MedNut Mail

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

B12 injection

Y Coleman

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https://medicationsandnutrition.online

Commentary

Abnormally high B12 levels are typically due to a medical disorder, however this article is specifically about elevated B12 levels due to ongoing therapeutic B12 interventions.

Vitamin B12 interventions are commenced upon diagnosis of low B12 status, typically comprise high dose injections until levels are within acceptable range, and then the intervention is changed to a maintenance dose that is typically administered every 3 months ad infinitum. B12 levels are rarely monitored once they are within acceptable range, and there is no concern if levels a higher than the deemed acceptable range.

A maintenance dose typically provides 1000 mcg; based on an adult requiring 2.4 mcg/day this provides the equivalent of 417 days of B12.

The administration dose is typically administered every 3 months therefore the patient receives 4000 mcg per year which is equivalent to 4.6 years provision of B12 – every year.

There is some interesting evidence that folate and B12 levels that are elevated due to supplements, can have negative impacts on cognitive function. This may be an early indication that some nutrients may have therapeutic ranges.

As a consequence of this article, we included in our clinical reports a recommendation to check B12 levels prior to the next injection to clarify status; if B12 levels were either at the high end of acceptable range, or higher than acceptable range, then the recommendation also included advice to review the frequency of the intervention and to consider changing from 3-monthly interventions to 6-monthly interventions.

Long term prescription of medications such as the following are likely to increase the cause of, or exacerbate the risk of B12 deficiency - the proton pump inhibitors (esomeprazole, lansoprazole, omeprazole, pantoprazole, rabeprazole), famotidine, ranitidine, metformin, glibenclamide, gliclazide, glimepiride, glipizide, sodium valproate, gabapentin, doxycycline, some oral contraceptives; some of these drugs can be prescribed for many years and even decades.

There is disagreement between pathology ranges and research findings with regard to appropriate B12 levels – with most of the focus on the lower level of acceptability. Neuro-imaging research found a direct causal link between B12 status, damage to the brain and consequent memory impairment; it also found increasing memory impairment as B12 levels

dropped even whilst within currently defined acceptable ranges and that B12 interventions are effective once levels are less than 300 pmol/L.

So not only do we need to be aware of the acceptable lower limit, but also the acceptable upper limit which is currently not well defined. My rule of thumb is – if the latest and most current B12 result is above the defined acceptable range then it is advisable to recommend a reduction in the frequency of the intervention.

So, next time you see someone prescribed B12 injections will you integrate the following into your clinical assessment?

- check their B12 status, and request it to be checked if it is not available,
- ensure the levels are more than 300 pmol/L and not above the recommended upper limit,
- recommend reducing frequency of the intervention if the levels are at the high end of normal range or above range.

Conclusions

Ultimately, the current maintenance dose of 1,000 mcg B12 every 3 months may confer long term harm, therefore it seems that once B12 levels are stabilised well within acceptable range, then the standard B12 intervention of 1000 mcg should be administered annually, and monitored with pre-injection annual testing of levels. However, if factors such as the prescribed medications are negatively impacting B12 status then the frequency may well need to be increased to either 6-monthly or 3-monthly.

Case study

Medical History with Nutritional Aspect

Note - Primary diagnosis has been excluded on the basis of individual identification

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: decreased sense of taste and smell, tires quickly

Other: moderate pain

Biochemistry with Pharmaconutritional Consequences

No recent relevant data available

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
METAMUCIL			☐					☐				☐	☐	☐
Risperidone			☑	NV	C	↑		☐		↑		☐	☐	☐
Sodium Valproate	B12, B6, biotin, Ca, carnitine, I		☑	NV	CD	↑	↕	☐				☐	☐	☑

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

A young man diagnosed with a rare neurodegenerative disorder about 10 years ago.

Relatively recent available (limited) biochemistry within acceptable ranges.

There was a suggestion for ammonia levels to be checked - am unable to locate the results. Sodium valproate is associated with increasing ammonia levels and decreasing carnitine status, and carnitine intervention has been found to normalise both.

Is at increased risk of developing diabetes due to the combination of dysfunctional mitochondria plus prescription of risperidone, and sodium valproate is associated with interference with insulin metabolism.

Is at increased risk of developing altered thyroid function due to prescription of sodium valproate.

Sodium valproate decreases both carnitine absorption and endogenous carnitine production – low carnitine is associated with increased risk of hyperammonaemia.

Sodium valproate decreases biotin absorption, decreases vitamin D metabolism, and decreases availability of folate.

Sodium valproate is associated with increased homocysteine levels, low folate levels, and normal or high B12 levels.

Risperidone inhibits OCT1 and OCT2 – major thiamine transporters that also convey choline.

Mr AAM's diagnoses include reduced sense of smell. Reduced sense of smell is now being considered to be an early warning signal of neuronal damage/injury, and consequent reduced life expectancy.

Mr AAM also "tires quickly and easily". Tiring may be due in part to lack of fitness and his underlying neurodegenerative disorder, and would be exacerbated by the inhibitory effect of risperidone on thiamine status.

Mr AAM's diagnoses include chronic pain. Nutritional factors that may be useful to consider in pain management -

- evidence indicates substantial relief of neuropathic pain by thiamine, pyridoxine and cyanocobalamin separately, and in combination there was a synergistic benefit,
- low B12 exacerbates elevated TNF- α which is an inflammatory response marker; elevation of the inflammatory response can include a pain response.

Nutrients that support neurons and that are affected by risperidone and/or sodium valproate include:

- Thiamine – deficiency causes mitochondrial dysfunction, energy shortage, chronic oxidative stress, defective myelin sheath, mild impairment of oxidative metabolism, and ultimately regionally selective neuronal death;
- biotin – targets both neurodegeneration and demyelination through 2 key pathophysiological functions -

1. triggers myelin synthesis by oligodendrocytes,
2. replenishes ATP in hypoxic neurons.

- carnitine - improves mitochondrial membrane dysfunction and alleviates oxidative stress thereby enhancing axonal plasticity and oligodendrocytic axonal myelination which forms the basis of carnitine's neuroprotective effects;
- choline - alone or in combination with other methyl donors (B12, folate) ameliorates neurological impairment, and is an important constituent of phosphatidylcholine which is a major component of all membranes;
- B12 – low levels cause defective production of choline and choline containing phospholipids, causes demyelination, followed by axonal degeneration and ultimately axonal death;
    - deficiency may worsen the inflammatory and demyelination processes and slow remyelination and repair processes. However, the repeated or continuous inflammatory and demyelinating processes plus endogenous attempts for remyelination and repair increase vitamin B12 consumption and may lead to its deficiency;
- vitamin D – inadequate status may be a contributor to remyelination failure, may facilitate myelin debris removal and thus support remyelination, has a regenerative component in demyelinating diseases.

Whilst only 2 prescribed medicines are considered - their combined negative impacts on this person's neurological physiology are potentially quite profound, especially given the underlying neurodegenerative disorder.

What else would you include?

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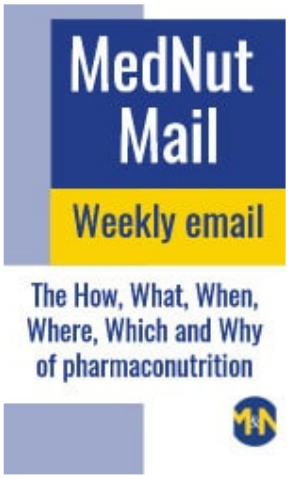

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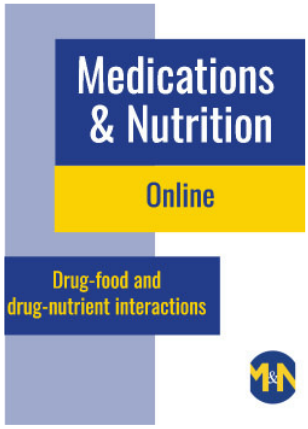

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