MedNut Mail

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

Guest case study - hypercalcaemia

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https://medicationsandnutrition.online

Editorial

This email is based on a question from a concerned clinician.

Oral calcium intake - no evidence of excessive calcium intake in diet, and no high-dose calcium supplements prescribed.

Pathology results -

- PTH (parathyroid hormone) normal;

- calcium ~ 2.7ish mmol/L (elevated), some degree of fluctuation.

Prescribed medications – fluoxetine, olanzapine.

Nutrient supplements – multivitamin, zinc.

Fluid intake - 3 L water/day (therefore not dehydrated).

Data summary

Olanzapine has not been found to be associated with altering calcium availability.

Fluoxetine has been found to alter calcium levels ie hypercalcaemia.

Fluoxetine is consumed daily between 7:30 and 8:30 am.

Fasted bloods are taken every Monday at about 9:00 am.

Meals and midmeals are consumed at nearly the same time (and very similar amounts) each day.

The concerned clinician contacted the biochemist to establish the margin of error on the serum calcium results – the biochemist indicated that the margin of error for a serum calcium over 2.5 mmol/L is 4% and also commented raised levels by 4-5% can be considered within the margin of error. The biochemist recommended the GP monitor parathyroid hormone (PTH) levels and if there are any changes then refer to an endocrinologist.

Transporter-mediated interactions and nutrients

Transporter	OCT1		OCT2		P-gp	
Nutrients - Sub	B1, choline, carnitine, TYR		B1, choline, creatinine, NMN, carnitine, TYR		B9, B12, vit D, lipids	
Nutrients - Inh					vit A, vit D	
DRUG	**Sub**	**Inh**	**Sub**	**Inh**	**Sub**	**Inh**
Fluoxetine		Y		Y		Y
Olanzapine		Y		Y	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, TYR - tryptophan

Pharmaconutrition comments

Both olanzapine and fluoxetine alter glycaemic status, therefore advisable to monitor glycaemia on a regular basis.

Regular measurement of serum sodium levels recommended whilst fluoxetine prescribed.

Currently prescribed a zinc intervention therefore advisable to monitor both zinc and copper levels as they both share the same transporter for absorption; sustained excessive zinc intake has been associated with copper deficiency.

Both prescribed medicines inhibit the OCT1/2 transporters and therefore likely compromise thiamine, choline and carnitine status. Advisable to both –

- clarify adequacy of dietary intake of thiamine, choline and carnitine, and whether well within acceptable ranges, and
- clarify the status of thiamine, choline and carnitine with blood tests and if results are low or high then question whether that is due to the inhibitory effects of the prescribed medicines on their organ and cellular uptake and/or excretion.

It is interesting to note that the two prescribed medicines have differing effects on P-gp (P-glycoprotein), therefore advisable to clarify current status and to monitor folic acid, B12 and vitamin D levels on a regular basis.

There are 4 primary causes for elevated calcium levels, and these causes are not mutually exclusive -

1. excessive dietary intake,
2. increased calcium release from bone,
3. inhibition of organ and/or cellular uptake of calcium,
4. inhibition of calcium excretion.

A thorough diet history has excluded excessive dietary intake therefore the hypercalcaemia is a medical issue.

The time between fluoxetine intake and fasted bloods is quite limited therefore it is likely fluoxetine is still having an effect on serum calcium results. The optimal timing for testing calcium status post fluoxetine intake seems to be currently unknown.

When I was a student in a WA general teaching hospital, the acceptable range for calcium was 2.25 - 2.65 mmol/L, and whilst working as a clinician in Victoria the general range seems to be about 2.10/2.15 - 2.50/2.55 mmol/L, so seemingly there is reasonable variability between pathology ranges. It seems to me that we, and perhaps other clinicians, need to be aware that there is variability between pathology laboratory ranges, and to factor that into our thinking, the questions we ask, and perhaps the decisions we then make.

The consequences of membrane transporters being inhibited and/or carrying non-nutritive substances are slowly being discovered, and their impacts on nutritional health are even more slowly being discovered. However, the outcome is that we can no longer attribute elevated/low nutrient levels in the blood to excessive/inadequate dietary intake alone.

Ultimately this case study highlights that we should question pathology ranges and results, even if they are within acceptable range - and especially if there is significant difference between food intake and the pathology result.

I suggest this case study be written up and both -

- submitted to a journal, and
- presented at one or more professional conferences.

Practical case studies are very useful for busy clinicians!

As a consequence of this case study what actions will you initiate when you see someone prescribed fluoxetine and/or olanzapine, will you –

- clarify adequacy of dietary intake of thiamine, choline, carnitine, folic acid, cobalamin and vitamin D, request blood tests, and then compare findings?
- consider the duration of time between taking of prescribed medicines and taking of bloods and whether that is also impacting the results?
- if there is disagreement between oral intake and blood test results, will you question whether altered membrane transporter availability is a contributor?
- recommend nutrient interventions be administered at different times from the prescribed medicines?

Conclusions

Due to direct and indirect impacts on availability, several identified nutrients should be monitored on a regular basis as a prophylaxis strategy.

It seems we can no longer accept blood test results at face value and consequently now need to factor in both margins of error and the potential impacts of relevant membrane transporters.

Accurate diet histories will/are becoming more relevant and broadly applicable in clinical care.

What else would you include?

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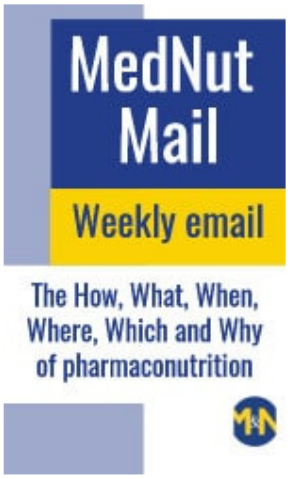

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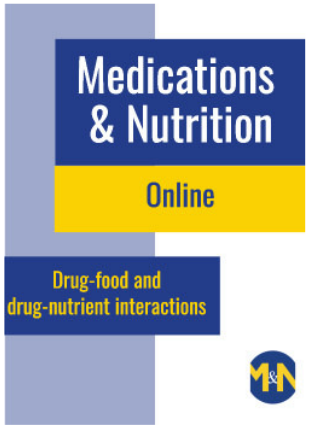

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