MedNut Mail

The How, When, Where, Which and Why of pharmacotnutrition

Are transporters really transit terminals?

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https://medicationsandnutrition.online

Commentary

Physiological transporters (aka "drug transporters") are seemingly a one-way gate for substances to pass from one carrier to another. Using an airport as an analogy, a range of carriers – cars, buses, trains, ferries, trams, other – carry a person from somewhere to the departure lounge of the airport, the person passes through one or more one-way gateways, and ultimately is guided to a relevant departure lounge to catch the next carrier – typically an aeroplane. Similarly, in the body, substances are passed from a carrier to a one-way terminal which they pass through to the departure point for the next carrier. Similarly to airline terminals, transporters are static ie they remain in the same location.

This scenario raises a number of questions -

What influences a substance to be carried by a specific carrier?

For example thiamine absorbed from the gut into the epithelial cells can be carried by OCT1 primarily to the liver, or OCT2 primarily to the kidneys, or OCT3 primarily to the muscles – what factor or factors determine which carrier thiamine will ride?

When will a comprehensive database be developed for the transporters and carriers of the substances that comprise foodstuffs?

Identification of transporters and their inhibitors and substrates is important for managing food, pharmaceutical and nutritional impacts. The pharmaceutical industry has been spending significant sums of money globally on this research however the food industry seems to be disregarding the importance of this information. This information is important because there is potentially a significant area for drug-nutrient interactions – and sadly is currently unrecognized.

Should all blood tests to establish nutrient status be fasting only?

If we refer to *MedNut Mail -Elevated pyridoxine and pharmaconutrition* the question could be asked whether the B6 levels in the case study were non-fasting? If the B6 results were based on non-fasting results then the second question is – were inhibitors in action that blocked B6 uptake by the kidneys which resulted in the seriously elevated B6 test results? Fasting test results would minimize inhibitor impact.

How reliable are the pathology results?

Example 1 – there are a number of variants for OCT1 – with OCT1.2 only transporting 50% thiamine instead of 100% thiamine into the liver; blood tests will show normal thiamine status however the liver is being deprived of sufficient thiamine and therefore changes metabolic pathways. Note OCT1.2 is apparently present in about 10% Mediterranean population.

Example 2 – if both pharmaceuticals and foodstuffs inhibit a particular transport then what is the duration of that inhibition, and will any non-fasting blood tests be reliable?

What interventions will you initiate when you see someone's blood test results, or request/suggest blood tests – will you -

- request all nutrient blood tests be fasting?
- be more discerning when viewing thiamine results for those with a Mediterranean background?
- propose a policy at a MAC (Medications Advisory Committee) meeting that all nutrient testing be fasting?

Conclusions

Transporter research is identifying many solutions to old questions, and also identifying many new questions for which we await answers. The more we learn about transporters the more we find out how much we don't know about many aspects of physiological function.

Case study

Medical History with Nutritional Aspect

Amputation	☐	Constipation	☐	Dysphagia	☐	MND	☐
Anaemia	☑	CVA	☐	Enteral Feed	☐	MS	☐
Arthritis	☐	CVD	☐	Falls	☐	Osteoporosis	☐
Cancer	☐	Dementia	☑	Fracture	☐	PD	☐
CCF	☐	Dentures	☑	Frailty	☐	Pressure Area	☐
Chest Infection	☐	Depression	☐	Gout	☐	Renal	☐
COAD	☐	DM Type 1	☐	Hypertension	☐	Ulcer	☐
Confusion	☐	DM Type 2	☐	Incontinent	☐	UTI	☐

Food Allergies: Pork

Other:

Biochemistry with Pharmaconutritional Consequences

No recent relevant results available that may have a pharmaconutrition component.

Medications That May Adversely Affect Nutritional Status

Drug	Vits + Mins	bpp	>90%	N/V	C/D	Wt	App	Tst	Thir	Sal	Drlg	d m	Dys	BSL
EPILIM	B12, B6, biotin, Ca, carnitine, I		☑	NV	CD	↑	↕	☐				☐	☐	☑
EXELON			☐	NV	CD	↓	↓	☐				☐	☐	☐
NEXIUM	(40 mg/day) B1, B12, Ca, Fe,		☑	NV	CD	↑		☑				☑	☐	☐
Quetiapine			☐		C	↑		☐				☑	☐	☐
			▩					▩				▩	▩	▩

Extra drug: enprocal (200 mL qid)

Comments – medication and nutrition impacts (direct and indirect) only

No recent relevant biochemistry available. Advisable to check plasma proteins (albumin, total proteins) as markers of nutritional status. The plasma proteins are the primary transporters for two of the prescribed drugs and hypoproteinaemia may alter their effects.

Epilim has been associated with drug-induced hypoalbuminaemia.

Epilim is associated with altered thyroid function and it's regular monitoring recommended.

Epilim may interfere with insulin metabolism in the liver resulting in peripheral hyperinsulinaemia and consequent weight gain.

Quetiapine may increase risk of glucose intolerance and diabetes.

Epilim decreases biotin and carnitine absorption and decreases availability of folic acid and vitamin D.

Nexium decreases B12, vitamin C, magnesium, zinc and iron absorption, may decrease calcium availability, and decreases thiamine availability.

Mr ABL has been prescribed nexium since admission ie 20 months, and probably before then. There is increasing evidence that proton pump inhibitors such as nexium significantly impair magnesium absorption - magnesium deficiency manifests as confusion, disorientation, personality changes, loss of appetite, depression, muscle cramps, tingling, numbness, hypertension, cardiac dysrhythmia, seizures, decreased absorption of thiamine, vitamin D, vitamin C and iodine. Magnesium is an intracellular ion therefore serum levels are unlikely to detect early depletion of status. Cellular magnesium status is unknown whilst magnesium levels within acceptable range however if magnesium levels are low then typically indicates significant cellular depletion and intervention recommended. Men require 420 mg magnesium per day; however there are side effects from magnesium interventions that provide 350+ mg elemental magnesium/day from non-food sources. Advisable to check magnesium levels and if still marginal then review current magnesium intervention and consider an intervention that provides about 300 mg elemental magnesium per day.

Bowels –

- no regular intervention prescribed

- oral PRN aperient prescribed; administered 2 x 12/14

- no Nurse Initiated interventions administered

Staff advise Mr ABL mostly eats well, that drowsiness at mealtimes is an issue, and that at times he refuses to open his mouth.

Since Mr ABL is pale, advisable to check iron levels and if low then short term (90-120 days) intervention recommended.

Mr ABL is a slender, pale man who was asleep in a chair in the Day Room - he did not stir to his name.

Mr ABL has been prescribed a proton pump inhibitor for 20 months. There is increasing evidence that longterm proton pump inhibitor prescription is associated with

- altered gut microbiome;

- increased risk of food sensitivities at a level of peanut allergy

- increased risk of coeliac disease due to partial protein digestion;

- increased risk of scurvy;

- generalised malnutrition due to impaired absorption of a range of nutrients such as B12, vitamin C, magnesium, zinc, iron, etc

- altered gastric pH which reduces absorption dynamics of a range of drugs and nutrients. Altered drug availability is relatively easily identified however reduced nutrient absorption is rarely identified due to the non-specific nature of their signs and symptoms.

Consequently advisable to reconsider reviewing current proton pump inhibitor prescription and consider

- whether proton pump inhibitor prescription is still required;

- if suppression of gastric acidity is still required then could it be managed with an H2 antagonist such as ranitidine (there is a general belief that they cause less nutritional harm than proton pump inhibitors).

Evidence indicates iron deficiency anaemia is unlikely to resolve whilst a proton pump inhibitor such as Nexium is prescribed. Advisable to consider a non-oral iron intervention to maximise effectiveness of the intervention.

Both Nexium and quetiapine inhibit OCT1 ie inhibits liver uptake of thiamine.

What else would you include?

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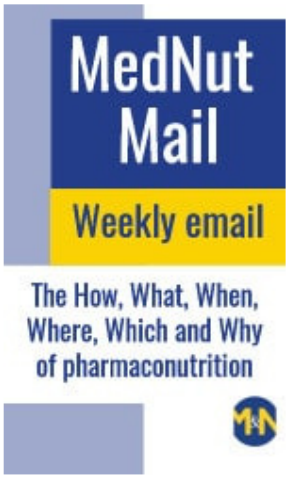

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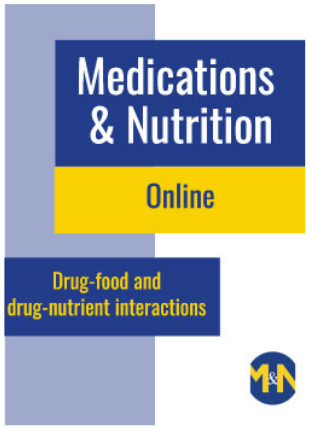

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