MedNut Mail

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

Some neuroinflammation markers and pharmaconutrition

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Commentary

Neuroinflammation occurs when the brain's innate immune system is challenged by factors such as injury, infection, toxin exposure, or neurodegeneration, and the responses can be both physiological and biochemical; neuroinflammation can both cause, and be caused by excitotoxicity and oxidative stress.

Is there evidence of an association between 3 common neuroinflammation markers and some nutrition factors?

Interleukin-1ß (IL1-ß).

- production decreased by – vitamin C, riboflavin, pyridoxine (via NLRP3 inhibition), magnesium;
- vitamin E reduces levels in hippocampus in animal models;
- inverse correlation with B12 status ie the higher the B12 levels then the lower the IL1-ß levels;
- overexpression caused by thiamine deficiency;
- inhibits thiamine uptake by brain cells;
- inhibits carrier (THTR1, THTR2) uptake of thiamine;
- inhibits mRNA expression of THTR1, but not THTR2, in brain cells;
- increasing duration of exposure further inhibits thiamine uptake;
- if levels are normalized then negative impacts on thiamine uptake and THTR1 levels are reversed.

Interleukin-6 (IL6).

- production decreased by – pyridoxine (via NLRP3 inhibition);
- inverse correlation with pyridoxine status ie the higher the pyridoxine levels then the lower the IL6 levels;
- inverse correlation with B12 status ie the higher the B12 levels then the lower the IL6 levels;
- overexpression caused by thiamine deficiency;
- inhibits thiamine uptake by brain cells;
- inhibits carrier (THTR1, THTR2) uptake of thiamine.

TNF-alpha.

- production decreased by – vitamin C, riboflavin, pyridoxine (via NLRP3 inhibition), magnesium;
- vitamin E reduces levels in hippocampus in animal models;
- inverse correlation with pyridoxine status ie the higher the pyridoxine levels then the lower the IL6 levels;

- inverse correlation with B12 status ie the higher the B12 levels then the lower the IL6 levels;
- overexpression caused by thiamine deficiency;
- inhibits thiamine uptake by brain cells;
- inhibits carrier (THTR1, THTR2) uptake of thiamine.

The physiological role of Thiamin Transporters (THTR ½) is the transfer of thiamine and pyridoxine.

- THTR1 – pharmaceutical substrates and inhibitors seem to be very limited with trimethoprim being the main contender for both.
- THTR2 – plethora of substrates and especially inhibitors with commonly prescribed (inhibitor) medications including amitriptyline, metformin, sertraline, telmisartan, verapamil.

There is likely to be a number of potential drug-nutrient interactions relating to neuroinflammation and for which there is currently no evidence – these would be identified by commonality of the transporters between the prescribed medications the relevant nutrients.

The nutrition contribution has seemingly attracted very little attention which is surprising given the extent of the interest in neuroinflammation globally.

What actions will you initiate when you see someone whose diagnoses include an inflammatory response, will you -

- clarify the status of the 3 key inflammatory response markers?
- check which prescribed medications are inhibiting relevant nutrient absorption and/or availability?
- clarify the status of the nutrients identified with modifying the inflammatory response?
- include pharmaconutrition impacts on neuroinflammation in your reports to colleagues?

Conclusions

Research into the nutritional contribution to neuroinflammation is very limited. Early evidence indicates mal-nutrition contributes to the risk of neuroinflammation throughout life.

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: poliomyelitis

Biochemistry with Pharmaconutritional Consequences

No recent relevant biochemistry available.

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
Alendronate sodiu	Ca	☐	NV	CD	↑		☑				☐	☑	☐
Aspirin	C, Fe	☑	NV				☐				☐	☐	☑
COLOXYL WITH S		☐		D			☐				☐	☐	☐
COVERSYL		☐	NV	D			☑				☑	☐	☐
FGF	Ca, Mg, Zn	☐					☐				☐	☐	☐
Fluoxetine	Na	☑	NV	CD	↑	↓	☑				☑	☑	☐
Galantamine		☐	NV	D	↓	↓	☐				☐	☑	☐
Irbesartan		☑	NV	CD	↑	↕	☑				☑	☑	☐
NEO-B12		☐	NV	D			☐				☐	☐	☐
NEXIUM	(20 mg/day) B1, B12, Ca, Fe,	☑	NV	CD	↑		☑				☑	☐	☐
OSTELIN	(1/day)	☐					☐				☐	☐	☐
Risperidone		☑	NV	C	↑		☐		↑		☐	☐	☐
		▩					▩				▩	▩	▩

Extra drug: osteoeze, enprocal (100 mL tds)

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

Advisable to check plasma proteins (albumin, total proteins) as markers of nutritional status. The plasma proteins are the primary transporters for five of the prescribed drugs and hypoproteinaemia may alter their effects.

Four prescribed medications may alter glycaemic control, being aspirin, fluoxetine, perindopril, risperidone.

Three prescribed medications associated with anaemia, being aspirin, perindopril and irbesartan.

Six prescribed medications associated with altered potassium status, being coloxyl with senna, perindopril, galantine, irbesartan, hydroxocobalamin, esomeprazole.

Alendronate requires an adequate intake of calcium and vitamin D to be effective - currently no calcium intervention and the vitamin D intervention is likely to be inadequate.

Administration of Alendronate sodium with coffee or orange juice reduces availability by ~ 60%

Vitamin C (960 mg/day) attenuates aspirin-induced gastric injury.

Caffeine increases aspirin absorption.

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

Ferrous sulfate component of FGF decreases zinc absorption.

Evidence indicates FGF (commenced 11/11) is unlikely to be effective whilst a proton pump inhibitor is prescribed.

Regular monitoring sodium levels recommended whilst fluoxetine prescribed.

Nexium (commenced 11/11) decreases B12, vitamin C, magnesium, zinc and iron absorption, may decrease calcium absorption, and decreases thiamine availability.

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; authors speculate the effect is likely drug class rather than specific drug.

Increasing number of recommendations for regular monitoring of magnesium levels whilst nexium is prescribed with a suggestion of urinary magnesium monitoring as an early indicator of depleting status.

Perindopril impairs zinc status.

A B12 intervention has been prescribed since November 2011 and likely before then. As evidence indicates elevated B12 levels are

associated with cognitive impairment, advisable to check B12 levels and clarify current status.

Currently prescribed ostelin (1/day). Advisable to check vitamin D levels and if still low then review current vitamin D management strategy.

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. 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.

Bowels –

- regular aperient prescribed

- oral PRN aperients prescribed; administered 4 x Nov, 2 x Oct

- Nurse Initiated anal intervention administered 1 x Nov

Staff commented that Mr ABV has been drowsy for the last couple of weeks and that temazepam was ceased last week.

Mr ABV is a slender man with cool hands, and who was dozing in a chair in the Day Room - he stirred to his name and promptly resumed dozing - he was definitely not interested in speaking to me which staff advise is now typical.

An iron supplement has been prescribed since admission (4+ years). Evidence indicates iron deficiency anaemia is unlikely to resolve whilst a proton pump inhibitor prescribed therefore advisable to clarify iron status and if still low then consider a non-oral intervention.

Loss of weight and longterm proton pump inhibitor prescription are associated with depletion of zinc status and zinc is important in a range of body functions, including sense of taste and release of the hunger hormone Neuropeptide Y. Since Mr ABV has lost about 6 kg weight, advisable to check zinc levels and if inadequate then short term (90-120 days) intervention and recheck status prior to cessation of the intervention; evidence indicates zinc interventions in the presence of a proton pump inhibitor are unlikely to be effective.

Mr ABV has been prescribed a proton pump inhibitor since November 2011 and likely before then. 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;

- 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)

Prescribed medications that inhibit liver uptake of thiamine and choline include fluoxetine, Nexium, risperidone, and that inhibit kidney uptake of thiamine and choline include fluoxetine, galantine, risperidone therefore blood tests may indicate thiamine levels as high-normal or elevated – this is due to a mechanism of inhibition and not due to oral intake.

What else would you include?

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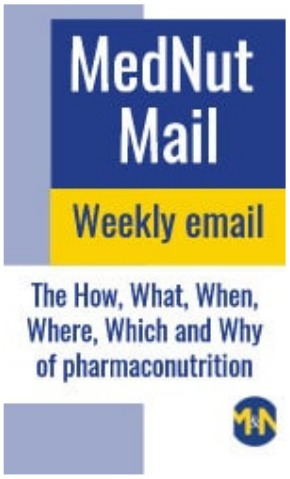

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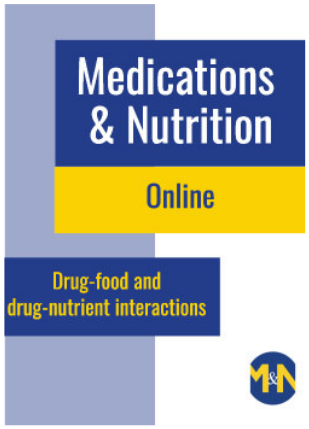

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