Clinical Application Guide

of medication impacts on nutritional factors

5 main areas of clinical application

by Yvonne Coleman

Contents

As this is a new area of expertise, we are still learning about its relevance and applicability in our daily clinical practice. Likely areas for the inclusion of medication impacts on nutritional factors are both direct and indirect.

There are probably 5 main areas of clinical application as summarised below:

- **Tabulated summary**

  Useful for identifying key nutrients and adverse reactions that may be of concern.

- **Blood test results**

  Are out-of-range results the consequence of and/or exacerbated by one or more prescribed medications?

- **Having a defined section for noting drug-nutrient impacts**

  Useful for highlighting nutrients of concern.

- **Having a defined section for diabetes drugs**

  Useful for identifying adequacy of coverage.

- **Inclusion in the management of general health issues**

  Inadequate nutrient availability delays and/or compromises responses to health-promoting interventions.

Each of these headings will include a range of examples.

Drugs, medicines and medications are used interchangeably.

From a time efficiency aspect, a good strategy to manage this information is to develop a file with your commonly used dot points and summary paragraphs. This means you can copy and paste these dot points and summary paragraphs into your reports ie create template, and then personalise to the individual's requirements - some example templates have also been included. Having templates means you are saving time because you do not have to repeatedly rethink and rewrite the pertinent points you wish to record, and you can quickly update as new information can be added.

Tabulated summary

The composite side effects of multiple medications (polypharmacy) are best presented in a table as outlined below. Write in drug name, vitamins and minerals affected (if any) and tick the adverse reactions pertaining to that drug.

Drug Name	Nutrients Affected	% BPP	N/V	C/D	Wt	Appetite	Δ Taste	Dry Mouth	BSL
drug a	Mg, Zn, Ca, Fe	90	N	√	⬆	⬆		√	√
drug b	B12, folate, B1	25	V	D	√		√		
drug c	B12, Fe, folate, biotin, B6	99	√	√	⬇	⬇	√	√	√
drug d	B12, I, Fe, B1	95	N	C		√	√	√	√

BPP – binding to plasma proteins, N – nausea, V – vomiting, C – constipation, D – diarrhoea, Δ - change in, BSL – blood sugar levels

Nutrients Affected

If two or more prescribed medications affect a specific nutrient then advisable to regularly monitor the status of each of those nutrients eg B12, Fe, folate, B1.

Side Effects

If the person experiences a specific side effect such as a dry mouth, and that problem is a side effect of some of their prescribed medications, then it is likely they are exacerbating that problem. It is then advisable to address the problem by reviewing the relevant prescribed medication(s) and also introducing strategies to address the adverse effect(s).

Binding to Plasma Proteins

The plasma proteins are the primary transporters for a significant number of medications. If there is greater than 90% binding of a drug to plasma proteins, then hypoproteinaemia (low plasma proteins) may alter the effects of the drug. There are now recommendations for dose titration for prescribed drugs such as furosemide/frusemide in the presence of hypoproteinaemia.

Useful to also record

- The dose of some medications as these can change eg diabetes, thyroid
- The times some medications are administered – especially relating to diabetes, parkinsons, thyroid
- The doses of the prescribed supplements – are they adequate?

Action

- Your Clinical Assessment form to include a table for a quick summary of nutrients affected, and adverse effects.
- Monitor identified nutrients at risk, and whether identified adverse effects are present (adverse events are often attributed to the diagnosis).

Blood test results

Useful to record

Recent relevant available biochemistry indicates:

- Low sodium - associated with increased risk of falls, and poor appetite; currently prescribed sertraline which includes hyponatraemia as a side effect.
- Low Hb - associated with increased risk of falls, and poor appetite; currently prescribed (an identified PPI) which decreases iron absorption.
- Low B12 - currently prescribed (an identified PPI) and metformin – both of which impair B12 absorption. There is disagreement between pathology ranges and research findings with regard to appropriate B12 levels. Neuro-imaging research 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.

No recent relevant biochemistry available:

- Advisable to check plasma proteins (albumin, total proteins) as markers of nutritional status. The plasma proteins are the primary transporters for (number eg 4) of the prescribed drugs and hypoproteinaemia may alter their effects including expression of their side effects.

Action

- [ ] Document any out-of-range results and which of the prescribed drugs, if any, may be impacting the identified results.
- [ ] Establish whether nutritional interventions may be necessary to address the negative effect. An example of this is the well-known clinical practice of prescribing a potassium intervention whilst furosemide/frusemide is prescribed.

Having a defined section for noting drug-nutrient impacts

In the same way blood test reports are reviewed for concerning results, so prescribed medications should be reviewed for nutritional issues of concern, the identified concerns highlighted and addressed.

Examples of simple issues

- Furosemide/frusemide increases urinary excretion of calcium, magnesium, potassium, sodium and thiamine.
- Glucocorticoid dose and duration associated with lower vitamin D levels; vitamin D enhances the anti-inflammatory effects of glucocorticoids.
- Regular monitoring sodium levels recommended whilst mirtazepine prescribed.
- Dietary levels of caffeine intake in conjunction with paracetamol inhibit antinocieception (pain relief).

Examples of more complex issues

- Phenothiazine derivatives such as amitriptyline are similar in structure to vitamin B2 (riboflavin) and riboflavin is now gaining importance in neuronal function therefore B2 intervention recommended.

- Commonly prescribed magnesium supplements typically provide 37.4 mg elemental magnesium per tab; women require 320 mg elemental magnesium/day (men require 420 mg elemental magnesium/day). Mr/Mrs XXX is prescribed (an identified PPI) which decreases magnesium absorption therefore advisable to check magnesium status and if low (< 0.80 mmol/L) then advisable to review current intervention and consider one that provides about 300 mg elemental magnesium/day.

- Zinc is important in a range of body functions, including sense of taste and release of the hunger hormone Neuropeptide Y. Mr/Mrs XXX is prescribed 2 drugs that decrease zinc availability, being (an identified PPI) and furosemide/frusemide. Advisable to check zinc levels and if inadequate then 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 PPI is prescribed.

- Evidence indicates iron deficiency anaemia is unlikely to resolve whilst a PPI such as (an identified PPI) is prescribed. Advisable to consider a non-oral iron intervention to maximise effectiveness of the intervention.

Action

- Monitor status of identified nutrients at risk.

- If ongoing monitoring identifies an ongoing decline in identified nutrient(s) at risk then intervention(s) advisable.

Having a defined section for diabetes drugs

Duration of effect of the various prescribed drug intervention(s) is an important component in diabetes management, and is integral to minimising periods of under- or over-dosing.

Examples of duration

- Insulin glargine has a time to onset of ~ 1 hour, minimal peak, and duration of 20-26 hours.
- Insulin aspart has a time to onset of 15 minutes, 30-90 minutes time to peak, and duration of 3-5 hours.
- Linagliptin has a duration of about 24 hours.
- Metformin has a time to onset of 1-3 hours and a duration of about 12 hours.

Examples of periods of coverage

- **Before breakfast BSLs**

  minimal coverage from previous morning's glargine, covered by previous evening's glargine.

- **Before midday BSLs**

  covered by previous evening's glargine, covered by current morning's glargine, linagliptin and metformin, some coverage from current morning's aspart.

- **Before evening meal BSLs**

  minimal if any coverage from previous evening's glargine, minimal coverage from current midday's aspart, covered by current morning's glargine and linagliptin.

- **Before-supper BSLs**

  minimal coverage from previous evening's glargine; covered by current morning's glargine and linagliptin, and current evening's aspart.

Example of duration of effect – allow time to onset and post-peak diminishing effect

Drug Name	Duration hrs	B/F	MT	M/day	AT	E/meal	Supper	B/F
Glargine	20-26	admin	Y	Y	**Y**	Y	Y	possibly
Aspart	3-5	admin	Y	admin	**Y**	admin	Y	N
Linagliptin	~24	admin	possibly	Y	**Y**	Y	Y	unlikely
Metformin	12	admin	possibly	Y	**Y**	Y	unlikely	N

Mr/Mrs XXX's late morning and early afternoon glycaemia is curious - realistically he/she should have very low BSLs because all the prescribed hypoglycaemic medications would be maximally impacting during that timeframe, however his/her BSLs are mostly high therefore one should ask why and there seem to be 5 options:

- The hyperglycaemic effects of the between-meal snack food, caffeine, and chlorogenic acid in the coffee are sufficient to offset the hypoglycaemic effects of the drugs.
- Current medication management strategy is undermedicating glycaemic control.
- Current medication management strategy is overmedicating glycaemic control and therefore causing the liver to release stored glucose as a physiological response to hypoglycaemia.
- Current medication management strategy is overmedicating glycaemic control and therefore he/she is eating/grazing, on typically sweet foods, to try and prevent a hypoglycaemic episode.
- Current medication management strategy is overmedicating glycaemic control and therefore causing both the liver to release stored glucose and him/her to eat sweet foods as a physiological response to preventing hypoglycaemia.

Therefore advisable to review current diabetes management strategy.

Action

- Identify the periods that have minimal and maximal drug effect.
- Monitor BSLs in periods of minimal drug effect, especially if they include a meal or snack time.
- Monitor BSLs in periods of maximal drug effect for evidence of hypoglycaemia - if they are already grazing then it may be too late.

Inclusion in the management of general health issues

Examples of common general health issues include loss of appetite, loss of weight, chronic pain, wound healing, history of falls, frequent UTIs and/or URTIs, insulin resistance/metabolic syndrome, dysfunctional mitochondria. Many people are likely to be prescribed medications as part of their health management strategy – these (medications) may negatively impact nutrients important to healing or recovery processes; these hidden impacts (commonly nutrient losses) are currently not considered in health management strategies

Loss of weight

A number of factors could be contributing to Mr/Mrs XXX's weight loss:

- **Overmedication with thyroxine**

  Thyroxine dose is weight dependent and change in weight status alters drug effectiveness. Since Mr/Mrs XXX has lost weight he/she is at high risk of overmedication therefore advisable to clarify thyroid function status.

- **Altered sense of taste**

  Likely exacerbated by (an identified PPI) prescription and weight loss as both deplete zinc status; simvastatin and moclobemide side effects include altered sense of taste.

- **Small food intake**

  Mr/Mrs XXX told me he/she feels like vomiting if he/she eats too much and so is self-limiting food intake; drugs A, B, C include vomiting and poor appetite as side effects.

- **Constipation**

  It seems likely to me the sense of vomiting may well be exacerbated by constipation.

PPI prescription

Mr/Mrs XXX has been prescribed (an identified PPI) since February 2016 and likely before then. There is increasing evidence that longterm (3+ years) PPI prescription is associated with:

- Altered gut microbiome,
- Increased risk of food sensitivities at a level of peanut allergy, due to partial protein digestion,
- Increased risk of coeliac disease due to partial protein digestion,
- Increased risk of scurvy due to inadequate availability of active vitamin C,
- Generalised malnutrition due to impaired absorption of a range of nutrients such as B12, vitamin C, magnesium, zinc, iron, etc,
- Increased risk of dementia,
- Altered gastric pH which reduces absorption dynamics of a range of drugs and nutrients.

Altered drug availability is relatively easily identified however reduced nutrient absorption is rarely identified due to the non-specific nature of their signs and symptoms.

Consequently advisable to review current (an identified PPI) prescription and consider.

- Whether the (identified PPI) prescription is still required.
- If suppression of gastric acidity is still required then could it be managed with an H2 antagonist such as ranitidine (there is a general belief that they cause less nutritional harm than PPIs).

Wound healing

Mr/Mrs XXX has been prescribed (an identified PPI) since February 2016 and likely before then. As several nutrients important in wound healing are negatively impacted, advisable to clarify whether the (identified PPI) prescription is still required:

- If the (identified PPI) is still required, can the potentially negatively impacted nutrients by supplemented non-orally?
- If suppression of gastric acidity is still required then could it be managed with an H2 antagonist such as ranitidine (there is a general belief that they cause less nutritional harm than PPIs).
- If the (identified PPI) intervention can be ceased until the wound is healed.

Vitamin C is important in collagen formation and the strength of the collagen; the (identified PPI) reduces 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 (an identified PPI) is prescribed.

Iodine

Mr/Mrs XXX is prescribed amiodarone which provides ~ 100 x iodine the body requires - this impacts thyroid function. Diabetes and thyroid have a genetic association therefore the presence of one indicates the increased likelihood of the other. Given Mr/Mrs XXX's diagnoses includes diabetes, he/she is prescribed amiodarone, he/she is reported to have very poor dietary preferences, and he/she is gaining weight, advisable to check thyroid function.

Chronic pain

Mr/Mrs XXX's diagnoses include chronic pain - nutritional factors that may be useful to consider in pain management include:

- **B12**. Low B12 exacerbates elevated TNF- α which is an inflammatory response marker; elevation of the inflammatory response can include a pain response; currently prescribed (an identified PPI) therefore advisable to monitor B12 status. There is disagreement between pathology ranges and research findings with regard to appropriate B12 levels - neuro-imaging research 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 mmol/L.

- **Magnesium**. Proposed mechanism - magnesium blocks the NMDA receptor channels in the spinal cord and thus limits the influx of calcium ie reduces the risk of excitotoxicity with consequent exacerbation of pain; currently prescribed furosemide/frusemide and (an identified PPI) both of which decrease magnesium availability therefore advisable to clarify magnesium status and if < 0.80 mmol/L then intervention recommended.

Thiamine transporters

At increased risk of thiamine and choline deficiencies as (number eg 4) drugs (drug a, drug b, etc) inhibit, and (number eg 6) drugs (drug a, drug b, etc) are substrates for their physiological transporters. Therefore interventions recommended and advisable to administer at a time when none of the prescribed medications that are inhibitors and/or substrates of these nutrients are administered to optimise effectiveness of the interventions. Very early evidence indicates nutrient interventions are effective if administered either 1 hour before or 2 hours after drug administration.

Action

- Monitor status of identified nutrients at risk.

- Consider non-oral interventions if nutrient levels continue to decline and prescribed medicines that affect the nutrients(s) continue(s) to be prescribed.

Conclusions

Ultimately medications are prescribed to address difficult chronic health issues. Both the underlying health issue(s) and the prescribed medications can also negatively impact nutritional factors with a consequent reduction in health responses and outcomes.

The current physiological responses are considered "normal", and further, there is some acknowledgement that various nutrients are important in healing and recovery processes. There is however, a serious lack of awareness and understanding about the mechanisms of action caused by inadequate nutrient status and how that alters physiological responses during healing or recovery. So when a prescribed medication negatively impacts the availability of one or more nutrients, clinicians neither "see" nor understand nor address the physiological consequences.

By addressing the negative nutritional impacts of many of the commonly prescribed medications there is likely to be a greater response to the interventions and therefore improved health outcomes for the individual, and reduced long term costs to society.

Acknowledgements

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Enabling busy Clinicians to integrate drug-nutrition information into their clinical practice

The negative impact of prescribed medications on nutritional health factors is a hidden cause of mal-nutrition. The integration of this expertise into daily clinical practice reduces the mal-nutrition impact of healing and recovery processes and therefore promotes improved health.