MedNut Mail

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

DOACs and pharmaconutrition

Y Coleman

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https://medicationsandnutrition.online

Commentary

DOACs (direct oral anticoagulants) are becoming the preferred option for coagulation management because they do not require the management strategies that warfarin administration necessitate such as regular and frequent INR monitoring, significant dietary restrictions, OH&S concerns relating to internal bleeds, etc especially for farmers, and elderly fallers.

Evidence indicates the individual macronutrients, being proteins, fats and carbohydrates, do not significantly affect the availability of apixaban, dabigatran, or edoxaban whilst high fibre diets (insoluble and/or soluble) have been found to reduce the availability of apixaban, dabigatran, and rivaroxaban. There is a suggestion that concurrent administration of a high-fibre diet and a DOAC is ill-advised.

Further, evidence indicates fasting alters drug effect and therefore regular meal consumption is recommended.

Unsurprisingly there do not seem to be any/many studies on interactions in humans between DOACs and a range of foodstuffs- likely mechanisms of action include the relevant cytochromes and transporters.

There are currently 4 DOACs, summarised from this excellent article, being –

1. **Apixaban**

   Can be taken with or without food; albeit after food ingestion time to maximum plasma concentration (Tmax) is shortened.

   Apixaban showed slight inhibitory effects on OAT1 (into liver), significant inhibitory effects on OAT3 (into muscles), and insignificant inhibitory effects on OCT2 (into kidneys).

   Inhibition of OAT1/3 are likely to negatively impact pantothenate and pyridoxine.

   Foodstuffs that inhibit OAT1 include - green tea, tea, coffee, cola, chocolate, some carbonated drinks, guarana, cola nuts, cocoa.

2. **Dabigatran**

   Dabigatran should not be crushed or chewed and contra-indicated for those fed enterally.

Is not metabolized by cytochrome P450 enzymes therefore food restrictions such as grapefruit juice are not relevant.

Renal excretion likely due to MATE (into urine) and MATE2K (into urine); MATEs also transport thiamine and pyridoxine.

Dabigatran showed slight inhibitory effects on OAT1, no effect on OAT3, and insignificant inhibitory effects on OCT2.

Inhibition of OAT1 is likely to negatively impact pantothenate and pyridoxine.

Foodstuffs that inhibit OAT1 include - green tea, tea, coffee, cola, chocolate, some carbonated drinks, guarana, cola nuts, cocoa.

3. Edoxaban

Food does not affect absorption.

Can be crushed and administered either in apple puree and taken orally or as a water suspension enterally.

Limited metabolism via CYP3A4 and CYP3A. It is not clear whether foods such as grapefruit juice, etc are contra-indicated.

Does not inhibit at clinically relevant concentrations OAT1, OAT3, OCT1, OCT2, P-gp or OATP1B1, OATP1B3.

It is unlikely the negative impacts of DOACs on nutrients has been investigated therefore it may be prudent to monitor nutrients that are likely to be impacted such as pantothenate, pyridoxine, thiamine and choline.

4. Rivaroxaban

Must be administered with food.

Can be administered by crushing and mixing with water or apple mousse.

Limited metabolism by CYP3A4, 3A5 and 2J2; it is not clear whether foods such as grapefruit juice, etc are contra-indicated.

Rivaroxaban showed slight inhibitory effects on OAT1, significant inhibitory effects on OAT3, insignificant inhibitory effects on OCT2, and substrate for OAT3.

Inhibition of OAT1/3 are likely to negatively impact pantothenate and pyridoxine.

Foodstuffs that inhibit OAT1 include - green tea, tea, coffee, cola, chocolate, some carbonated drinks, guarana, cola nuts, cocoa.

As DOACs are a relatively recent development it is likely there are more DOAC-nutrient and DOAC-food interactions to be identified.

What actions will you initiate when you see someone who has been prescribed a DOAC, will you –

- review regularity of meal intake?
- recommend monitoring pantothenate, pyridoxine and biotin levels?
- check whether other prescribed medications are also negatively impacting these nutrients?

Conclusions

The DOAC drugs reduce the impost that warfarin prescription necessitated – however their drug-nutrient and drug-food interactions are still being identified.

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: asthma

Other: ABI, epilepsy, Ca def, vit D def, psychosis

Biochemistry with Pharmaconutritional Consequences

No recent relevant available results

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		☑	NV				☐				☐	☐	☑
Atorvastatin			☑	NV	CD	↑	↓	☑				☐	☐	☐
Bisacodyl			☐	N	CD			☐				☐	☐	☐
Carbamazepine	B6, biotin, carnitine, D, folate,		☐	NV	CD	↑	↑	☑				☑	☐	☐
Cholecalciferol	(1/day)		☐					☐				☐	☐	☐
Citalopram	Na		☐	NV	CD	↑	↕	☑		↑		☑	☑	☑
COLOXYL WITH S			☐		D			☐				☐	☐	☐
Domperidone			☑	N	CD		↕	☐	↓			☑	☐	☐
Mirtazapine			☐	N	D	↑	↑	☐				☑	☐	☐
Olanzapine			☑		C	↑	↑	☐				☑	☐	☐
Perindopril			☐	NV	D			☑				☑	☐	☐
Phenytoin	B6, biotin, Ca, carnitine, D, fol		☑	NV	C	↓	↓	☑				☐	☐	☑

Extra drug: natural b complex

Summary of medications, nutrients and transporters

Organ (transporter)	Thiamine	Choline	Carnitine
Inhibitor function			
Liver	Citalopram Olanzapine	Citalopram Olanzapine	
Into kidneys	Citalopram Mirtazapine Olanzapine	Citalopram Mirtazapine Olanzapine	
Substrate function			
Into muscles	Citalopram	Citalopram	Citalopram

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

Data summary

Biochemistry

No recent relevant available biochemistry. Advisable to check plasma proteins (albumin, total proteins) as they are the primary transporters for five of the prescribed drugs and hypoproteinaemia may alter their effects and side effects.

Glycaemia
Currently prescribed 5 medications that alter glycaemia, being aspirin, atorvastatin, citalopram, olanzapine, perindopril and phenytoin.

Pharmaconutrition
Currently prescribed 9 medications that include nausea as a side effect.

Currently prescribed 6 medications that include vomiting and dry mouth as side effects.

Currently prescribed 11 medications with side effects that negatively impact appetite either directly and /or indirectly.

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

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

Carbamazepine decreases biotin and carnitine absorption and decreases availability of folate and vitamin D.

Regular monitoring sodium levels recommended whilst citalopram and mirtazepine prescribed.

Perindopril impairs zinc status.

Phenytoin decreases biotin and carnitine absorption and decreases availability of thiamine, folate, vitamin K, vitamin D.

Since two drugs (carbamazepine, phenytoin) decrease folate availability advisable to check folate status and if low then consider a low-dose management strategy.

Evidence now indicates biotin (B vitamin) is important in glycaemic control. Longterm inadequate biotin intake is likely to increase risk of development of diabetes, and currently prescribed carbamazepine and phenytoin therefore advisable to monitor Mr AGI for diabetes on a regular basis (at least 6-monthly).

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

Meta-analysis of statin therapy on plasma CoQ10 concentrations found statins significantly reduced plasma CoQ10 status.

Statins interfere early in the cholesterol metabolic pathway and consequently decrease -
- conversion of sun to vitamin D - vitamin D intervention recommended,
- production of CoQ10 - important in cellular energy production; CoQ10 intervention recommended,
- DHEA production - low DHEA associated with increased risk of metabolic syndrome; intervention recommended.

Advisable to clarify cholesterol status.

Bowel management
- regular x 2 aperients prescribed,
- oral PRN aperient prescribed,
- no Nurse Initiated interventions administered.

Currently prescribed 7 medications that include constipation as a side effect.

Staff comments
Staff advise Mr AGI was eating well until he was commenced on a vitamised meat diet due to his coughing. Staff also commented Mr AGI does not like desserts, and does enjoy bananas and banana-flavoured milk drinks.

Observations
Mr AGI is a tall, slender, softly-spoken man who was sitting in the Day Room when I went to speak to him - he told me he dislikes the sight of vitamised meat and that he really likes fish and chips.

Mr AGI's weight status is currently indeterminate ie it is unclear whether he is remaining weight stable or whether he is losing weight.

Pharmaconutrition comments
The Scottish lipid study found that a 5-year prescription of atorvastatin confers 20 years of benefit - atorvastatin has loss of appetite as a side effect. Given Mr AGI's currently poor food intake, and indeterminate weight status, advisable to clarify duration of statin prescription and consider its cessation if > 5years.

Mr AGI's diagnoses include falls - nutritional factors that may be useful to consider in falls management include -
- loss of weight – prescribed 11 drugs with side effects that negatively impact food intake;
- low calcium - more likely to be low if potassium or magnesium low; important in muscle function, currently prescribed phenytoin therefore advisable to clarify status;
- vitamin D – associated with muscle weakness and consequently falls; currently prescribed atorvastatin, carbamazepine and phenytoin therefore advisable to clarify vitamin D status.
- low Hb - advisable to check status and if low, and SIS within acceptable range then may indicate carbamazepine and phenytoin are affecting biotin absorption - biotin is important in five stages of Hb formation;
- low zinc – can decrease food intake through altered sense of taste and poor appetite, and consequently reduced muscle mass; currently prescribed carbamazepine therefore advisable to check status;
- low carnitine - carnitine is both absorbed and produced de novo, and is important in a range of muscle functions; carbamazepine and phenytoin decrease

carnitine absorption; magnesium is important in de novo carnitine production. Advisable to clarify status.

Currently prescribed natural B complex – advisable to clarify that all 8 B vitamins are included in the product, and that the doses are not excessive to recommendations.

Caffeine increases aspirin absorption - food sources include tea, coffee, cola, chocolate, some carbonated drinks, guarana and cola nuts. It is likely the caffeine intake from beverages will be relatively constant however chocolate intake is much more likely to be irregular!

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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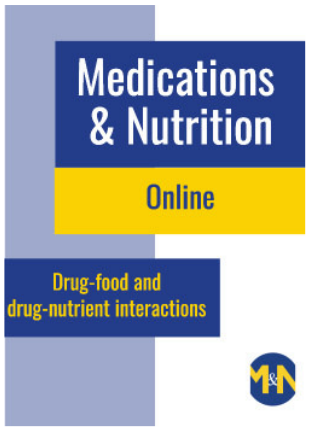

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