MedNut Mail

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

Sodium Multivitamin Transporter (SMVT) and pharmaconutrition

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https://medicationsandnutrition.online

Editorial

Sodium Multivitamin Transporter (SMVT) facilitates the uptake of biotin, pantothenic acid, lipoic acid, and iodine from the gut and across the Blood Brain Barrier. SMVT is the only currently known intestinal biotin transporter.

SMVT is present in the small and large intestines, liver, kidney, heart, lungs, brain, cornea, retina, and placenta tissues.

As a consequence of facilitating the uptake of its substrates ie biotin, pantothenate, lipoic acid, and iodide, SMVT is important in -

- fatty acid metabolism, and cellular energy production and metabolism,
- maintaining normal mucosal integrity,
- being a prognostic marker for gastric cancer,
- being a drug delivery transport system to increase the availability of prodrugs as conjugates of its biological substrates. For example, biotin-conjugates decrease access to the efflux membrane transporter MDR1 (P-gp).

SMVT deficiency can be due to -

1. **Inherited metabolic disorder** – is likely to manifest at a young aged, and typically encompasses feeding problems, failure to thrive, metabolic acidosis, and mild to severe neurological deficits; biotin and pantothenic acid supplementation may confer benefit in some of these disorders;
2. **Polymorphisms** – likely to manifest at a young aged, and is typically due to mutations in the SLC5A6 gene; biotin and pantothenic acid supplementation may confer benefit in these disorders;
3. **Environmental** – likely to manifest at any age and is dependent upon the environmental insult; biotin and pantothenic acid supplementation are likely to confer benefit in these disorders; identified causes include -
    - cytokine activation of the NF-kB pathway that typically results in decreased SMVT levels – colitis is an example,
    - chronic alcohol exposure that results in a significant inhibition in both carrier-mediated biotin uptake and SMVT expression,

- prescribed medicines that inhibit SMVT function (for an unknown duration) and include cefmetazole, captopril, norfloxacin, aspirin, methotrexate, enoxacin, lomefloxacin, levofloxacin, 6-mercaptopurine, indomethacin, salicylic acid.

Signs and symptoms that are common to most of SMVT's substrates include –

Likely SMVT deficiency signs and symptoms	Adult	Child
altered energy and other metabolic pathways	Y	Y
dermatitis	Y	
developmental delay	?	Y
failure to thrive	Y	Y
immune dysfunction	Y	Y
impairment in bone development	?	Y
intestinal disturbances	Y	Y
neurological disorders such as ataxia	Y	Y
seizures	Y	Y
likely others	Y	Y

Neonatal screening (aka heel prick test) records are maintained until the person is aged 18 or 21 years, as per State regulations, at which time the records are destroyed. The sample may be used for further testing at the request of the parent or guardian, to provide new medical information for the benefit of the family.

What actions will you initiate when you see someone whose prescribed medications include SMVT inhibitors, will you –

- request clarification of biotin, pantothenic acid and iodine status?
- trial an intervention program and monitor for benefit?
- recommend nutrient interventions be administered at different times from the prescribed medicines?
- document the expressed signs and symptoms that support your request, the intervention(s) trialled, and submit as a Case Study at relevant conferences?
- if the person is young then recommend accessing the person's neonatal screening and exclude inherited and/or polymorphism contribution?

Conclusions

SMVT downregulation and its consequences are not front of mind considerations when reviewing someone with a range of neurological, gastrointestinal and other signs and symptoms, and especially not in adults. Awareness of transporter downregulation is steadily increasing our skill base and consequently improving the outcomes in those in our care.

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: wound on (L) toe

Biochemistry with Pharmaconutritional Consequences

Na:	141	mmol/l	Hb:	122	g/L	Albumin:	37	g/L	BSL:		mmol/l
K:	4.4	mmol/l	Lymph:	1.3		Total Protein:	64	g/L	HbA1C:		
Urea:	6.1	mmol/l	MCV:	90	mmol/l	B12:		pmol/L	INR:		
Creatinine:	0.062	mmol/l	Zn:		umol/l	Folate:		nmol/L	TSH:		mIU/L

Other: Ca 2.10, corr 2.16, chol 2.5, Tg 1.0, vit D 18

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
Aspirin	C, Fe		☑	NV				☐				☐	☐	☑
CALCIA D	(1/day)		☐					☐				☐	☐	☐
COLOXYL WITH S			☐		D			☐				☐	☐	☐
EPILIM	B12, B6, biotin, Ca, carnitine, I		☑	NV	CD	↑	↕	☐				☐	☐	☑
Metoprolol			☐	NV	CD	↑		☑				☑	☐	☑
Mirtazapine			☐	N	D	↑	↑	☐				☑	☐	☐
Paracetamol			☐	NV	CD			☐				☐	☐	☐
Perindopril			☐	NV	D			☑				☑	☐	☐

Extra drug: arginaid mane

Transporter-mediated interactions and nutrients

Transporter	OCT1		OCT2		OCT3		OCT6		OCTN1		OCTN2		MATE1/2	
Nutrients - Sub	B1, choline, carnitine		B1, choline, creatinine		B1		carnitine		carnitine		carnitine		B1, creatinine	
Nutrients - Inh														
Location	intestines, liver		kidney		intestines, liver, kidney		testis, endometria		Intestines, kidney		Intestines, liver, kidney		kidney	
DRUG	Sub	Inh	Sub	Inh	Sub	Inh	Sub	Inh	Sub	Inh	Sub	Inh	Sub	Inh
Metoprolol				Y										
Mirtazepine				Y										
Epilim												Y		
Sub – substrate, Inh – inhibitor, B1 - thiamine														

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

Data summary

Biochemistry

Recent relevant biochemistry indicates -

- low chol 2.5 - atorvastatin ceased 3 months ago;

- low vit D - commenced vitamin D intervention 3 months ago. Advisable to check vitamin D levels and if still low then review current vitamin D management strategy.

Glycaemia

Currently prescribed 5 medications that alter glycaemia, being aspirin, Epilim, metoprolol, paracetamol, perindopril.

Pharmaconutrition

Currently prescribed 6 medications that include nausea as a side effect.

Currently prescribed 5 medications that include anaemia, diarrhoea as a side effect.

Currently prescribed 4 medications that include vomiting as a side effect.

Currently prescribed 3 medications that include constipation, dry mouth, sweating as a side effect.

Currently prescribed 2 medications that include hyponatraemia, tremor, altered appetite as a side effect.

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

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

Epilim decreases biotin and carnitine absorption, decreases availability of folic acid and vitamin D, and may decrease pantothenic acid availability

Regular monitoring sodium levels recommended whilst mirtazepine prescribed.

Dietary levels of caffeine intake in conjunction with paracetamol inhibit antinocieception.

Concurrent ingestion of paracetamol and iron resulted in increased rate of iron absorption and decreased extent of drug absorption; the authors advise drug and iron to be administered at different times from each other.

Perindopril impairs zinc status.

Prescribed 2 medications that negatively impact riboflavin status, being metropolol and perindopril. Riboflavin is the rate-limiter in one-carbon metabolism and therefore has an important role in metabolic pathways. Advisable to clarify riboflavin status however if direct testing is unavailable then check pyridoxine and/or niacin status as both these require adequate riboflavin status so they can be activated ie functional.

Prescribed 2 medications that negatively impact zinc status, being sodium valproate and perindopril. Zinc is important in a range of body functions, including sense of taste, release of the hunger hormone Neuropeptide Y, hearing, bone development, protects thyroid function, protects the mitochondria from oxidative stress and glycation, and altered glomerular function, as well as modifying the inflammatory response pathway and activation of the polyol pathway (a part of intracellular signalling and metabolism). Advisable to monitor zinc status on a regular basis ie at least annually and if low then short term (90-120 days) intervention recommended.

Bowel management

Regular aperient prescribed.

Oral PRN aperient prescribed; administered 1 x Jun, 1 x Apr,

Nurse Initiated anal intervention administered 1 x Apr.

Staff comments

Staff advise Mr AGV eats well.

Observations

Mr AGV is a slender, pale Turkish man who had just finished eating his midday meal when I went to speak to him - he had eaten everything.

Mr AGV has remained weight stable for the last year.

Pharmaconutrition assessment

Staff expressed concern about the delayed wound-healing on Mr AGV's (L) toe. Nutritional factors that contribute to wound healing include -

- adequate vitamin D status - evidence indicates low vitamin D status is associated with delayed wound healing. Currently prescribed both a vitamin D intervention and a medicine that decreases vitamin D availability, being Epilim. Advisable to clarify current vitamin D status and if still very low then recommend reviewing current intervention with a view to increasing current dose.

- adequate vitamin and mineral intake – current combination of prescribed medications negatively impact iron, zinc, sodium, vitamin C, B12, folic acid, thiamine, biotin, carnitine, and likely pantothenic acid therefore advisable to consider either monitoring all these nutrients on a regular basis (at least annually) or commence a prophylactic intervention that is administered at a different time from the other prescribed medications (some authors are now advocating this strategy as their preferred option).

Mr AGV's diagnoses include falls - nutritional factors that may be useful to consider in falls management include -

- loss of weight – most of the prescribed medications include side effects that negatively impact food intake either directly or indirectly;

- vitamin D – associated with muscle weakness and consequently falls; currently prescribed Epilim therefore advisable to clarify vitamin D status;

- low B12 - is important in the righting reflex when a person stumbles; prescribed Epilim therefore advisable to monitor status;

- low iron – currently prescribed aspirin therefore advisable to monitor status;

- low zinc – can decrease food intake through altered sense of taste and poor appetite, and consequently reduced muscle mass; currently prescribed Epilim and perindopril therefore advisable to monitor status;

- low carnitine - carnitine is both absorbed and produced de novo, and is important in a range of muscle functions; Epilim decreases carnitine absorption; magnesium is important in de novo carnitine production. Advisable to clarify carnitine status.

What else would you include?

Medications have profoundly and positively changed health outcomes however they do generally come with some nutritional harms. By identifying and addressing the nutritional harms, optimal health outcomes are closer to being achieved.

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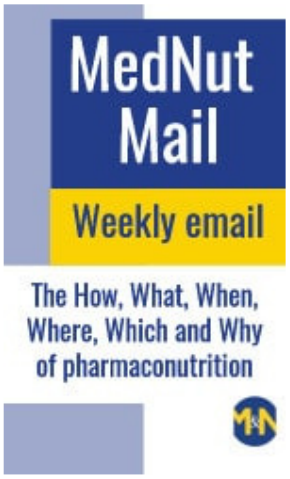

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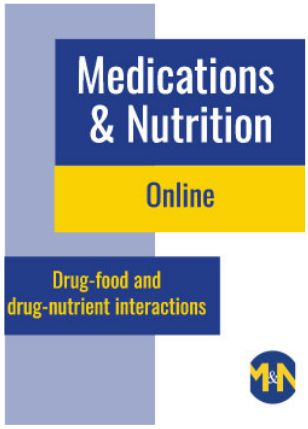

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