MedNut Mail

The How, What, Which, Where, When and Why of pharmaconutrition

Aspirin-vitamin C interaction

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Editorial

The aspirin-vitamin C interaction was discovered in the early 1970's. Much of the evidence is based on short term, high-dose interventions and there is minimal evidence in relation to low-dose, long term interventions. Currently there are no commonly prescribed clinical interventions for this interaction.

Vitamin C transporters include -

- SVCT1 (Sodium Vitamin C Transporter 1) – primarily involved in maintaining vitamin C status in the body; interaction with aspirin seems unlikely;
- SVCT2 –primarily involved in cellular uptake of ascorbic acid; no interaction with aspirin;
- SVCT3 – function unknown therefore likely interaction with aspirin unknown;
- GLUT1 (Glucose Transporter 1) – involved in the transport of ascorbic acid into the mitochondria where it acts as an antioxidant and protects cells from oxidative damage. Dehydoascorbic acid (DHA) enters cells through GLUT1 and is reduced to ascorbic acid; aspirin is an inhibitor and/or regulator of GLUT1;
- GLUT2/3/4/8 – can transport DHA; likelihood of interaction with aspirin unknown.

DHA and glucose have similar three-dimensional structures and some GLUT transport proteins have a higher affinity for DHA than glucose, consequently the glucose concentration in plasma also affects DHA transport.

How aspirin negatively impacts vitamin C status remains speculative, with a strong contender being depletion of intracellular vitamin C status due to increased antioxidant defences in response to aspirin-induced mucosal damage.

However, utilization of the technological combination of voltammetry, infrared, three-dimensional fluorescence and circular dichroism in 2020 (https://doi.org/10.1016/j.saa.2020.118356), has ascertained that aspirin influences the binding process of Vitamin C to albumin. Further, the authors conclude Vitamin C should be administered first because it does not alter aspirin absorption whereas if aspirin is administered first then there is a consequent reduction in vitamin C absorption.

There is a recommendation that the daily dose of ascorbic acid may need to be increased during long term aspirin therapy from the daily dose of 30 –60 mg ascorbic acid to 100 – 200 mg.

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Consequently, aspirin apparently inhibits vitamin C absorption by 2 mechanisms –

1. inhibition of GLUT1 cellular uptake of DHA;
2. inhibition of vitamin C binding to albumin.

Being a drug-protein interaction, this aspirin-vitamin c interaction is indicative of a new mechanism of action in drug-nutrition interactions.

Clinical Considerations

If a vitamin C intervention is to be considered when aspirin is prescribed then when would be the best time to administer it? The recommended timing for aspirin administration is with food, therefore perhaps vitamin C should be administered either one hour prior to the same meal, or administered at another defined time.

Clinical Questions

What actions will you initiate as you a review a person whose prescribed medications include aspirin, will you –

- clarify duration of prescription and consider recommending a vitamin C intervention, and at what dose?
- recommend an administration time of the vitamin C intervention?
- recommend the Medications Advisory Committee develop guidelines for administration of vitamin C when aspirin is prescribed?

Conclusions

The aspirin-vitamin C interaction is rarely clinically addressed. Recent evidence highlights the importance of administering a vitamin C intervention at a different time from aspirin administration.

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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: chronic pain, PA (L) heel, B12 def, Zn def, IDA

Biochemistry with Pharmaconutrition Consequences

Na:	147	mmol/l	Hb:	111	g/L	Albumin:	41	g/L	BSL:		mmol/l
K:	3.9	mmol/l	Lymph:	1.6		Total Protein:	71	g/L	HbA1C:		
Urea:	7.1	mmol/l	MCV:	108	mmol/l	B12:	731	pmol/L	INR:		
Creatinine:	0.079	mmol/l	Zn:		umol/l	Folate:	37.7	nmol/L	TSH:	2.70	mIU/L

Other: eGFR 55, Ca 2.28, Ca corr 2.26, phos 1.11, Mg 0.76, Fe 9, TRF 1.9, satn 19%, ferritin 191, CRP 26, ESR 60, vit D 68

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
Cholecalciferol	(50000 IU/day)	☐					☐				☐	☐	☐
COLOXYL WITH S		☐		D			☐				☐	☐	☐
Metoprolol	B2	☐	NV	CD	↑		☑				☑	☐	☑
MICARDIS	Zn, B1, B2	☑	NV	CD			☑				☑	☐	☐
MOVICOL		☐	N	D			☐				☐	☐	☐
NEO-B12	3/12ly; due 09/19	☐	NV	D			☐				☐	☐	☐
PANADOL	Fe	☐	NV	CD			☐				☐	☐	☐
Pregabalin		☐	NV	CD	↓	↑	☑		↑		☑	☑	☐
URAL		☐	N			↓	☐				☐	☐	☐

Extra drug: prolia, norspan

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Transporter-mediated interactions and nutrients

Transporter	OCT1		OCT2		OCT3		THTR2		OCTN1		OAT1		OAT2	
Nutrients - Sub	B1, choline, carnitine		B1, choline, NMN, carnitine,		B1		B1, B6		carnitine		B1, NMN		B1, NMN	
Nutrients - Inh														
DRUG	Sub	Inh	Sub	Inh	Sub	Inh	Sub	Inh	Sub	Inh	Sub	Inh	Sub	Inh
Metoprolol				Y										
Micardis				Y				Y						Y
Paracetamol												Y		
Pregabalin									Y					
Sub – substrate, Inh – inhibitor, B1 – thiamine, B2 – riboflavin, B3 – niacin, B5 – pantothenic acid, B6 – pyridoxine, B7 – biotin, B9 – folic acid, B12 – cobalamin, NMN – N-methylnicotinamide														

Comments – medication and nutrition effects only

Data summary

Biochemistry with Nutritional Aspect

Recent relevant available biochemistry indicates –

- marginal Hb + elevated MCV – currently prescribed paracetamol therefore advisable to monitor status and ensure marginal status is resolving;
- elevated normal TSH - evidence indicates increased risk of altered thyroid function in the elderly once TSH > 2.5;
- high-normal B12 status – currently prescribed a B12 intervention therefore advisable to review either necessity for its continued administration or reduce frequency of the intervention;
- elevated TSH – is diagnostic for altered thyroid function; currently prescribed metoprolol which masks altered thyroid function therefore advisable to clarify thyroid;
- elevated CRP+ESR - inflammatory response markers; associated with increased resting metabolic rate and consequent increase in energy (food) requirements; influenced by vitamin D status, and currently prescribed a vitamin D intervention;
- marginal vit D - currently prescribed an intervention. Advisable to check vitamin D levels and if still low then review current vitamin D management strategy.

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Glycaemia
Currently prescribed 3 medications that include hyperglycaemia and/or hypoglycaemia as side effects.

Pharmaconutrition
Currently prescribed 6 medications that include nausea aside effect.

Currently prescribed 5 medications that include diarrhoea a side effect.

Currently prescribed 4 medications that include hypokalaemia, vomiting and constipation as side effects.

Currently prescribed 3 medications that include altered taste, dry mouth and sweating as side effects.

Coffee inhibits vitamin D uptake by osteoblasts (bone builders) by inhibiting their vitamin D receptors, and consequently decreases calcium and zinc absorption.

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 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.

The identified membrane transporters inhibit the absorption and/or organ and cellular uptake of thiamine, choline, carnitine, pyridoxine and NMN (B3) 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. Advisable for blood tests to be conducted several hours after administration of relevant prescribed medicines.

Bowel management
Regular aperient prescribed.
Oral PRN aperient prescribed; administered 1 x this month.
No Nurse Initiated interventions administered.

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Staff comments
Staff advise Mrs ACP is recovering from a recent significant infection, that during the duration of the infection she ate sparingly, and now her appetite is improving

Observations
Mrs ACP is a small, pale, frail lady who was sitting up in bed when I went to speak to her - she answered all my questions appropriately and briefly - she seems to be quite a character.

Mrs ACP remained relatively weight stable about 50 kg from admission until 6 months ago then lost weight - staff attribute the weight loss to her recent unwellness.

Pharmaconutrition comments

Ordinarily, since Mrs ACP is pale, I would recommend a short term iron intervention however latest SIS results indicate IDA is resolving.

Mrs ACP's diagnoses include B12, zinc and iron deficiencies - an intervention has been initiated for B12 deficiency only. If iron and zinc interventions are initiated then advisable to administer at different times from each other as they share the same absorption mechanism.

Mrs ACP's diagnoses include a pressure area - nutritional interventions that support to wound healing include -
- ensure adequate status of B12, zinc and iron – currently commenced a B12 intervention, micardis impairs zinc availability and paracetamol masks iron status;
- adequate vitamin D status - evidence indicates low vitamin D status is associated with delayed wound healing and currently prescribed a vitamin D intervention**.**

Mrs ACP's diagnoses include 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;
- evidence indicates substantial relief of neuropathic pain by thiamine, pyridoxine and cyanocobalmin separately, and in combination there was a synergistic benefit;
- low B12 exacerbates elevated TNF- α which is an inflammatory response marker; elevation of the inflammatory response can include a pain response - currently prescribed a B12 intervention;

What else would you include?

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The information in this article is provided to support Health Professionals. It is not an exhaustive protocol and Health Professionals are advised that adequate professional supervision is accessed to ensure that Duty of Care obligations with respect to safe administration of medicines is met for each consumer.

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