MedNut Mail

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

SVCTs and pharmaconutrition

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https://medicationsandnutrition.online

Editorial

The Sodium Vitamin C Transporters (SVCTs) regulate vitamin C homeostasis (system stability) such that excessive intakes result in reduced intestinal absorption and renal reabsorption, and inadequate intakes result in increased intestinal absorption and renal reabsorption.

The SVCT1/2 substrate is the reduced form of vitamin C/ascorbic acid ie ascorbate.

There are 3 identified SVCTs, being –

SVCT1

SVCT1 is responsible for maintaining the correct concentration of circulating vitamin C in the body by regulating the intestinal absorption and renal re-absorption of vitamin C.

SVCT1 is expressed in the intestines (with a higher expression in the small intestine), kidneys, liver, and lungs.

SVCT2

SVCT2 regulates the intracellular concentration of ascorbate and is responsible for its antioxidative effect.

SVCT2 is expressed in the intestines, most body tissues (excepting red blood cells, and lungs), heart, brain, adrenal glands, articular cartilage, bones, eyes, retina, placenta, spleen, prostate, and the central nervous system (CNS) including the epithelial cells of the choroid plexus.

There is disagreement regarding SVCT2 presence in the skeletal muscles.

SVCT3

SVCT3 does not transport vitamin C, and its function is still unknown.

SVCT deficiencies can be long term or short term, and are likely due to -

1. **Inherited metabolic disorders** – examples do not seem to be readily available therefore the question is whether they have been identified yet;

2. **Polymorphisms (variants)** - variations of a specific DNA sequence that can involve either a single nucleotide (aka single-nucleotide polymorphism, or SNP), or a longer DNA sequence; examples include –
    a. SNPs are likely associated with transcriptional and post-translational modifications such as glycosylation and phosphorylation;
    b. SVCT2 polymorphisms are associated with more health conditions than SVCT1 polymorphisms, and include cancer, cardiovascular diseases, optic neuropathy, and inflammatory bowel disease;
    c. the polymorphism SNP 10063949 is associated with IBD and the proposed mechanism of action is downregulation of SVCT1;
    d. in Huntington's Disease there are fewer SVCT2 transporters and many of them are deformed;
    e. there is reduced expression of SVCT2 in the articular cartilage in arthritis.
3. **Environmental** – likely to manifest at any age and is dependent upon the environmental insult; identified causes include –
    a. lipopolysaccharide (LPS) consistently inhibits vitamin C uptake by downregulating SVCT1/2;
    b. sepsis downregulates SVCTs and the mechanism of action is TNF inducing downregulation of SVCT1;
    c. enteropathogenic E. coli (EPEC) dysregulates SVCT1/2 expression in the intestines with consequent inhibition of vitamin C absorption;
    d. high dose vitamin C supplementation has been found to downregulate the SVCTs;
    e. the transporters' binding affinity for ascorbate diminishes with increasing acidity (lower pH); both transporters have an optimum pH of approximately 7.5;
    f. some flavonoids inhibit the SVCTs - for example, the flavanol quercetin acts as a reversible, non-competitive SVCT1 inhibitor;
    g. reduced availability of calcium and magnesium inactivates SVCT2, even if sodium status is within acceptable range.

Magnesium is a known SVCT2 activator ie increases SVCT2 expression.

What actions will you initiate when you see someone whose prescribed medicines alter availability of the SVCTs, will you –

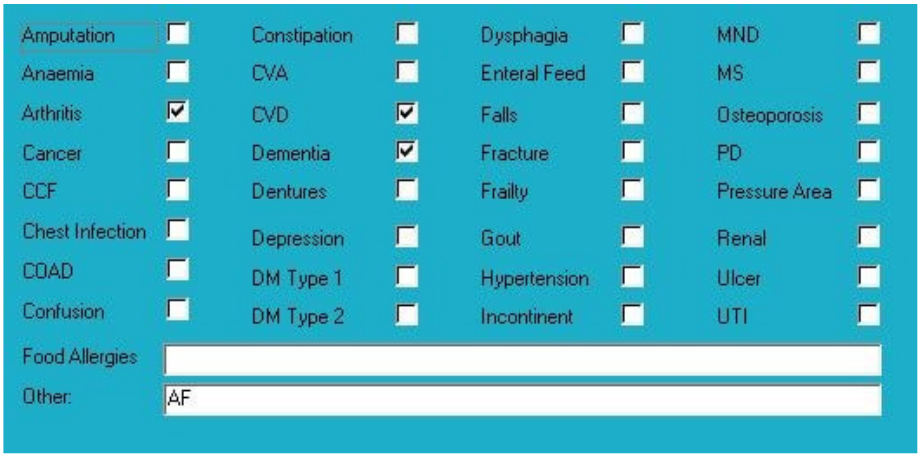
- clarify adequacy of dietary intake of vitamin C, calcium and magnesium, request blood tests, and then compare findings?
- If there is disagreement between oral intake and blood test results, will you question inhibition of the SVCTs?
- recommend nutrient interventions be administered at different times from the prescribed medicines?

Conclusions

The SVCTs have very important roles in body metabolism ie ensuring an adequate, consistent availability of vitamin C, however they also seem to be remarkably overlooked, with key regulators still not including them in the drug discovery process.

Case study

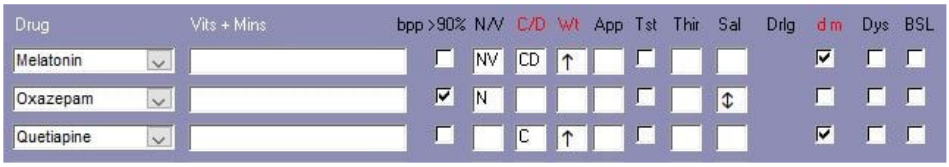
Medical History with Nutritional Aspect



Biochemistry with Pharmaconutrition Consequences

No recent relevant results available.

Medications That May Adversely Affect Nutritional Status



Transporter-mediated interactions and nutrients

Transporter	OCT1		OCT2		OCT3		THTR1		THTR2		MATE1		MATE2	
Nutrients - Sub	B1, choline, carnitine		B1, choline, creatinine		B1		B1, B6		B1, B6		B1, creatinine		B1, carnitine, creatinine, NMN	
Nutrients - Inh														
Location	intestines, liver		kidney		intestines, liver, kidney		Intestines, skeletal muscle, BAT		Intestines, breast, adipose tissue, placenta		Liver, kidney		kidney	
DRUG	**Sub**	**Inh**	**Sub**	**Inh**	**Sub**	**Inh**	**Sub**	**Inh**	**Sub**	**Inh**	**Sub**	**Inh**	**Sub**	**Inh**
Oxazepam				Y										
Quetiapine		Y												

Sub – substrate, Inh – inhibitor, B1 – thiamine, B2 – riboflavin, B3 – nicacin, B5 – pantothenic acid, B6 – pyridoxine, B7 – biotin, B9 – folic acid, B12 – cobalamin, NMN – N-methylnicotinamide, BAT – brown adipose tissue

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 medicines.

Glycaemia

Currently prescribed 1 medication that alters glycaemia, being quetiapine.

Pharmaconutrition

Currently prescribed 2 medications that include altered lipids, altered salivation, nausea, constipation, dry mouth and increased weight as side effects.

Bowel management

No regular intervention prescribed.

Oral PRN aperient prescribed; administered 1 x Mar.

Nurse Initiated oral aperient administered 1 x Feb.

Staff comments

Staff advise variable, mostly minimal appetite, and that Mr AGZ is fully assisted with his meals. Staff commented family advised Mr AGZ had similar food behaviours at home, that he liked ice cream at home but does not now, and that he likes porridge which is about to be trialled.

Observations

Mr AGZ is a tall, big-framed man who has bony shoulders which indicates significant loss of weight at some time. I asked Mr AGZ his height, and in a moment of lucidity he told me 6 foot - it was his only moment of lucidity as he did not respond appropriately to any of my other questions.

Weight status indeterminate due to significantly different admission weights.

Pharmaconutrition assessment

Both oxazepam and quetiapine inhibit thiamine transport from intestines and into liver and kidneys therefore there is a risk that blood test results for thiamine will be unreliable.

This is an unusual case study as there is a limited pharmaconutrition input!

What else would you include?

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