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DRUG INDUCED MALABSORPTION – A REVIEW

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ABSTRACT
Drug-induced malabsorption occurs when medications impair nutrient absorption by inhibiting enzymes, damaging mucosal tissue, or altering gut microbiota. Medications such neomycin, cholestyramine, antacids, and methotrexate may induce deficits in vitamins A, D, E, K, B12, calcium, and iron, thereby exacerbating nutritional condition. The processes encompass enzyme inhibition, direct mucosal injury, compound formation, and modified gut motility. Clinical symptoms vary from persistent diarrhoea to subclinical deficits. Management techniques encompass the identification of causal medications, modification of therapy, and supplementation of lacking nutrients. Research underscores the significance of vitamin A in mitigating methotrexate-induced malabsorption. Healthcare professionals should oversee vulnerable persons and execute early interventions via food adjustments and medication evaluations. Future investigations should examine specific therapeutics to reduce drug-induced intestinal damage while maintaining therapeutic efficacy.

KEYWORDS: Drug-induced malabsorption, vitamins A, D, E, K, B12, calcium, diarrhoea.

INTRODUCTION

Malabsorption refers to the inadequate absorption of nutrients when they are eat, it's also correlate with maldigestion the refer to poor digestion to absorb the nutrient in intestinal lumen.[1] The phrase "drug-induced malabsorption" refers to the way certain medications can hinder the gastrointestinal tract's capacity to absorb nutrients.[2] Medication like antibiotic and PPI significantly alter the intestinal flora, impacting gut sensory and motor capabilities. While some medications (such as iron and gold compounds) affect intestinal permeability.[3] Because drug-induced malabsorption has many different origins and individual responses to drugs vary, it is difficult to pinpoint its precise prevalence. A study of patients using antihypertensive drugs revealed that 51 (0.11%) of the 44,775 participants had intestinal malabsorption or enteropathy. However, when comparing several types of antihypertensive medications, this investigation did not identify a significant difference in the incidence of intestinal malabsorption or enteropathy.[4] consequence of the DI-Malabsorption like direct mucosal damage, enzyme inhibition, complex formation, altered gut motility and vitamin deficiencies.[5] Clinical implement for DI-malabsorption like following ESPEN guideline on choric intestinal failure, otherwise medication interaction or adverse monitoring, alternative therapies, monitor the nutrient level, therapy adjustment to monitor the malabsorption patient for managing the DI-malabsorption.[6] Management of DI-malabsorption is finding the drug cause the syndrome, discontinue or change the medicine and nutrient supplementation and monitor the level of nutrient.[1]

Drugs may disrupt the digestion of food. A-glucosidase inhibitors, such as acarbose, utilised in diabetic patients, and lipase inhibitors like orlistat, commonly used for obesity treatment, may induce symptoms indicative of malabsorption. Certain medications induce selective malabsorption, including tetracycline (which chelates calcium), cholestyramine (which binds bile acids and vitamin B12), and aluminium (which precipitates calcium); however, they infrequently result in clinical complications. Other medications may induce structural damage resulting in subtotal villous atrophy, which can produce malabsorption symptoms or specific nutritional deficits. These adverse events are extremely rare, with the primary offenders being mefenamic acid (a nonsteroidal anti-inflammatory drug commonly utilised for symptomatic relief of dysmenorrhea), colchicine, neomycin, methotrexate, ,metformin, fenemates, and chemotherapeutic drugs disrupt nutrition absorption via inducing mucosal injury. Drug-induced malabsorption may aggravate the patient's inadequate nutritional condition.[7]

Malabsorption occurs when dysfunction in any of these components results in inadequate nutrient absorption due to various causes, which can be categorised into three pathways. (i) maldigestion, associated with mixing and digestive mediators; (ii) mucosal or mural aetiologies, including coeliac disease (CD)and (iii) microbiological

aetiologies. There are three physiological phases of absorption: luminal digestion, mucosal digestion, and mucosal absorption. The luminal phase entails the degradation of proteins, carbohydrates, and fats by digestive enzymes and bile, whereas the mucosal phase involves the hydrolysis of carbohydrates and peptides by enterocyte membrane enzymes (disaccharidases and peptidases). The absorption phase encompasses the transepithelial transport of nutrients, fluids, and electrolytes into the blood vessels via enterocytes.[8][9]

Clinical manifestations of malabsorption

Patients experience symptoms that can be categorized into two categories: intestinal and extraintestinal manifestations. Typically, intestinal characteristics predominate in such types of clinical manifestation of severe malabsorption. Chronic diarrhea is a distinctly subjective symptom. At times, a clear understanding is not achieved, particularly in individuals with chronic symptoms. Watery, diurnal and nocturnal, voluminous, frequent stools are the clinical hallmark of overt malabsorption, although they may not always be present. The color of stool may be affected by its fat content.

Patients with steatorrhea exhibit light, yellow, floating, spongy faces. This subjective assessment must be validated with a thorough inspection of faces. This examination must include faecal weight, stool frequency, and color assessment. Additional gastrointestinal manifestations include anorexia, hyperphagia, nausea, vomiting, abdominal distension, borborygmi, and excessive flatulence. While stomach discomfort is common, abdominal pain is atypical. The cramping discomfort indicates the existence of obstructed intestinal segments (such as Crohn's disease or malignancies), particularly if it continues post-defecation.[10]

Subclinical malabsorption is extensively acknowledged, particularly in coeliac disease. Patients do not exhibit gastrointestinal symptoms; instead, they have persistent and often overlooked extraintestinal manifestations that are infrequently linked to intestinal issues (such as low stature, infertility, bone disease, hematological disorders, etc.) Once again, an asymptomatic progression might be found among relatives of individuals with coeliac disease who exhibit small intestinal mucosal atrophy.[11,12]

When a patient's medical history and physical examination suggest malabsorption disorders without indicating a specific diagnosis, general testing may be initiated. This is especially pertinent in instances where non-specific symptoms, such inadvertent weight loss, prolonged diarrhea, or impaired wound healing, are evident. Laboratory tests serve a supplementary function in the diagnostic process but are not conclusive independently. Blood tests often employed in this context comprise a thorough metabolic panel to evaluate electrolyte imbalances, hepatic, and renal function, alongside a complete blood count to determine anemia. Supplementary tests encompass the quantification of albumin, magnesium, zinc, and phosphorus levels, in addition to evaluations of vitamins like B12, folate, and D.

An iron panel, comprising serum iron, total iron-binding capacity, and ferritin levels, is commonly conducted to assess dietary inadequacies.

Faecal examinations are essential for detecting fat malabsorption diseases, employing diverse procedures that provide varying degrees of sensitivity and precision. A single specimen faecal fat measurement acts as an initial assessment, and if positive or if clinical suspicion persists, a 72-hour faecal fat excretion analysis is conducted as the definitive standard for diagnosing steatorrhea. This test necessitates rigorous compliance with dietary and collecting protocols for precise outcomes. The Sudan III stain, conducted on a spot stool sample, is an effective technique for identifying fat in stool. The acid steatocrit is an additional assay employed to assess fat malabsorption. Near-infrared reflectance analysis (NIRA) serves as a more expedient substitute for the 72-hour faecal fat excretion test, delivering similar accuracy while additionally assessing nitrogen and carbohydrate levels alongside faecal fat.[13][14]

DRUG CAUSING MECHANISM OF MALABSORBTION

Drug-induced malabsorption can result from a variety of medications, including neomycin, cholestyramine, antacids, laxatives, paraminosalicyclic acid, colchicine, methotrexate and oral hypoglycemic medicines.

NEOMYCIN

Neomycin, an aminoglycoside antibiotic, is known to be linked with malabsorption syndromes, especially those that impact lipid absorption. Research has shown that neomycin can cause the precipitation of micellar lipids by interacting with ionized fatty acids and bile acids, which can result in steatorrhea and low cholesterol levels.[15] Neomycin can lead to malabsorption, structural changes in the small intestine, and a secondary deficiency in intestinal disaccharidases. Fortunately, these effects are reversible once the medication is stopped.[16] In tropical populations, a small single dose of neomycin has been found to reduce the absorption of d-xylose and sucrose within six hours, based on tolerance tests.[17]

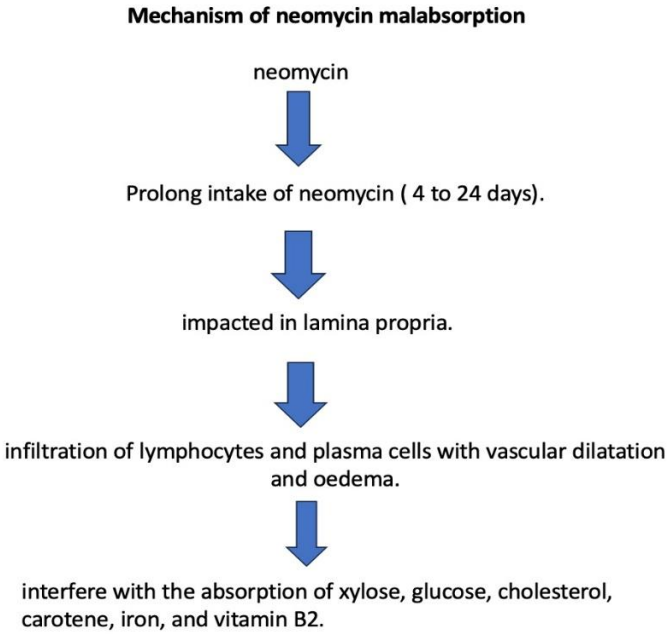

Figure 1.1: Mechanism of neomycin malabsorption.[18]

CHOLESTYRAMINE

Cholestyramine is a bile acid sequestrant primarily used to manage hypercholesterolemia and certain types of chronic diarrhea associated with bile acid malabsorption. By binding to bile acids in the gastrointestinal tract, cholestyramine disrupts their enterohepatic circulation, leading to their excretion and a subsequent reduction in cholesterol levels. This mechanism also makes it effective in treating diarrhea resulting from excessive bile acids entering the colon, a condition known as bile acid malabsorption.[19] Cholestyramine therapy can cause malabsorption of fat-soluble vitamins such as A, D, E, and K, as well as certain medications. By binding to bile acids, cholestyramine may hinder the emulsification and absorption of dietary fats and these vitamins, which could lead to deficiencies. It can also affect the absorption of various drugs, including warfarin, diuretics, thyroid hormones, and beta-blockers. To reduce these interactions, it's advisable to take other medications at least one hour before or four hours after taking cholestyramine.[20]

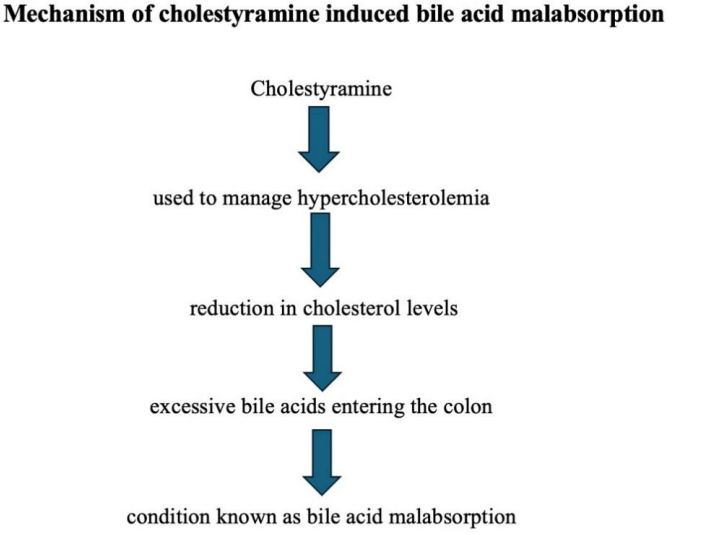

Figure 2: Mechanism of cholestyramine induced bile acid malabsorption.[21]

ANTACID

Calcium: Certain antacids, especially those with aluminum, may contribute to greater calcium loss. This happens because aluminum binds with dietary phosphate, creating insoluble complexes that are eliminated from the body, which in turn decreases calcium absorption.[22]

LAXATIVE

Laxative abuse syndrome (LAS) is a form of Munchausen syndrome marked by the secretive misuse of laxatives. The clinical symptoms can be confusing and may resemble those of inflammatory bowel disease or malabsorption disorders. Patients often report experiencing diarrhea that alternates with constipation, and they may also suffer from nausea, vomiting, and weight loss.[23] Habit-forming properties have been noted in patients with constipation when using stimulant laxatives, unlike osmotic laxatives like milk of magnesia or lubricant laxatives such as liquid paraffin. A combination of milk of magnesia and liquid paraffin could be advantageous for patients with constipation due to their quick and lasting effects, lack of habit-forming characteristics due to their different mechanisms of action, and the absence of side effects like bloating and flatulence.[24]

ANTICONVULSANTS

Some research suggests that phenytoin may have a direct impact on the absorption of calcium in the intestines. Given that phenytoin is known to influence ion movements in the central nervous system, it is reasonable to assume that it could also affect ion movements in other organ systems, including the intestinal tract.[25]

COLCHICINE

The absorption studies utilizing the Schilling technique clearly show significant malabsorption of vitamin B during colchicine treatment. In four subjects, the results dropped to abnormal or borderline abnormal levels, and distinctly abnormal Schilling tests were observed when colchicine was administered directly into the ileum.[26]

BIGUANIDE

The criteria accepted for diagnosing metformin-induced malabsorption of vitamin B12 include evidence of malabsorption during the course of drug therapy and a return to normal absorption after stopping the medication. This pattern was observed in seven patients. The exact mechanism behind this effect remains unclear, but it may involve competitive inhibition or inactivation of enzymes that play a role in absorption.[27]

Reduction of Methotrexate-Induced Malabsorption by Vitamin A

Studies demonstrate that vitamin A helps alleviate malabsorption caused by methotrexate. Yamamoto et al. conducted a study indicating that the coadministration of vitamin A with methotrexate protected the small intestine from injury, enhancing the permeability and bioavailability of nutrients such as D-glucose in rats.[28] In a similar, Dagdemir et al. discovered that the administration of vitamin A before high-dose methotrexate decreased D-xylose malabsorption in paediatric patients with leukaemia and lymphoma. A improved the permeability and bioavailability of nutrients like D-glucose, suggesting it may help reduce the malabsorption associated with Methotrexate.[29]

CLINICAL MANAGEMENT OF MALABSORPTION

The role of proton pump inhibitors in contributing to or even promoting drug-induced intestinal damage is becoming more evident. As a result, there is a strong recommendation to limit their use to genuinely necessary situations, and practical guidelines have been established on when and how to reduce the dosage or discontinue their use.[30] Neomycin antibiotic stop the prolong use or change the medication.[18] phenytoin may have a direct impact on the absorption of calcium in the intestines but did not affect the vitamin D. so if calcium and vitamin D role are similar using vitamin D instead of calcium.[25]

CONCLUSION

Drug-induced malabsorption occurs when drugs inhibit enzymes, damage mucosa, or change the gut flora, which hinders the absorption of nutrients. Drugs such as neomycin, cholestyramine, antacids, and methotrexate might affect nutritional status by causing deficiencies in vitamins A, D, E, K, B12, calcium, and iron. Medication adjustments, vitamin supplements, and patient monitoring are all part of management. According to studies, vitamin A may lessen the malabsorption caused by methotrexate. Clinicians should identify risk factors, make sure that early intervention occurs, and implement individualised care plans that include dietary changes. Targeted therapeutics should be investigated in future studies to reduce intestine damage caused by drugs while maintaining therapeutic efficacy.

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