MedNut Mail

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

Aspirin and various nutrients

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https://medicationsandnutrition.com/mednutmail/

Editorial

Interactions between aspirin and various nutrients have been identified over a number of decades and are either old, forgotten, or have no supporting references, and therefore require clarification with regard to current status.

Nutrients for which there is relatively recent evidence -

1. **Vitamin E.**
   The proposed aspirin-vitamin E interactions generally refer to possible additive antithrombotic effects, ie their co-administration increases the risk of bleeding.

   Whether there is any benefit in combining vitamin E with aspirin has been equivocal as the evidence is limited – small studies generally indicate benefit is conferred whilst expert opinions generally negate the findings.

   However, a 2017 study looked at the effect of vitamin E and aspirin on the uterine artery blood flow in women with recurrent miscarriages, and found that all 3 combinations ie aspirin alone, vitamin E alone, aspirin + vitamin E combination, conferred benefit by improving uterine blood flow, with the aspirin + vitamin E combination conferring the most benefit; proposed mechanism of action is decreased uterine artery PI (pulsatility index).

   Other evidence has found that Vitamin E can inhibit MultiDrug Resistance (MDR) by inhibiting the activity of ATPase to prevent P-gp's eviction of defined drugs from cells, thus increasing their within-cells presence and consequently enhancing therapeutic benefit. Speculatively, as aspirin is a P-gp substrate (carried by P-gp), Vitamin E could inhibit aspirin function via this mechanism of action.

2. **Magnesium stearate.**
   Magnesium stearate, a common excipient (ingredient), has been found to reduce the effectiveness of aspirin, and its use was associated with a higher risk of composite events than non-Mg stearate preparations ie the implied meaning being that not all aspirin products have equivalent antiplatelet effect. One author actually states magnesium stearate is an incompatible excipient for aspirin

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These are nutrients that aspirin is deemed to have a negative impact and for which there does not seem to be any recent (within 10 years) evidence -

- Niacin **-** aspirin alters niacin metabolism,
- Potassium **-** aspirin increases and/or decreases potassium excretion.

Unreferenced evidence stated within a VERY reliable source and for which I have not been able to locate evidence is that aspirin may increase serum levels of - chromium, magnesium chloride, magnesium trisilicate, potassium, selenium, tocopherol.

Potential interactions include those associated with aspirin transporters such as -

- OAT1 – aspirin inhibits function; substrates include pantothenate, pyridoxic acid (B6), biotin, folate;
- OAT3 - aspirin inhibits function; substrates include pantothenate, pyridoxal, pyridoxate, pyridoxic acid (B6), flavin mononucleotide (B9), dehydroascorbic acid (vitamin C), carnitine;
- P-gp – substrates include aspirin, niacin, pantothenate, pyridoxine, folate, cobalamin, vitamin D; inhibitors include vitamin A.

Clinical Considerations

If aspirin is prescribed, then what would be an appropriate scenario for these potential nutrient interactions to be considered? There are a number of scenarios to consider –

Given there is an additive effect if aspirin and vitamin E are administered concurrently, if there is excessive bleeding then is it possible/probable that excessive vitamin E could be a contributing factor? The excessive vitamin E could be due to nutrient supplements, excessive high vitamin E-containing food intake, and/or inhibition of relevant transporters.

Given magnesium stearate is deemed incompatible with aspirin, advisable to check excipients to ensure it is not present in any of the prescribed medications that are administered concurrently with aspirin.

Since vitamin A is a P-gp inhibitor, and aspirin is a P-gp substrate, then there is a potential risk that vitamin A interventions could inhibit aspirin function and effectiveness.

Otherwise, if the recorded Diet History intakes do not match with blood test results, then it would be reasonable to ask why and whether there is a potential risk of an interaction with aspirin.

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Clinical Questions

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

- compare the Diet History nutrient intakes with blood test results and question any disparities?
- consider recommending nutrient interventions to be administered at a different time from aspirin to minimize the risk of adverse drug-nutrient interactions?
- recommend the Medications Advisory Committee develop guidelines for nutrient interventions when aspirin is prescribed?

Conclusions

Whilst interactions between aspirin and various nutrients have been identified over several decades, clinical management strategies have not been developed, and so these drug-nutrient interactions are not considered.

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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: diverticulosis, gastritis, micralbuminaemia, pain

Other: choreaform move't disorder/? Huntingtons, RA, IDC

Biochemistry with Pharmaconutrition Consequences

Na:	139	mmol/l	Hb:	109	g/L	Albumin:	37	g/L	BSL:		mmol/l
K:	4.8	mmol/l	Lymph:	1.7		Total Protein:	72	g/L	HbA1C:	7.1	
Urea:	8.1	mmol/l	MCV:	94	mmol/l	B12:		pmol/L	INR:		
Creatinine:	0.071	mmol/l	Zn:		umol/l	Folate:		nmol/L	TSH:	0.74	mIU/L

Other:), Ca corr 2.36, phos 1.13, Mg 0.82, uric acid 0.42, chol 4.6, Tg 2.5, HDL 1.08, LDL 2.4, LDL:HDL 2.2, chol:HDL 4.3, Fe

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, folate	☑	NV				☐				☐	☐	☑
Baclofen		☐	NV	CD	↑	↓	☑				☑	☐	☑
Cholecalciferol	(1000 IU/day)	☐					☐				☐	☐	☐
COLOXYL WITH S		☐		D			☐				☐	☐	☐
Lactulose		☐	NV	D		↓	☐				☐	☐	☑
Metformin	(08:00, 17:00) Mg, Zn, B1, B6	☐	NV	D	↓	↓	☑				☐	☐	☑
Pantoprazole	(40 mg/day) B1, B12, Ca, Fe,	☑	NV	CD		↓	☑				☑	☐	☐
Paracetamol	Fe	☐	NV	CD			☐				☐	☐	☐
Perindopril	Zn, B2	☐	NV	D			☑				☑	☐	☐
Pregabalin		☐	NV	CD	↓	↑	☑		↑		☑	☑	☐
URAL		☐	N			↓	☐				☐	☐	☐

Extra drug: magnesium aspartate (1 tab/day), empagliflozin

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Transporter-mediated interactions and nutrients

Transporter	OCT1		OCT2		OCT3		THTR2		OCTN1		MATE 1		MATE 2		OAT1		OAT3		P-gp		BCRP	
Nutrients - Substrates	B1, ch, car		B1, B3, ch, car		B1		B1, B6		car		B1, B3		B1, B3		B9, B5, B6, B7		B5, B9, car, B6, DHA (vit C),		B9, B12, vit D, B6, B3, B5		B2, B9, B5, vit K3	
Nutrients - Inh																			vit A		vit D2	
DRUG	S	I	S	I	S	I	S	I	S	I	S	I	S	I	S	I	S	I	S	I	S	I
Aspirin																Y		Y	Y			Y
Pregabalin									Y													
Pantoprazole		Y		Y		Y	Y									Y					Y	
Metformin	Y	Y	Y		Y				Y		Y		Y									
Other – aspirin inhibits SMVT																						
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, ch – choline, car - carnitine																						

Comments – medication and nutrition effects only

Data summary

Biochemistry

Recent relevant available biochemistry indicates
- low Hb - associated with increased risk of falls, and poor appetite; currently prescribed pantoprazole;
- elevated MCV - advisable to check B12 levels; currently prescribed metformin and pantoprazole. Neuro-imaging research that B12 interventions are effective once levels are less than 300 pmol/L;

Glycaemia

BSLs (Apr-May)
- daily range - 5.3-11.7; recommended range 4-10;
- monitored monthly;
- unable to locate reportable limits.

Diabetes drugs
- metformin has a duration of 12 hours;
- empagliflozin time to peak is 1.5 hour.

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Diabetes drugs coverage

- before breakfast BSLs - minimal, if any, coverage from previous morning's metformin or previous evening's metformin;
- before evening meal BSLs - covered by current morning's metformin.

Currently prescribed 4 medications that alter glycaemia.

Pharmaconutrition

Currently prescribed -

- 9 medications that include nausea as a side effect.
- 7 medications that include vomiting and diarrhoea as side effects.
- 6 medications that include altered potassium status and altered appetite as side effects.
- 5 medications that include altered taste as a side effect.
- 4 medications that include dry mouth and sweating as side effects.
- 3 medications that include anaemia, altered sodium status, altered zinc status, constipation and weight change as side effects.

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

Aspirin decreases vitamin C and folic acid availability.

Drug-coffee interaction – coffee alters gastric pH resulting in increased drug absorption.

Currently prescribed colecalciferol - coffee inhibits vitamin D uptake by osteoblasts (bone builders) by inhibiting their vitamin D receptors.

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

Magnesium aspartate provides 37.4 mg/day elemental magnesium - women require 320 mg magnesium per day; currently prescribed metformin and pantoprazole. Advisable to monitor magnesium levels on a regular basis.

Metformin decreases B12, thiamine, pyridoxine, folate, magnesium and zinc absorption – therefore advisable to monitor levels on a regular basis ie at least annually.

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

Paracetamol decreases iron status.

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

Perindopril decreases availability of zinc and riboflavin – advisable to monitor status.

Currently prescribed the daily double ie 2 drugs that decrease B12 absorption - being pantoprazole and metformin; there is also evidence that this combination has an additive depletion effect on B12 status.

The identified membrane transporters inhibit the absorption and/or organ and cellular uptake of thiamine, choline, carnitine, pyridoxine, NMN (B3), folate and pantothenate which means blood test results are likely to indicate low, normal or elevated status whereas these nutrients may be in the blood because they are prevented from entering or exiting relevant organs and cells. Advisable for blood tests to be conducted several hours after administration of relevant prescribed medicines.

Bowel management

- regular aperients prescribed;
- oral + anal PRN interventions prescribed; oral - 1 x Apr, 2 x Mar; anal - 1 x Mar;
- no Nurse Initiated interventions administered.

Staff comments

Staff advise Mrs ACR eats well, and is able to say if she would like more food.

Observations

I was unable to locate Mrs ACR to have a chat.

Mrs ACR has been losing weight for the last 6 months.

Pharmaconutrition comments

Mrs ACR’s diagnoses include arthritis and therefore chronic pain. Nutritional factors that may be useful to consider in pain management include -

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- vitamin D - current intervention may not be adequate to attain adequate range. Evidence indicates increasingly brittle pain control with decreasing vitamin D levels therefore advisable to monitor status;
- 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 pantoprazole 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 and currently prescribed pantoprazole and metformin therefore advisable to monitor B12 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 metformin and pantoprazole which decrease magnesium availability.

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

- low calcium - more likely to be low if potassium or magnesium low; important in muscle function, currently prescribed pantoprazole therefore advisable to clarify status;
- low B12 - is important in the righting reflex when a person stumbles; prescribed metformin and pantoprazole therefore advisable to check status;
- low Hb - advisable to monitor status on a regular basis as currently prescribed aspirin, pantoprazole and paracetamol;
- low zinc – can decrease food intake through altered sense of taste and poor appetite, and consequently reduced muscle mass; currently prescribed pantoprazole and perindopril therefore advisable to monitor status;
- low magnesium - magnesium is important in vitamin D activation and muscle function, amongst other functions. Also currently prescribed metformin and pantoprazole which significantly decrease magnesium availability. Magnesium is an intracellular ion therefore serum levels are unlikely to detect early depletion of status Advisable to monitor magnesium status.

Mrs ACR's diagnoses include osteoporosis - nutritional factors that may be useful to consider in osteoporosis management include -

- sodium – excessive intake competes with calcium for reabsorption in the renal tubules ie excessive sodium intake increases calcium loss;

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- homocysteine – elevated levels associated with impaired collagen crosslinking and thus compromised bone strength, also negatively impacts osteoblast and osteoclast activities. Homocysteine levels are likely to be elevated if low riboflavin, low B12, low folate, or low pyridoxine therefore advisable to monitor their levels on a regular basis.

What else would you include?

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