MedNut Mail

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

Research numbers vs case numbers

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https://medicationsandnutrition.online

Commentary

Welcome to the first edition of our weekly email - and thank you for your interest in pharmaconutrition.

The content format is based on a short editorial plus a case study - questions and comments are welcome.

“I am not interested in any research that is not randomized, blinded and includes a control group” was stated to a group of colleagues at a clinical meeting; another colleague at a different institution made a similar statement and added the caveat “… and has large numbers”.

These statements are promoted and supported by the institutions training our health professional clinicians – it is idealistic and reflects a perfect world. These large-scale, randomized, blinded, control group studies are usually designed to address an already-identified issue and examples include incidence, prevalence, and treatment strategies for health problems such as heart disease, diabetes, dementia, etc.

Whilst idealistic, it is also very limiting in the research read and the issues addressed – what do these clinicians do if there aren’t any large-scale, randomized, blinded, controlled studies addressing an issue of concern?

In practice, our initial red flags seem to be case studies – an issue has been identified, a number of treatment strategies trialed until an effective one is identified, and then the case and its findings are published to advise other clinicians of an effective treatment strategy with that combination of circumstances; and this usually includes the underlying reasons as to why different strategies did not, and ultimately did, prove effective.

Once a number of case studies on a particular issue are published, then there is often a small research project evaluating the effectiveness of the trialed treatment strategies – and usually they are randomized, have a control group and are typically blinded.

These are two classic examples supporting the importance of case studies in the research process - and especially in clinical practice.

Excessive zinc-induced copper-deficiency myeloneuropathy. A case study identified a person with copper-deficiency myeloneuropathy and found the copper deficiency was induced by an excessive zinc intake; the source of zinc was denture cream. Subsequently a number of other similar case studies were published supporting the initial finding, and

finally a small study was conducted that also supported the initial finding.

Many denture creams now do not contain zinc, and the finding is an accepted form of copper deficiency causation.

It is unlikely this issue will ever attract the gold-standard research criteria of being randomized, control group, blinded, and large numbers, and yet the findings are important and clinically applicable.

Proton pump inhibitor induced magnesium deficiency. As a consequence of a case study by two Australian clinicians, who found that a specific proton pump inhibitor interfered with magnesium availability, a plethora of case studies with similar findings have subsequently been published.

We are now at the stage whereby contradictory evidence is being published – which causes confusion at best -

- do we need further research to clarify causation and treatment? – certainly;

- is it likely to be conducted? – perhaps;

- will it attract large trial support? – unlikely.

The nutritional consequences of the pharmacological intervention in this second case study is an excellent example of application of case study research and application of clinical first principles; both case studies are examples of health issues that are unlikely to attract large-scale, randomized, blinded, control-group-based research and yet their findings are clinically very important.

What will these clinicians do if there aren't even any case studies or small research projects to refer to?

What do you do?

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: blindness

Other: pain, AF, multiple toes amputated, asthma

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
ACTILAX		☐	NV	D		↓	☐				☐	☐	☑
Amiodarone		☑	NV	C	↑	↓	☑				☐	☐	☐
Cholecalciferol	(1000 IU/day)	☐					☐				☐	☐	☐
DIAFORMIN XR	(08:30) B12	☐	NV	D	↓	↓	☑				☐	☐	☑
Domperidone		☑	N	CD		↕	☐	↓			☑	☐	☐
Frusemide	(160 mg/day) Ca, Cl, K, Mg, Na	☑	NV	CD		↓	☐				☑	☐	☑
MOVICOL		☐	N	D			☐				☐	☐	☐
Pantoprazole	(40 mg/day) B1, B12, Ca, Fe,	☑	NV	CD		↓	☑				☑	☐	☐
Prazosin		☑	NV	CD			☐				☑	☐	☑
Sertraline	Na	☑	NV	CD	↑	↑	☐				☑	☐	☐
TROVAS		☑	NV	CD	↑	↓	☑				☐	☐	☐
		▩					▩				▩	▩	▩

Extra drug: lantus 30U bd, novorapid sliding scale, norspan

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

No recent relevant biochemistry available. Advisable to check plasma proteins (albumin, total proteins) as they are the primary transporters for 7 of the prescribed drugs and hypoproteinaemia may alter their effects including expression of their side effects.

Diabetes drugs

- lantus time to onset ~ 1 hour, minimal peak, duration 20-26 hours
- novorapid time to onset 15 minutes, time to peak 30-90 minutes, duration 3-5 hours
- diaformin XR duration of 24 hours

Diabetes drugs coverage

- before breakfast BSLs - minimal, if any, coverage from previous morning's diaformin XR or lantus; coverage from previous evening's lantus;
- before evening meal BSLs - covered by current morning's diaformin XR and lantus.

Mr AAB has 3 prescribed medicines impacting his afternoon glycaemia - are his afternoon BSLs being monitored? Is he grazing? and if so then why? Is his afternoon glycaemia low (expected) or high? and if high then why? If his afternoon glycaemia is high in the presence of 3 powerful drugs then is it because he is grazing to prevent a hypo or has the liver released sugar back into the system to prevent a hypo?

Chronic use of actilax may promote excessive loss of water and electrolytes, especially potassium, and their regular monitoring recommended.

Amiodarone comprises approximately 37% iodine by weight, a maintenance dose of 200-600 mg amiodarone/day will provide approximately 7-21 mg iodide/day; optimal iodine intake is 150-200 mcg/day ie about 100 x more than the body needs.

Metformin XR decreases B12 absorption and thiamine availability.

Frusemide increases urinary excretion of calcium, magnesium, potassium, sodium and thiamine.

Currently prescribed ostelin 1000 IU/day. Advisable to check vitamin D levels and if low then advisable to review current vitamin D management strategy.

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

Regular measurement sodium levels recommended whilst sertraline prescribed.

Three prescribed medicines impact thiamine status, being metformin directly as it is a substrate for many of the thiamine transporters, and both frusemide and pantoprazole indirectly by decreasing magnesium availability – adequate magnesium status is important for activation of thiamine and vitamin D.

Two prescribed medicines decrease B12 availability, being metformin and pantoprazole. B12 is very important in neurological physiology as well as many other functions, therefore advisable to monitor levels on a regular basis and ensure > 300 pmol/L; neuroimaging evidence indicates loss of memory function once B12 levels < 300 pmol/L.

Statins interfere early in the cholesterol metabolic pathway and consequently decrease

- production of vitamin D
- production of CoQ10 - important in cellular energy production.

Advisable to check lipid levels and ensure within acceptable range, and if low then review necessity for its continued prescription. There is variability between pathology laboratories with regard to appropriate lower acceptable cholesterol level - some pathology ranges have set the lower acceptable limit at 3.5, others 3.0, and some do not set a lower limit. Cholesterol is important in brain structure and function amongst many other roles.

Mr AAB told me the food does not have much taste which is contributing to his limited range of food choices. Zinc is important in a range of body functions, including sense of taste and release of the hunger hormone Neuropeptide Y. Mr AAB is prescribed 2 drugs that decrease zinc availability, being pantoprazole and frusemide. Advisable to check zinc levels and if inadequate then consider a short term (90-120 days) intervention and recheck status prior to cessation of the intervention however success of any mineral intervention is questionable whilst a proton pump inhibitor is prescribed.

Mr AAB is in the difficult position of being prescribed a proton pump inhibitor and having a wound that is unlikely to heal properly whilst a proton pump inhibitor is prescribed therefore advisable to consider -

- whether proton pump inhibitor prescription is still required;
- whether suppression of gastric acidity is still required and whether it could be managed with an H2 antagonist such as ranitidine (there is a general belief that they cause less nutritional harm than proton pump inhibitors);
- if the proton pump inhibitor intervention can be ceased until the wound is healed.

Vitamin C is important in both collagen formation and its strength; proton pump inhibitors reduce availability of active vitamin C. It is likely wound healing will be delayed, and of poor quality whilst there is reduced availability of active vitamin C. It is also likely vitamin C interventions are unlikely to be effective whilst a proton pump inhibitor is prescribed.

Mr AAB is prescribed amiodarone which impacts thyroid function. Diabetes and thyroid have an association therefore the presence of one indicates the increased likelihood of the other. Given Mr AAB's diagnoses includes diabetes, he is prescribed amiodarone, he is reported to have very poor dietary preferences, and he is gaining weight, advisable to check thyroid function.

Reduced availability of nutrients such as vitamins B12 and D could contribute to the brittleness of Mr AAB's pain control.

Reduced availability of vitamin B12 could increase Mr AAB's risk of falls.

Ultimately the impact of Mr AAB's prescribed medicines could be negatively impacting a number of his diagnoses such as NIDDM, falls, incontinence, pressure area and pain, through decreased nutrient availability; it could also be seen as the consequences of a hidden form of malnutrition.

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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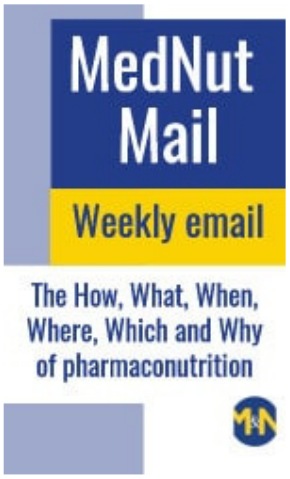

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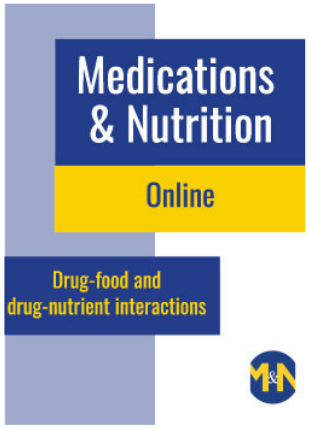

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