MedNut Mail

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

Caffeine and pharmaconutrition

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6th July 2022

https://medicationsandnutrition.online

Commentary

Caffeine is a commonly consumed foodstuff, typically found in beverages such as coffee, tea, cola, energy drinks, and foods such as guarana, cocoa and chocolate.

Caffeine can alter the absorption, distribution, excretion, and induction or inhibition of metabolizing enzymes for a range of prescribed medications by -

1. Altering absorption

- changing the dissolution profile - increasing or decreasing absorption by altering solubility;
- changing the gastrointestinal pH – by increasing hydrochloric acid secretion which can alter the solubility of a drug ie increased or decreased solubility;
- interacting with a third party – for example coffee interacts with osteoblasts to alter the absorbed amount of vitamin D;
- affecting the gastrointestinal emptying time - increased hydrochloric acid secretion can also alter the rate of dissolution, and the rate of gastric transit ie the faster the dissolution of some drugs, then the faster the rate of absorption;
- the formation of complexes – caffeine can complex with a drug that ultimately results in an increased or decreased absorption of both components;
- inhibiting glucose-6-phosphate dehydrogenase activity - results in reduction in the intracellular levels of NADPH and reactive oxygen species (ROS), and altered the expression of redox-related proteins in Renal Cell Carcinoma cell.

2. Altering distribution

- by altering the permeability of the blood-brain barrier – to enable increased or decreased substance entry and excretion;
- by slowing the rate of conversion of L-Dopa to dopamine which results in extended distribution in brain tissues and increased therapeutic effect.

3. Altering metabolism

- by saturating or inducing enzymes – resulting in an altered rate of drug elimination and altered blood levels for a variable duration.

4. Altering excretion

- by increasing urinary volume – partly by inhibiting Anti-Diuretic Hormone, and partly by antagonising adenosine receptors.

Caffeine effect is dose related ie high caffeine intake is associated with pain relief and indeed caffeine is now an active ingredient in some of the pain management interventions, whilst dietary caffeine intake (6-8 cups coffee/day) is associated with reduced pain relief as evidenced by reduced paracetamol effect.

Some common drugs that interact with caffeine include allopurinol, alprazolam, amlodipine, aspirin, clozapine, esomeprazole, fluvoxamine, lansoprazole, lithium, melatonin, nifedipine, nitrazepam, omeprazole, oxazepam, paracetamol, rabeprazole, theophylline, warfarin.

The authors of the paper **The Effect of Coffee on Pharmacokinetic Properties of Drugs: A Review** make the following recommendations –

- that consumption of caffeine-containing foods and beverages be restricted as appropriate unless a lack of interaction has already been established for a particular drug,
- that medications that interact with coffee should be appropriately labelled,
- that the time required to minimise interactions between intake of drug and coffee be identified and recommended,
- that relevant drug regulatory agencies and researchers support further research in this area.

The recommendation to label medications that interact with caffeine seems obvious as caffeine-containing beverages are ubiquitously consumed globally (~ 87% global population consume caffeine daily) – especially at mealtimes and most social occasions, however it's very ubiquity makes limiting and regulating caffeine intake difficult to manage. There is a requirement that medications that interact with ethanol are identified during the drug discovery process, therefore it should not be difficult for a similar requirement to apply to caffeine.

What is the best strategy for busy clinicians to integrate caffeine-prescribed medications interactions into their daily practice? I suggest if a person has a stable intake and their health status is stable then advisable not to make changes, however if the person has an unstable intake and their health status is also unstable then advisable to discuss with GP/Consultant and pharmacist the potential benefit of limiting caffeine intake and regulating its timing, prior to initiating the action.

What actions will you initiate when you see someone prescribed a medication that interacts with caffeine - will you -

- clarify whether caffeine intake is an issue?
- start discussing the benefits of regulating and limiting caffeine intake if the person has unstable health status? Substituting water for caffeinated beverages may lead to improved bowel function!

Conclusions

Caffeine has the capacity to alter many aspects of prescribed medication availability, and the outcomes may range from therapeutic failures to toxic responses.

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: hypercholesterolaemia, cholecystectomy

Biochemistry with Pharmaconutritional Consequences

Na:		mmol/l	Hb:		g/L	Albumin:		g/L	BSL:		mmol/l
K:		mmol/l	Lymph:			Total Protein:		g/L	HbA1C:	5.8	
Urea:		mmol/l	MCV:		mmol/l	B12:	252	pmol/L	INR:		
Creatinine:		mmol/l	Zn:		umol/l	Folate:	26.9	nmol/L	TSH:		mIU/L

Other: Fe 12, TRF 3.1, satn 16%, ferritin 21, vit D 72, holotranscobalamin 67

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	(1000 IU/day)		☐					☐				☐	☐	☐
MOVICOL			☐	N	D			☐				☐	☐	☐
PANADOL			☐	NV	CD			☐				☐	☐	☐
Pantoprazole	(40 mg/day) B1, B12, Ca, Fe,		☑	NV	CD		↓	☑				☑	☐	☐
Risperidone			☑	NV	C	↑		☐		↑		☐	☐	☐
			▩					▩				▩	▩	▩

Extra drug: novomix 16U mane, 6U nocte

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

Recent relevant available biochemistry indicates

- low B12 – relatively recent research shows a direct causal link between B12 status and memory impairment; they also found increasing memory impairment as B12 levels dropped even whilst within acceptable range. The authors recommend B12 interventions once levels are less than 300 pmol/L.

Diabetes drugs

- novomix has a time to onset of 5-15 minutes, variable time to peak, and duration of 10-16 hours.

Risperidone may increase risk of glucose intolerance and may increase requirements for antidiabetic agents.

BSLs

- before breakfast - 5.1-10.5; recommended range 4-6,
- daily range - 5.1-15.8, mostly 5-10; recommended range 4-10,
- tested daily bd,
- reportable limits: < 4 and > 20,
- HbA1c indicates good glycaemic control.

Diabetes drugs coverage

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

Bowels

- regular aperient prescribed,
- oral PRN aperient prescribed,
- no Nurse Initiated interventions administered.

Staff advise Mrs ABS eats well.

Mrs ABS is a small, curvaceous lady with thyroidy eyes and who was eating her midday meal when I went to speak to her - I did not interrupt her mealtime.

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

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.

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

Longterm PPI use such as pantoprazole, alters gut microbiome by increasing in Fimicutes and reducing Bacteriodetes.

Longterm prescription of proton pump inhibitors is associated with both lower baseline zinc stores and an incapability of adequately increasing zinc plasma levels with oral zinc supplements; authors speculate the effect is likely drug class rather than specific drug.

The time to manifestation of severe hypomagnesaemia may reflect the time required to deplete body stores of magnesium.

There is increasing evidence that proton pump inhibitors such as pantoprazole 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 check magnesium status and if marginal or low then intervention recommended.

Nutritional factors that may be contributing to falls include -

- low potassium - advisable to check status, especially since pantoprazole is prescribed;
- low calcium - more likely to be low if potassium or magnesium low; currently prescribed pantoprazole;
- low vitamin D – currently prescribed an intervention therefore advisable to monitor status to clarify effectiveness of the intervention;
- low B12 - is important in the righting reflex when a person stumbles therefore advisable to check status; currently prescribed pantoprazole;
- low Hb - advisable to check status and if low then intervention advisable; currently prescribed pantoprazole;
- low zinc - more likely to be low if prescribed a proton pump inhibitor; advisable to check status as pantoprazole prescribed;
- low magnesium - magnesium is important in muscle function, especially cardiac muscle, amongst other functions. Also currently prescribed pantoprazole 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 as pantoprazole prescribed.

Two prescribed medications, pantoprazole and risperidone, inhibit thiamine transporters into the liver, kidney and muscles therefore advisable to monitor thiamine status. Given the degree of organ inhibition of thiamine uptake, normal thiamine levels may not indicate actual physiological status.

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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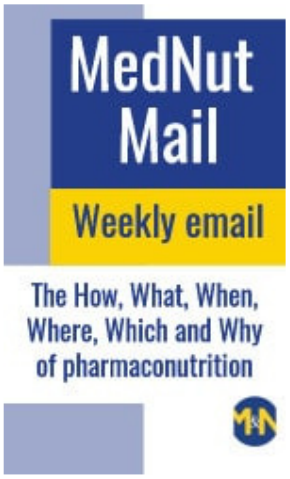

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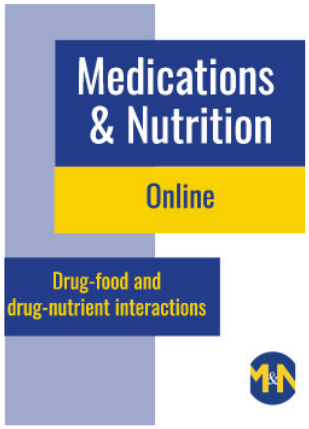

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