MedNut Mail

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

Astrocytes and pharmaconutrition

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https://medicationsandnutrition.online

Commentary

Astrocytes are overlooked essential intermediaries in neurological physiology. Astrocytes operate on a network system whereby they service hundreds, if not thousands of neurons. Therefore, if anything damages one astrocyte then the harm is expressed extensively.

Astrocytes have 2 primary functions -

1. provision of all the substances essential for neurons to survive and thrive,
2. removal of neuronal garbage.

If anything interferes with these functions then the neurons become damaged and typically die – dying neurons cause neuropathic pain which is difficult to manage.

Three key nutrients essential for astrocytes to function adequately are -

1. **Thiamine (B1)**. Inadequate thiamine availability is associated with altered availability of glutamate transporters, lactic acidosis, altered water channel protein AQP4 likely contributing to brain oedema, disruption to the blood-brain barrier, increased vitamin C excretion from the cells;
2. **Magnesium**. Necessary for thiamine to be activated;
3. **Cobalamin (B12).** Inadequate cobalamin availability causes astrogliosis, a reaction that if chronic, hinders axon generation, synapse formation, seemingly a cause of multiple sclerosis, and releases neurotoxic substances.

Drugs that are known to negatively impact the status of all 3 nutrients ie thiamine, cobalamin, magnesium include –

- Aluminium hydroxide
- Esomeprazole
- Esomeprazole + amoxycillin + clarithromycin
- Famotidine
- Lansoprazole
- Metformin
- Metformin + Rosiglitazone
- Neomycin sulfate
- Omeprazole
- Pantoprazole
- Rabeprazole
- Ranitidine

Worryingly, most these prescribed generics are very commonly prescribed – often by brand name with the most common being those with acid-inhibiting functions, whilst metformin is the fourth most commonly prescribed medication globally.

There are about 39 combinations of the above prescribed medications that negatively impact two of the three key nutrients.

Potential drug-nutrient interactions are likely when prescribed medications that are substrates and/or inhibitors of the various transporters utilised by the nutrients.

The “don’t knows” are becoming very apparent – and potentially dire -

- duration of inhibition of each prescribed medication;
- how to address the chronic lack of availability of relevant nutrients;
- identification of the best time(s) to compensate for the negative impact on our astrocytes;
- identification of all the transporters and nutrients associated with astrocytes and their functions;
- availability of credible pathology laboratory ranges for all our nutrients, and especially our key nutrients such thiamine, magnesium and cobalamin.

What actions will you initiate when you see someone whose prescribed medications negatively impact thiamine, magnesium or cobalamin status – will you –

- check B1, B12, and magnesium levels and ensure they are within acceptable range? Whose range will you use – the pathology labs or something more recent such as the neuroimaging research for B12? The recommended minimum ranges for magnesium, and what for thiamine?
- recommend regular monitoring of the status of these 3 nutrients on an annual basis?
- recommend interventions at the lower end of acceptable ranges?

Conclusions

Astrocytes require an adequate supply of some key nutrients in order to be functional. Longterm prescription of some medications can reduce the availability of these nutrients.

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:

Other: AF, PPM, ? FTD Korsikov/late Alzheimers, GORD

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
Cholecalciferol	(1/day)		☐					☐				☐	☐	☐
Clopidogrel			☑	N	CD	↓		☑				☐	☐	☐
COLOXYL WITH S			☐		D			☐				☐	☐	☐
Diltiazem			☐	NV	CD	↑	↓	☑	↓			☑	☐	☑
PANADOL OSTEO			☐	NV	CD			☐				☐	☐	☐
Pantoprazole	(40 mg/day) B1, B12, Ca, Fe,		☑	NV	CD		↓	☑				☑	☐	☐
			▩					▩				▩	▩	▩

Extra drug: ferrous fumarate

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.

BSLs (Jul-Aug)

- before breakfast - 5.1-5.8; recommended range 4-6,
- tested weekly,
- advisable to check HbA1c and clarify overall glycaemic control.

Currently prescribed one medication that may alter glycaemia, being diltiazem.

Mr ABR seemingly has well-controlled glycaemia without medication intervention.

Chronic use of coloxyl + senna may promote and excessive loss of water and electrolytes, especially potassium, and their regular monitoring recommended.

Ferrous fumarate decreases zinc absorption and zinc decreases iron absorption.

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

B12 deficiency is a risk factor associated with chronic use of acid-lowering agents such as pantoprazole, and regular monitoring B12 status is consequently recommended. Neuro-imaging evidence indicates changes to brain structure and function once B12 levels < 300 pmol/L. Advisable to clarify B12 status and if lower than 300 pmol/L then intervention recommended.

Longterm prescription of proton pump inhibitors is associated with both lower baseline zinc stores and an incapability of adequately increasing zinc plasma levels with oral zinc supplements. Advisable to clarify zinc status and if low then advisable to consider a non-oral zinc intervention.

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

Currently prescribed thiamine and vitamin D on a daily basis; both thiamine and vitamin D require magnesium in order to be activated therefore advisable to consider a magnesium intervention to optimise the effectiveness of these interventions.

Currently prescribed vitamin D (1 tab/day). Advisable to clarify current vitamin D status and establish

effectiveness of the intervention – if levels are still low then advisable to review adequacy of current intervention.

There is increasing evidence that proton pump inhibitors such as pantoprazole significantly impair magnesium absorption - magnesium deficiency manifests as confusion, disorientation, personality changes, loss of appetite, depression, muscle cramps, tingling, numbness, hypertension, cardiac dysrhythmia, seizures. 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. Advisable to clarify magnesium status and if low then intervention recommended however effectiveness of the intervention is questionable whilst pantoprazole prescribed.

Bowels

- regular aperient prescribed
- oral PRN aperient prescribed
- no Nurse Initiated interventions administered

Staff advise a variable, mostly poor appetite since return from hospital (subsequent to a recent fall).

Mr ABR is a tall, slender, anxious-looking man who was standing in the Day Room when I went to speak to him - we were unable to communicate.

Mr ABR's diagnoses include? FTD Korsikov/late Alzheimers. I am uncertain what? FTD Korsikov means however Kosikoff's psychosis is related to irreversible thiamine deficiency typically induced by chronic alcohol consumption. I am also uncertain whether? FTD Korsikov/late Alzheimers relates to confusion of diagnosis - advisable to clarify diagnosis.

Further to discussion with staff there seem to be several main issues that result in poor appetite, including -

- total number of prescribed drugs with side effects that include poor appetite – 2,
- total number of prescribed medications with side effects that include nausea and/or vomiting – 4.

Mr ABR has been prescribed pantoprazole since admission ie for 15 months, and probably before then. There is increasing evidence that proton pump inhibitors such as pantoprazole 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 C, vitamin D 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 low or marginal then consider an intervention that provides about 300 mg elemental magnesium per day.

Mr ABR has been prescribed a proton pump inhibitor for many years. There is increasing evidence that longterm (3+ years) proton pump inhibitor prescription is associated with -

- altered gut microbiome;
- increased risk of food sensitivities at a level of peanut allergy, due to partial protein digestion;
- 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;
- increased risk of dementia;
- 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).

Time to dissolution of ferrous fumarate at pH 1.2 (ie gastric environment) about 57 minutes, and at pH 5.8 (ie intestinal environment) about 85 minutes; gastric emptying time for adults is 3-6 hours, therefore any undissolved tablet will pass into the large intestine and be excreted.

Poorly absorbed iron, typically from sources such as iron supplements, results in increased iron availability to the gut microbiota with consequent -

- increase in the virulence of faecal enteropathogens,
- increase in the ratio of faecal enteropathogens to protective microbiota such as bifidobacteria and lactobacillus,

- favouring of the colonisation of the gut microenvironment by potentially pathogenic strains,
- increase in gut inflammation.

The growth and colonisation of Lactobacillus and other similar bacteria, is not dependent upon the availability of iron. Lactobacillus and other similar bacteria provide an important barrier effect against colonisation and invasion by pathogens – iron fortification may actually reduce their numbers and consequently weaken the protective effect they confer.

Evidence indicates beneficial gut microbiota have low iron requirements and that enteropathogens thrive once iron is available. Non-haem iron, such as in iron supplements, is poorly absorbed therefore it is unlikely the anaemia will resolve and the increased supply of iron to the enteropathogens increases the risk of GI infections. Iron absorption is significantly improved x 10 if administered attached to protein and potentially minimises pathogen harm ie animal-based high-iron foodstuffs are more effective than supplements; concurrent administration of iron tablet with a probiotic such as yakult or vaalia will also increase the beneficial bacteria.

Recent evidence found a direct correlation between level of cognitive impairment and degree of elevation of homocysteine levels, and that if homocysteine levels are reduced to acceptable range then early cognitive impairment can be reversed. Homocysteine status is altered by 4 B vitamins – being B12, folate, pyridoxine and riboflavin. Mr ABR is currently prescribed pantoprazole which decreases B12 absorption therefore advisable to check homocysteine levels and if elevated then intervention recommended. Pantoprazole negatively impacts these nutrients by -

1. altering gastric pH and therefore limiting absorption - B12, folic acid.
2. OAT3 inhibition - B6.

Currently prescribed pantoprazole which decreases thiamine availability. Thiamine is important in glycaemic and lipid control, neurological function and energy production; when there is insufficient thiamine then food is converted to alternatives such as fat stores, cholesterol and triglycerides; people with diabetes have a significantly increased urinary excretion of thiamine A short term (90-120 days), low dose (~ 10 mg/day) thiamine intervention on a regular basis such as annually may confer benefit.

Also prescribed 3 medications that decrease thiamine uptake by liver and/or kidney and/or urinary system – being clopidogrel, diltiazem, pantoprazole.

Nutritional factors that may be contributing to falls include -

- low vitamin D – currently prescribed an intervention. Advisable to check status if low then advisable to review adequacy of current intervention.

- low B12 - is important in the righting reflex when a person stumbles; currently prescribed pantoprazole; advisable to check status.

- low Hb – currently prescribed an intervention; currently prescribed pantoprazole. Advisable to check status and if low, then advisable to review adequacy of current intervention.

- low iron - currently prescribed an intervention; currently prescribed pantoprazole. Advisable to check status and if low, then advisable to review adequacy of current intervention.

- low zinc - currently prescribed pantoprazole. Advisable to check status and if low, then advisable to consider a non-oral intervention.

- low magnesium - magnesium is important in muscle function, especially cardiac muscle, amongst other functions; currently prescribed pantoprazole. Advisable to clarify magnesium status and if low then consider a non-oral intervention.

What else would you include?

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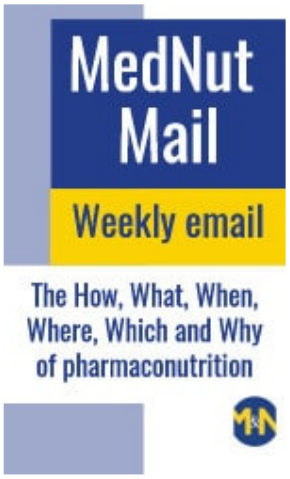

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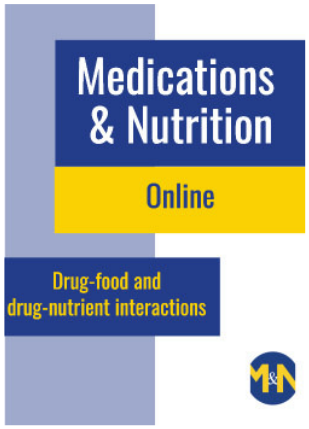

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