MedNut Mail

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

Organic Cation Transporters (OCTs) and pharmaconutrition

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11th April 2023

https://medicationsandnutrition.online

Editorial

The organic cation transporters regulate the transfer of many essential organic cations across biological membranes and therefore have an essential role in many metabolic processes.

OCTs are known as being polyspecific transporters because they recognize and transport a broad range of substances such as the organic amines choline and carnitine, the neurotransmitters dopamine and serotonin, and the vitamin thiamine. OCTs can act as influx, efflux or bi-directional systems.

OCTs include OCT1, OCT2, OCT3, OCT6, OCTN1, OCTN2, MATE1, MATE2.

OCT1

OCT1 is primarily expressed on the basolateral membrane of enterocytes (intestines) and hepatocytes (liver).

Transports thiamine, choline, acylcarnitine, the toxic substances aflatoxin, ethidium, monocrotaline and paraquat, and toxic metals such as cadmium.

Thiamine uptake by OCT1 may be relevant if there are high levels of thiamine in the food.

OCT1 deficiency/downregulation includes -

(1) a change in energy production from glucose to fatty acid oxidation due to inadequate thiamine availability;

(2) increased gluconeogenesis and hepatic glucose output, and consequent increases in liver glycogen and glucose levels;

(3) increased peripheral adiposity due to altered energy metabolism;

(4) altered cholesterol homeostasis.

There is early evidence that sustained OCT1 deficiency/downregulation may be associated with diagnoses such as obesity and diabetes.

OCT2

OCT2 is expressed on the basolateral membrane of proximal tubular cells (kidneys), several regions of the brain, hepatocytes, small intestine, placenta, and the ciliated epithelial cells of the lung and trachea.

Transports thiamine, choline and creatinine.

OCT2 is involved in the uptake and secretion of many organic cations predominantly via the kidneys.

There are currently 10 known polymorphisms (variants).

OCT3

OCT3 is expressed in the luminal membrane of enterocytes, the sinusoidal hepatocyte membrane, the basolateral side of proximal tubule cells, skeletal muscle and adipose tissue (mature adipocytes only).

Transports thiamine – which may be relevant if the food contains high levels of thiamine.

Oct3 is the predominant transporter for catecholamines, particularly norepinephrine, in White Adipose Tissue (WAT). By regulating catecholamines levels in adipocytes OCT3 has an essential role in the browning of WAT during adaptive thermogenesis.

Oct3 deficiency/downregulation results in increased core body temperature, oxygen consumption, and whole-body energy expenditure as well as hepatic fibrosis progression.

OCT6

OCT6 is specifically expressed in the testis and endometria.

Transports carnitine.

There is an inverse correlation between OCT6 and SIRT1. OCT6 ameliorates neural tube defects whereas environmental stresses such as oxidative stresses, starvation, and DNA damage inducers directly activate SIRT1.

OCTN1

OCTN1 is expressed in the apical brush border membrane of the small intestine, the renal proximal tubules, liver, lungs, trachea, bone marrow, skeletal muscle, prostate, pancreas, placenta, heart, uterus, spleen, spinal cord and bronchial epithelial cells.

OCTN1 transports carnitine and ergothioneine.

OCTN2

OCTN2 is expressed in the apical brush border membrane of enterocytes, on the sinusoidal membrane of hepatocytes, on the apical membrane of the proximal tubular cells, in heart, placenta, skeletal muscle, pancreas, brain, lungs and bronchial epithelial cells.

OCTN2 transports carnitine and choline.

OCTN2 is important in carnitine absorption and reabsorption.

Insulin has been associated with an increase in carnitine uptake, and expression of OCTN2 in skeletal muscle.

MATE1/2

Are renal efflux transporters ie transfer organic cations from kidney to urinary system.

Transport thiamine and creatinine.

Hyperuricaemia downregulates MATE1.

The essentiality of the OCTs in a range of metabolic processes emphasizes the importance of being aware of prescribed medications and their substrates and/or inhibitors and their potential to cause nutritional harm.

As we are still developing familiarity with the transporters, the nutrients they transport, the organs impacted, and the role of prescribed medicines, I have created this downloadable form that you can modify to your requirements.

Transporter	**OCT1**		**OCT2**		**OCT3**		**OCT6**		**OCTN1**		**OCTN2**		**MATE1/2**	
Nutrients	B1, choline, carnitine		B1, choline, creatinine		B1		carnitine		carnitine		carnitine		B1, creatinine	
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**
Drug a	**Y**		**Y**	**Y**										
Drug b		**Y**		**Y**		**Y**		**Y**		**Y**		**Y**		**Y**
Drug c			**Y**											
Drug d	**Y**	**Y**												
Sub – substrate, Inh – inhibitor, B1 - thiamine														

What actions will you initiate when you see someone whose prescribed medications include OCT substrates and/or inhibitors, will you –

- request clarification of thiamine, choline and carnitine status?
- question whether low nutrient levels are due to inadequate dietary intake or to iatrogenic transporter inhibition via their prescribed medications?

- recommend nutrient interventions to be administered at a different time from the prescribed medicines?

Conclusions

Downregulation of the organic cation transporters can profoundly alter health outcomes ranging from neural tube defects to beiging white fat. We are slowly becoming familiar with transporters and their impacts on nutrition.

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: Ca bowel, GORD, B12 def, PPM

Biochemistry with Pharmaconutritional Consequences

No recent relevant results 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
Cholecalcifero	(0.2 mL/day ~ 12 mcg)		☐					☐				☐	☐	☐
COLOXYL WITH S			☐		D			☐				☐	☐	☐
NEXIUM	(80 mg/day) B1, B12, Ca, Fe,		☑	NV	CD	↑		☑				☑	☐	☐
PANAMAX			☐	NV	CD			☐				☐	☐	☐
			▩					▩				▩	▩	▩

Extra drug: norspan

Transporter-mediated interactions and nutrients

Transporter	OCT1		OCT2		OCT3		OCT6		OCTN1		OCTN2		MATE1/2	
Nutrients	B1, choline, carnitine		B1, choline, creatinine		B1		carnitine		carnitine		carnitine		B1, creatinine	
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**
Nexium		**Y**												
Sub – substrate, Inh – inhibitor, B1 - thiamine														

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

Data summary

Biochemistry

No recent relevant biochemistry available. Advisable to check plasma proteins (albumin, total proteins) as they are the primary transporters for one of the prescribed drugs and hypoproteinaemia may alter its effects.

Glycaemia

Currently prescribed 0 medication that alters glycaemia.

Pharmaconutrition

Currently prescribed vitamin D intervention. Advisable to check vitamin D levels and if still low then review current vitamin D management strategy.

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

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

Concurrent ingestion of paracetamol and iron resulted 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.

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.

Bowel management

Regular aperient prescribed.
Oral PRN aperient prescribed; administered 1 x Sep.
No Nurse Initiated interventions administered.

Staff comments

Staff advise variable mostly poor appetite and that Mrs AGU recently had a UTI during which time her appetite was very poor.

Observations

Mrs AGU is a pale, big-framed lady who was having afternoon tea with her husband when I went to speak to her - she refused to speak to me.

Mrs AGU has been steadily losing weight for the last 3 months ie very sudden weight loss.

Pharmaconutrition assessment

Since Mrs AGU is pale, advisable to check iron levels and if low then short term (90-120 days) intervention recommended. There is some evidence that oral iron interventions are not effective whilst a proton pump inhibitor is prescribed and that non-oral interventions are more effective.

Current diagnoses include B12 deficiency and was prescribed neo-B12 until 5 months ago. Currently prescribed Nexium therefore advisable to clarify B12 status and if still low then recommencement of intervention advisable.

Nutritional factors that may be useful to include in UTI management include -
- vitamin C – currently prescribed Nexium therefore advisable to consider a vitamin C intervention;
- vitamin D – recurrent UTIs associated with vitamin D deficiency however

intervention prescribed therefore advisable to clarify its status;

- zinc – recurrent UTIs deplete immune system and consequently zinc status. Also prescribed Nexium therefore advisable to check zinc status and if low then short term (90-120 days) intervention recommended. However, since Nexium prescribed then it is unlikely the zinc intervention will be effective unless non-oral.

Mrs AGU's diagnoses include arthritis which is associated with chronic pain. Nutritional factors that may be useful to consider in pain management include -

- vitamin D - current intervention may not be adequate to attain adequate range. Evidence indicates increasingly brittle pain control with decreasing vitamin D levels. Advisable to clarify vitamin D levels and if still low then review current vitamin D management strategy.

- vitamin C - pain increases the reactive substances (formerly Reactive Oxygen Species) within cells. Vitamin C is important in quenching reactive substances and if there is insufficient vitamin C then cell status becomes compromised and the cells typically die which also causes pain. Vitamin C is not considered part of the pain management armament however it won't cause harm and evidence suggests it may confer benefit. Currently prescribed Nexium which decreases conversion of vitamin C to its active form.

- low B12 exacerbates elevated TNF- α which is an inflammatory response marker; elevation of the inflammatory response can include a pain response. Currently prescribed Nexium therefore advisable to clarify B12 status and if low then intervention recommended.

- magnesium – proposed mechanism is that magnesium blocks the NMDA receptor channels in the spinal cord and thus limits the influx of calcium ie reduces the risk of excitotoxicity and consequent exacerbation of pain. Currently prescribed Nexium which decreases magnesium absorption.

Nutritional factors that may be contributing to falls include -

- low potassium – currently prescribed Nexium therefore advisable to check status,

- low calcium - more likely to be low if potassium or magnesium low,

- low vitamin D – intervention prescribed therefore advisable to clarify status and if low advisable to review current intervention,

- low B12 - is important in the righting reflex when a person stumbles; currently prescribed Nexium therefore advisable to clarify its status,

- low Hb - advisable to clarify status and if low then advisable to check iron status, and if iron studies are low then intervention recommended – preferably non-oral,

- low zinc - more likely to be low if loss of weight or prescribed a proton pump inhibitor. As Mrs AGU has both lost weight and is prescribed Nexium advisable to clarify status and if low then intervention recommended – preferably non-oral,

- low magnesium - magnesium is important in muscle function, especially cardiac muscle, amongst other functions. Also currently prescribed Nexium which significantly decreases magnesium absorption. Magnesium is an intracellular ion therefore serum levels are unlikely to detect early depletion of status. Advisable to clarify magnesium status and if low then intervention recommended – preferably non-oral.

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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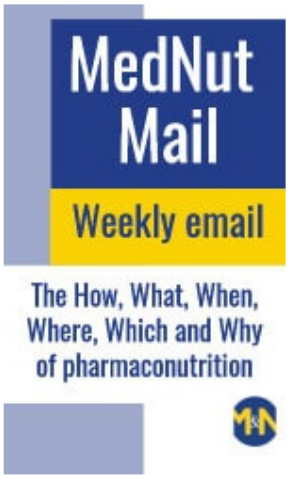

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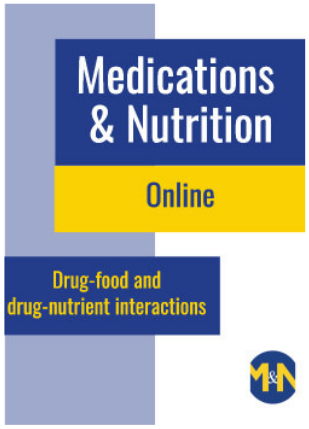

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