MedNut Mail

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

Carnitine and 3 epilepsy medications

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https://medicationsandnutrition.online

Guest case study

This email is based on a question from a reader.

I have a client who is tube fed, currently on XXX enteral feed as she can't tolerate regular/standard formula.

She is on a few medications that affect carnitine levels/absorption- including Frisium, Epillim and Lamictal.

She has been experiencing a lot of the symptoms also associated with carnitine deficiency, (her last blood test also indicated low Carnitine level).

How much would you usually recommend to start with?

Also any carnitine supplements that you have used for tube feeding clients?

Carnitine enables the transport of long-chain fatty acids across the inner mitochondrial membrane for beta-oxidation. It also allows for the removal of the toxic acyl-coenzyme-A metabolites from the mitochondria. Consequently low carnitine levels reduce fatty acid concentration within mitochondria resulting in decreased energy production.

Carnitine homeostasis reflects the balance between -

(i) absorption from the diet – about 75% of adult intake, predominantly from animal-based foodstuffs;

(ii) endogenous biosynthesis - from the amino acids lysine and methionine;

(iii) efficient renal reabsorption – as evidenced by normal carnitine levels in strict vegetarians (vegans) and lacto-ovo-vegetarians.

Normal serum carnitine levels do not reflect muscle carnitine levels as most body carnitine is stored in skeletal muscle however low serum carnitine levels reflect low muscle carnitine levels – and are an indication of the time lag between depletion of body carnitine stores and plasma carnitine levels.

L-Carnitine supplementation may contribute to restoring free carnitine levels and remove accumulating toxic acyl complexes as well as raising free fatty acids in the mitochondria and decreasing serum triglycerides. One author stated there is no published research evidence that carnitine supplements induce seizures and the authors further acknowledge that this finding contradicts authorised, formal product information.

Administration of L-carnitine (100 mg/kg/day to a maximum of 2 g/day) recommended.

Secondary carnitine deficiency can result from:

(i) acquired medical conditions (eg chronic liver failure, renal failure, etc);

(ii) malabsorption or malnutrition (such as vegetarians, coeliac diagnosis, inflammatory bowel disease, etc);

(iii) a high catabolic state (eg trauma, malignancy, acutely ill patients); and

(iv) prescribed medications, including chemotherapeutic agents, antiretrovirals, antiepileptics and antibiotics.

All 3 identified prescribed medications (Epilim, Frisium, Lamictal) negatively impact carnitine status.

Mechanisms by which Epilim decreases carnitine availability include:

- inhibition of endogenous carnitine production,

- urinary excretion of valproylcarnitine (produced in the mitochondrial intermembrane space),

- decreased renal reabsorption of carnitine.

There is a correlation between carnitine deficiency, urea cycle disorders and hyperammonaemia secondary to valproate – carnitine deficiency results in a shift from β-oxidation towards ω-oxidation, resulting in increased 4-en-VPA, which interferes with the urea cycle, thus increasing plasma ammonia levels.

Non-carnitine factors to consider -

- What other medications are prescribed and do they directly or indirectly impact the effectiveness of these 3 identified prescribed medications?
- Epilim and Lamictal negatively impact B12 status; B12 is important in myelin and astrocytic functions therefore advisable to monitor B12 status, and aim to maintain levels > 300 pmol/L as per findings from neuroimaging evidence.
- Epilim increases the risk of altered thyroid function and negatively impacts insulin levels with consequent weight gain as an outcome.
- Epilim is associated with depletion of biotin status; various studies also identified negative impacts on B12 and/or folate and/or homocysteine levels.
- Epilim and Frisium negatively impact vitamin D availability, consequently several authors recommend regular monitoring vitamin D status whilst this/these drug(s) prescribed.
- Lamictal negatively impacts thiamine status via common-to-both transporters and thiamine supplementation may be advisable, however best to administer the thiamine supplements at a different time from Lamictal.

- Is the lack of formula tolerance indicative of formula intolerance or is it a drug side effect.?
- Both Epilim and Lamictal are associated with increased risk of drug malabsorption with jejunostomy feeding.
- Epilim enteral nutrition osmolality is 5010 mOsm/kg (acceptable upper limit < 500 mOsm/kg) therefore increased likelihood of diarrhoea.

What interventions will you initiate when you see someone prescribed Epilim and/or Frisium and/or Lamictal – will you -

- request carnitine status be clarified?
- recommend a prophylactic carnitine intervention with regular monitoring? especially if there are symptoms?
- ensure vitamin D, B12, folate and homocysteine levels are within acceptable ranges?
- monitor glycaemic control and thyroid function?
- recommend a thiamine intervention (administered at a different time from these 3 drugs)?

Conclusions

Carnitine is an overlooked essential nutrient in energy metabolism and mitochondrial function. The dysfunctional mitochondria umbrella encompasses a broad range of medical diagnoses therefore carnitine status is likely to be more important than currently considered thus those with carnitine-medication interactions are likely to benefit from carnitine interventions.

My response to the request.

I have never worked with a doctor who was interested in trialling carnitine interventions.

The evidence suggests a maximum dose of 2 g/day. Given the carnitine depletion is longstanding, sustained and ongoing I suggest commencing with the maximum dose for at least a month or two or three to ensure there is an adequate supply of the nutrient available to meet this person's metabolic requirements.

I also suggest monitoring on a regular basis ie at least weekly -

- carnitine levels to ensure they're improving and identify when they are within acceptable range, and
- monitoring degree of expression of carnitine deficiency symptoms and how quickly they resolve.

and establish what dose was required to achieve resolution of the symptoms.

We don't know a number of factors such as -

- the level of carnitine intake from dietary sources,
- the level of impact of any or all 3 of the prescribed meds on carnitine availability,
- whether these 3 prescribed meds alter gut micro flora,
- the optimal carnitine dose to meet metabolic requirements; estimated doses for most nutrients are based on a dose whereby there is a lack of observed expression of a deficiency.

Further I would question whether the lack of tolerance for the formula is related to the enteral formula or whether it is a side effect of one or more of the prescribed medications - Epilim is likely to cause diarrhoea when enteral formula administered.

I also suggest you write it up this person as a case study and submit to a journal and also present it at a professional conference. Practical case studies are very useful for busy clinicians!

What else would you include?

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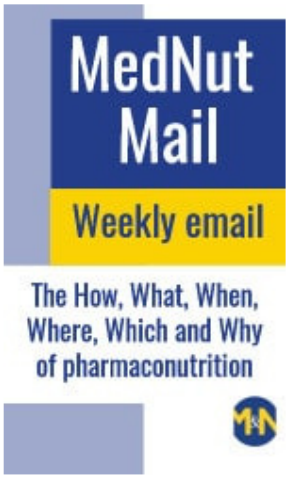

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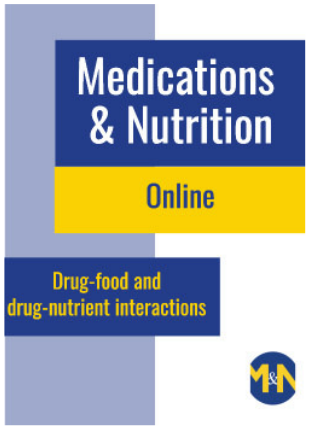

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