MedNut Mail

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

Altered glycaemia and Vitamin C

Y Coleman

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Editorial

The side effects of many prescribed medicines include altered glycaemic status which is associated with physical harm to the body. Glycaemia (blood sugar levels) are variable and at times can be either too high (hyperglycaemia) or too low (hypoglycaemia). Both hyperglycaemia and hypoglycaemia are associated with oxidative stress which is considered a primary cause of diabetes-related within-cell harm. The current stable of diabetes management medicines are glycaemia-only agents and do not reverse the complications caused by altered glycaemic status.

Oxidative stress occurs when there is inadequate antioxidant available to quench/negate oxidative reactions that result in cell damage and ultimately cell death.

Vitamin C is a key within-cell antioxidant and as such protects cell content from harm – especially from oxidative stress.

The evidence fairly consistently finds that those diagnosed with diabetes generally have lower vitamin C levels than those who are not diagnosed with diabetes – and the proposed range of causes is diverse; whether vitamin C confers benefit on glycaemic status in those with diabetes, remains contentious.

One of the many consequences of hyperglycaemia is inhibition of vitamin C uptake by cells which means that at the time when significant harm is being conferred there is no/limited antioxidant support and the end result is damaged and dying cells.

Hypoglycaemia is also associated with oxidative stress-induced harm, and there is also very limited evidence that vitamin C administered after a hypoglycaemic episode may modify consequent cellular harm.

Drug-induced altered glycaemic status falls into 2 categories whereby the timing and duration of altered glycaemic status is either **known** or **unknown**. For example, prednisolone-induced afternoon hyperglycaemia is well-documented and even includes recommendations that glycaemic management focus on this critical timeframe. However, the timing and duration of critical glycaemia periods for most prescribed medicines is generally not documented.

There seems to be a requirement during the drug discovery process to identify whether newly developed medicines will negatively impact glycaemia, however there does not seem to be a requirement to identify altered glycaemia patterns in relation to their timing and duration. A regulatory requirement that altered

glycaemia patterns be both identified during the drug discovery process and included in each brand's Product and Consumer Information documents, is likely to improve clinical outcomes as strategies could be developed to manage those key periods of harm.

Harm minimization is effectively about finding simple solutions to modify significant longterm harm. If we consider initiating a vitamin C intervention to minimize harm then there are a number of matters to be considered such as –

- are these interventions effective if administered both pre and post known altered glycaemic episodes?
- are single or multiple interventions per episode more effective?
- when are the most appropriate times to administer these interventions?
- what is the most effective vitamin C dose per intervention?

Given the trifecta of (i) reduced vitamin C availability in those with diabetes, (ii) that hyperglycaemia episodes inhibit cellular uptake of vitamin C, and (iii) that altered glycaemic status is associated with oxidative stress, in conjunction with Vitamin C being a key within-cell antioxidant, it seems there is an opportunity to initiate a harm minimization strategy. The research evidence to administer Vitamin C interventions as a strategy to modify oxidative stress harms in those with diabetes, is remarkably limited therefore First Principles should underpin the decision-making.

I propose strategies for two scenarios for managing the duration and timing of altered glycaemia status, based on administration of 500 mg vitamin C per dose –

- **Known** eg prednisolone – I hour pre and immediately post episode,
- **Unknown** eg most medicines – immediately post episode.

Application of First Principles –

- **Will doing nothing cause harm?** Yes as harm is caused every time there is an altered glycaemic episode;
- **Will the intervention cause harm?** No as this is an episodic intervention based on glycaemic status and known transporter capacity;
- **Will the intervention confer benefit?** This is the big unknown - based on theory and related research evidence, benefit is likely but has not been effectively researched.

Perhaps the most vulnerable group in this scenario are children, and introducing a strategy whilst they are still young (single digit years), may become one that will survive the Terrible Teens rebellion and potentially modify the consequent profound

harm such as seriously impaired vision, kidney transplants etc. Children seem to love the Gummies vitamin C tabs and so would be more likely to find this strategy acceptable.

Many people with diabetes experience afternoon hyperglycaemia that is likely due to overmedication with diabetes management medicines – it is essential this cause of hyperglycaemia be addressed.

What will you do as you identify altered glycaemia patterns, will you -

- review all other prescribed medicines for their contribution to the altered glycaemia?
- recommend a 3-day qid charting of BSLs to clarify the timing, duration and regularity of altered glycaemia episodes?
- recommend trialling vitamin C interventions pre and post known onsets of hyperglycaemia eg prednisolone?
- recommend trialling a vitamin C intervention post each unknown altered glycaemic episode?
- write up your first ten case studies and present at your next professional conference?

Conclusions

Both hyperglycaemia and hypoglycaemia are associated with profound physiological harm – much of which is related to oxidative stress. A simple harm minimization strategy such as the administration of vitamin C interventions after each altered glycaemic episode has the potential to confer logterm benefit.

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: vit D def, poor appetite

Other: behaviours, chronic pain, lower leg oedema

Biochemistry with Pharmaconutrition Consequences

Na:	139	mmol/l	Hb:	144	g/L	Albumin:	44	g/L	BSL:		mmol/l
K:	4.5	mmol/l	Lymph:	1.8		Total Protein:		g/L	HbA1C:		
Urea:	15.2	mmol/l	MCV:	94	mmol/l	B12:		pmol/L	INR:		
Creatinine:	0.114	mmol/l	Zn:		umol/l	Folate:		nmol/L	TSH:		mIU/L

Other: eGFR 45, Ca 2.41, Ca corr 2.35, phos 1.23, Mg 0.99, CRP 9

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
Frusemide	(20 mg/day) Ca, Cl, K, Mg, Na,		☑	NV	CD		↓	☐				☑	☐	☑
Lactulose			☐	NV	D		↓	☐				☐	☐	☑
Paracetamol			☐	NV	CD			☐				☐	☐	☐
VITA-D GEL CAPS	(1000IU/day)		☐					☐				☐	☐	☐
			▩					▩				▩	▩	▩

Extra drug: norspan, multivit

Transporter-mediated interactions and nutrients

Transporter	OCT1		OCT2		OCT3	
Nutrients - Sub	B1, choline, carnitine		B1, choline, creatinine		B1	
Nutrients - Inh						
DRUG	Sub	Inh	Sub	Inh	Sub	Inh
Asasantin				Y		
Citalopram		Y		Y	S	
Omeprazole		Y		Y		Y
Targin				Y		

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

NO PORK - COPTIC ORTHODOX

Data summary

Biochemistry

Recent available biochemistry not relevant to pharmaconutrition.

Glycaemia

Currently prescribed 2 medications that alter glycaemia.

Pharmaconutrition

Currently prescribed 3 medications that include hypokalaemia, nausea, vomiting, diarrhoea as side effects.

Currently prescribed 2 medications that include hyponatraemia, constipation and poor appetite as side effects.

Frusemide increases urinary excretion of calcium, magnesium, potassium, sodium and thiamine.

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

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

Concurrent ingestion of drug 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.

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

Bowel management

Regular aperient prescribed.

Oral and anal PRN interventions prescribed; oral administered 4 x Jan, 3 x Nov.

No Nurse Initiated interventions administered.

Staff comments

Staff advise a variable food intake - eating well some days but not others.

Observations

Mr ACK is a frail man with 100 years to develop his guile and determination skills - he did not want to answer any of my questions and so didn't!

Mr ACK's current weight status is indeterminate ie is he continuing to lose, is he stabilising or is he gaining?

Pharmaconutrition comments

I was unable to ascertain whether food has an acceptable taste for Mr ACK, therefore since he has been prescribed frusemide for at least a couple of years, and since there has been loss of weight which is associated with depletion of zinc levels, advisable to clarify zinc status.

Loss of weight is 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 ACK has an indeterminate weight, advisable to clarify zinc levels and if inadequate then short term (90-120 days) intervention and recheck status prior to cessation of the intervention.

Advisable to clarify whether Mr ACK's pain is well-controlled - nutritional factors that may be useful to consider in pain management include -

- vitamin D - current intervention may not be adequate to attain adequate range as evidence indicates increasingly brittle pain control with decreasing vitamin D levels. Advisable to clarify status;

- magnesium – proposed mechanism 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 frusemide which decreases magnesium absorption therefore advisable to clarify status.

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

- loss of weight – several of Mr ACK's prescribed medicines include side effects that directly and indirectly negatively impact food intake;

- calcium – currently within acceptable range; important in muscle function, currently prescribed frusemide therefore advisable to monitor status;

- vitamin D – associated with muscle weakness and consequently falls; currently prescribed intervention therefore advisable to clarify vitamin D status to clarify whether current intervention is effective;

- zinc – can decrease food intake through altered sense of taste and poor appetite; currently prescribed frusemide therefore advisable to check status;

- low magnesium - magnesium is important in vitamin D activation and muscle function, amongst other functions. Also currently prescribed frusemide which significantly decreases magnesium absorption. Magnesium is an intracellular ion therefore serum levels are unlikely to detect early depletion of status Advisable to monitor magnesium status;

The identified membrane transporters inhibit the absorption and/or organ and cellular uptake of a range of nutrients as identified which means blood test results are likely to indicate normal or elevated status whereas these nutrients may be in

the blood because they are prevented from entering relevant organs and cells, therefore recommended to –

- conduct a comprehensive Diet History to clarify adequacy of potentially compromised nutrients intakes,
- clarify whether the blood samples were drawn several hours before or after administration of relevant prescribed medicines?

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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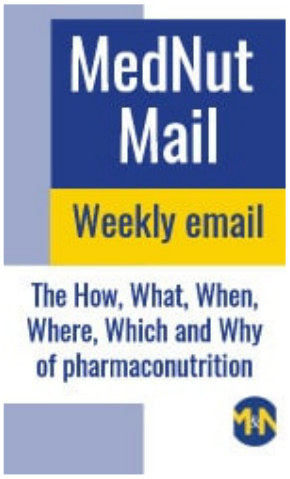

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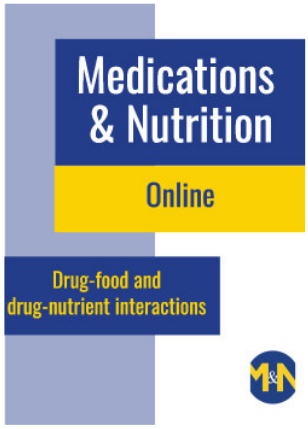

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