distribution

These interactions occur when drugs and nutritional element entered the systemic circulation. They are related to changes of cellular or tissue distribution or transport. For example, fat soluble drugs may have a longer half life as a consequence of an increment in fat mass because of a slower release from fatty tissues.

Type IV - Interaction with excretion

These interactions involve drug/nutrient clearance and elimination modulated by enterohepatic and/or renal metabolism. An example of this type of interactions is represented by CYP450 drug metabolizing enzymes and some nutrients. Grapefruit juice is a selective intestinal CYP 3A4 inhibitor and the overall concentration of some drugs can be increased by more than fivefold when taken with grapefruits. Drugs that undergo extensive first-pass effect are similarly involved in these kinds of interactions: propranolol, metoprolol can have an increased bioavailability after a high protein meal owing to enhanced hepatic blood flow [7] whereas methyldopa can have a decreased bioavailability when ingested with a protein-rich meal [8].

In addition, some dietary protein can interact with medications (Table 2). For example, MAO-I drug class can interact with the amino acid tyramine that is contained in aged cheese, fermented food and red wines. Tyramine is an indirect sympathomimetic amine that releases norepinephrine from the adrenergic neurons, causing a significant pressor response. Tyramine is metabolized by the enzyme monoamine oxidase before any significant increases in blood pressure. If the activity of the enzyme is reduced by MAO-I drugs, severe and potentially fatal increment in blood pressure can occur. Finally, Vitamin K-rich foods (broccoli, green leafy vegetables) can alter response to anticoagulant agents as warfarin. When ingested in high amounts they could be associated with anticoagulants failure with consequent need for higher dose. Similarly, an increased risk of bleeding is observed when elderly who have been stable on warfarin suddenly decrease their intake of this vitamin k-rich food.

Polypharmacy, Adverse Drugs Reactions and Nutritional Status

Older adults show the co-occurrence of multiple chronic diseases (comorbidity) and conditions that cannot be ascribed to a specific organ

Food-Drug Interactions	Drug-Nutrient Interactions
Changes in lean body mass total body fluids and plasma protein concentrations Compromised nutritional status due to chronic disease Impairing in gastrointestinal, hepatic e/o renal function On prolonged polypharmacy	Drugs that need to be taken for prolonged periods Drugs with a narrow therapeutic windows (warfarin, digoxin) Drugs that require dietary restriction or regulation (warfarin and vit k rich food) Drugs associated with impaired gastric motility Drugs associated with anorexia, nausea, vomiting or taste alterations

Table 1: Risks factors for food-drug and drug-nutrient interactions in the elderly.

Drug	Food-Nutrient	Effect
Acid Blocker	Calcium, Phosphorus, iron	Drug binds minerals and reduce their absorption
Antihyperlipidemic	Fat soluble vitamins(A,E,D,K)	Drug decreases vitamin absorption
Antihypertensive drugs, E.g ACEI	Electrolytes	Drugs elevates potassium levels, increase sodium excretion
Bisphosphonates	Calcium, iron	Calcium, iron and other divalent cations determining the formation of insoluble chelates that hinder the absorption of drug
Laxatives	Vitamins and minerals	Drug increases motility reducing absorption
Levodopa	Amino acids	Drug reduces its absorption
MAO inhibitors	Thyramine in cheese	Drugs inhibits breakdown of amine contained in dietary products. Interaction can cause hypertensive crisis.
Proton Pump Inhibitors	Calcium, iron, magnesium, B12	PPI reduces their adsorption

Table 2: Drugs- food interactions.

system pathology and have multiple causes (the so-called geriatric syndromes) This high degree of complexity is further complicated by the presence of cognitive and functional impairment, which are common in this population. Pharmacological treatment of this complex patient represents a challenge for prescribing physicians, as confirmed by the high prevalence of polypharmacy, defined as the concomitant use of multiple drug therapies, and resulting iatrogenic illness observed in this population. According to a recent study, more than 10% of older adults living in the community receive ≥ 10 drugs and this rate rises among institutionalized elderly [9]. Although the evidence of benefits, including prevention or control of disease and symptom relief, is compelling, there is also evidence that in the elderly a greater consumption of medications contributes to decreased medication adherence [10], increased risk of adverse drug events [11] and it is strongly associated with decline in nutritional status, functional ability and cognitive capacity [12].

Drug treatment and polypharmacy may worsen nutritional status, most commonly as a manifestation of adverse drug effects [12-14]. Several studies have shown an inverse association between the number of drugs and nutritional status [15-17]. In particular, a recent cross-sectional study performed among community-dwelling elderly aged 65 or older found a significant reduction in the intake of fiber, several fat –soluble vitamins (A,D, E) and water-soluble vitamins (B1, B3 and B7) and an increased intake of glucose, sodium, and dietary cholesterol with increasing number of drugs used.

In the elderly, drugs most likely to have nutritional implication are those with a narrow therapeutic window (i.e. Warfarin, Clozapine, Digoxin), those with sharp dose-concentration profile (i.e. MTX, Phenytoin) or those requiring an high plasma concentration (i.e. Cordarone or antibiotics). However, drugs taken for prolonged periods (such as those used to treat chronic conditions or those requiring specific rules in term of the timing of food intake, dietary restrictions or regulation) are at high risk for nutritional problems and drug-nutrient interaction.

In addition, drugs can reduce food intake through a variety of mechanisms. Several drugs may affect appetite by either central or peripheral effects, inducing sedation or evoking adverse response when food is ingested [18]. Centrally acting mechanisms include catecholaminergic or dopaminergic (L-dopa) modulators which act to suppress appetite. Peripherally acting mechanisms lead to a reduction of appetite directly by inhibition of gastric emptying (L-Dopa) or indirectly by causing nausea and diarrhea (Table 3), xerostomia, ageusia (Table 4) or olfactory disturbances [19]. Interestingly, a recent study performed in hospitalized older adults [20] showed that advanced age (>75years) and polypharmacy were positively and independently related to an increased risk of reduced sour taste perception. Indeed, several drugs have been associated clinically with taste complaints such as "loss of taste" (ACE inhibitors, Cephalosporins, Clopidogrel, Metformin), "bitter taste" (aspirin, L dopa, carbamazepine) or "metallic taste" (allopurinol, captopril, nifedipine).

Nutritional implications of polypharmacy can be also mediated by a drug-induced malabsorption of nutrient such as vitamins or fluid and electrolytes imbalance (Table 2). For instance, chronic corticosteroid use can determine a net negative calcium balance and decrease bone mineral density owing to suppression of intestinal absorption of calcium or increment in renal calcium and phosphate excretion [21]. Metabolic effects of a long treatment with corticosteroids include also impaired glucose tolerance, gastric damage, increased protein catabolism and reduced protein synthesis with consequent reduction of muscle's mass, factor already involved in physiological modification age related and elderly frailty. Proton pump inhibitors (PPIs) are widely used in older people to treat acid peptic disorders and to reduce risk of gastrointestinal (GI) bleeding related to the use of non-steroidal anti-inflammatory drugs (NSAIDs) and low-dose aspirin. Noticeably, only 38.6% of PPI prescribing was appropriate according to National Institute for Clincal Excellence (NICE) recommendations and long term therapy was shown to be associated with several risks. *Chronic PPI use seems to affect iron* [22], *magnesium* [23-25] *calcium absorption and increase the risk of hip fractures. Interestingly also vitamin B12 serum levels inversely correlates with the time of PPI use, suggesting that this drug may interfere with vitamin B12 absorption and this phenomenon is not reduced by oral supplementation of vitamin B12.* [22]. Several studies [26] confirm the relationship between the use of PPIs and prevalence of diarrhea caused by alteration in gastric and intestinal wall. Treatment with PPIs induces a clinical state similar to atrophic gastritis with markedly reduced gastric acid production and pepsin activity because of high gastric pH. This condition is frequently associated with bacterial overgrowth [27,28] which may result in malabsorption of fat, carbohydrate, protein, micronutrients and clinical manifestations of abdominal pain, diarrhea, and even malnutrition [29].

Conclusion

The aging process is characterized by a high level of complexity which makes the care of the elderly a challenging task. A progressive decline in several physiological systems coexists with multiple chronic diseases (comorbidity), presence of cognitive and functional impairment and several geriatric syndromes. Polypharmacy and problems in nutritional status are relevant components of this complex spectrum. Limiting drug prescriptions to essential medications and periodic revaluations of drug regimens are essential to minimize drug–nutrient interactions, ultimately leading to improvement in nutritional status [30]. Similarly, evaluation of nutritional status is a key step to improve quality of prescribing: it is crucial to identify nutritional problems which can be related to drug use and assessment of nutritional factors which may influence drug efficacy.

Drugs associated with nausea and vomiting	Drugs associated with diarrhoea
Antibiotics Cytotoxic Iron preparations Levodopa Nicotine Opioatyes Potassium Selective serotonin reuptake inhibitors(SSRI)	Broad-Spectrum antibiotics Colchicine Digoxin Erythromicine Lithium Metformin Metoclopramide and domperidone Proton Pump inhibitors

Table 3: Drugs associated with nausea, vomiting and diarrhea.

Drugs associated with dry mouth	Drugs associated with ageusia/ hypogeusia
Amitryptiline Atropine Captopril Chlorphenamine Citalopam Codeine Diazepam Enalapril Fluoxetine Levodopa Paroxetine	ACEI Ampicillin Benzodiazepines Clopidogrel Diltiazem Levodopa Metformine Nifedipine Spironolactone Tricyclic antidepressants

Table 4: Drugs associated with dry mouth, hypogeusia or ageusia.

References

1. Crogan NL, Shultz JA, Adams CE, Massey LK (2001) Barriers to nutrition care for nursing home residents. J Gerontol Nurs 27: 25-31.
2. Russell TL, Berardi RR, Barnett JL, Dermentzoglou LC, Jarvenpaa KM, et al. (1993) Upper gastrointestinal pH in seventy-nine healthy, elderly, North American men and women. Pharm Res 10: 187-196.
3. Pickering G (2004) Frail elderly, nutritional status and drugs. Arch Gerontol Geriatr 38: 174-180.
4. Pan SH, Lopez RR Jr, Sher LS, Hoffman AL, Podesta LG, et al. (1996) Enhanced oral cyclosporine absorption with water-soluble vitamin E early after liver transplantation. Pharmacotherapy 16: 59-65.
5. Guengerich FP (1995) Influence of nutrients and other dietary materials on cytochrome P-450 enzymes. Am J Clin Nutr 61: 651S-658S.
6. Chan LN (2006) Drug-Nutrient interactions, Modern Nutrition in Health and Disease, Baltimore, Lippincott Williams & Wilkins.
7. Melander A, Danielson K, Scherstén B, Wåhlin E (1977) Enhancement of the bioavailability of propranolol and metoprolol by food. Clin Pharmacol Ther 22: 108-112.
8. Roe DA (1994) Medications and nutrition in the elderly. Prim Care 21: 135-147.
9. Kaufman DW, Kelly JP, Rosenberg L, Anderson TE, Mitchell AA (2002) Recent patterns of medication use in the ambulatory adult population of the United States: the Slone survey. JAMA 287: 337-344.
10. Gray SL, Mahoney JE, Blough DK (2001) Medication adherence in elderly patients receiving home health services following hospital discharge. Ann Pharmacother 35: 539-545.
11. Onder G, Petrovic M, Tangiisuran B, Meinardi MC, Markito-Notenboom WP, et al. (2010) Development and validation of a score to assess risk of adverse drug reactions among in-hospital patients 65 years or older: the GerontoNet ADR risk score. Arch Intern Med 170: 1142-1148.
12. Jyrkkä J, Enlund H, Lavikainen P, Sulkava R, Hartikainen S (2011) Association of polypharmacy with nutritional status, functional ability and cognitive capacity over a three-year period in an elderly population. Pharmacoepidemiol Drug Saf 20: 514-522.
13. Agostini JV, Han L, Tinetti ME (2004) The relationship between number of medications and weight loss or impaired balance in older adults. J Am Geriatr Soc 52: 1719-1723.
14. Fabian E, Bogner M, Kickinger A, Wagner KH, Elmadfa I (2011) Intake of medication and vitamin status in the elderly. Ann Nutr Metab 58: 118-125.
15. Griep MI, Mets TF, Collys K, Ponjaert-Kristoffersen I, Massart DL (2000) Risk of malnutrition in retirement homes elderly persons measured by the "mini-nutritional assessment". J Gerontol A Biol Sci Med Sci 55: M57-63.
16. Chen CC, Tang ST, Wang C, Huang GH (2009) Trajectory and determinants of nutritional health in older patients during and six-month post-hospitalization. J Clin Nurs 18: 3299-3307.
17. Schilp J, Wijnhoven HA, Deeg DJ, Visser M (2011) Early determinants for the development of undernutrition in an older general population: Longitudinal Aging Study Amsterdam. Br J Nutr 106: 708-717.
18. Welling PG (1996) Effects of food on drug absorption. Annu Rev Nutr 16: 383-415.
19. Van Zyl M (2011) The effect of drugs on nutrition. S Afr J Clin Nutr 24: S38-S41.
20. Toffanello ED, Inelmen EM, Imoscopi A, Perissinotto E, Coin A, et al. (2013) Taste loss in hospitalized multimorbid elderly subjects. Clin Interv Aging 8: 167-174.
21. Gura KM, Couris RR (2002) Drug-induced bone disease. US Pharmacacist 27: HS43-57.
22. Ito T, Jensen RT (2010) Association of long-term proton pump inhibitor therapy with bone fractures and effects on absorption of calcium, vitamin B12, iron, and magnesium. Curr Gastroenterol Rep 12: 448-457.
23. Epstein M, McGrath S, Law F (2006) Proton-pump inhibitors and hypomagnesemic hypoparathyroidism. N Engl J Med 355: 1834-1836.
24. Cundy T, Dissanayake A (2008) Severe hypomagnesaemia in long-term users of proton-pump inhibitors. Clin Endocrinol (Oxf) 69: 338-341.
25. Mackay JD, Bladon PT (2010) Hypomagnesaemia due to proton-pump inhibitor therapy: a clinical case series. QJM 103: 387-395.
26. Teramura-Grönblad M, Hosia-Randell H, Muurinen S, Pitkala K (2010) Use of proton-pump inhibitors and their associated risks among frail elderly nursing home residents. Scand J Prim Health Care 28: 154-159.
27. Maton P (1993) Omeprazole administration as a model for atrophic gastritis. Chronic gastritis and hypochlorhydria in the elderly. Boca Raton, FL: CRC.
28. Saltzman JR, Kowdley KV, Pedrosa MC, Sepe T, Golner B, et al. (1994) Bacterial overgrowth without clinical malabsorption in elderly hypochlorhydric subjects. Gastroenterology 106: 615-623.
29. Badenoch J, Bedford PD, Evans Jr (1955) Massive diverticulosis of the small intestine presenting with steatorrhea and megaloblastic anemia. Q J Med 24: 321-330.
30. Schmidt LE, Dalhoff K (2002) Food-drug interactions. Drugs 62: 1481-1502.