MedNut Mail

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

Metformin and weight loss

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https://medicationsandnutrition.online

Commentary

"Can you see Mr EYOM (Eighty Year Old Man) – he's been losing weight?"

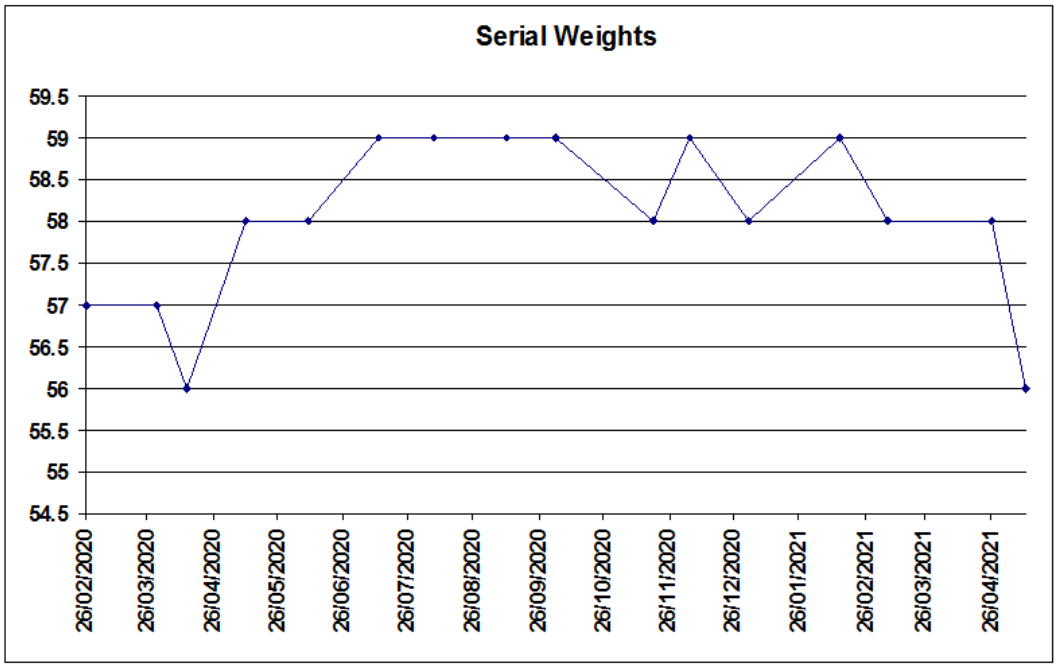
The weight graph showed a stable weight until a defined moment when the loss was dramatic – steep enough to abseil down.

The standard causes were excluded – no amputation, no gastro, no unwellness, no hospitalization, no falls, no nasty wound, no bad news in the family, no complaints of feeling upset in the tummy.

The Notes around that time indicated commencement of metformin – the metformin was ceased and both appetite and weight improved.

"Mrs EYOW (Eighty Year Old Woman) was losing weight so quickly all meds were ceased, her appetite improved, and re-introduction of prescribed medicines established metformin as the cause" was the comment that greeted me as I walked into Unit. The weight loss trigger in this seriously demented lady was that her metformin dose had been increased – fortunately cessation of metformin resulted in return of her appetite and she was quite happily eating to regain the weight she had lost so dramatically.

As can be seen from Mrs NTYOW's (Ninety Two Year Old Woman) weight graph, she gained weight at admission, stabilized, and there is a recent apparent weight loss of 2 kg. Has she really lost weight or is this part of the weight fluctuation we often see? This apparent weight loss coincides with the commencement of metformin. If weekly weighs over the next 4 weeks show ongoing weight loss then it is likely the weight loss is due to the commencement of metformin.



Metformin is the fourth most commonly prescribed drug in the world, and yet we rarely identify it as a significant cause of weight loss. So there are further questions -

- should the metformin be ceased as a consequence of causing the weight loss and an alternative intervention be initiated?
- which is more important – diabetes control or weight stability – especially in a frail elder?
- would continuation of metformin and consequent weight loss result in increased frequency of hypoglycaemic events and possible consequences such as falls and fractures?

These are 3 personal stories, commented upon to highlight a potential side effect that does not seem to be considered when initial causes of weight loss are being excluded.

Will you now scrutinize weight status a little more closely if metformin is prescribed?

Conclusion

Metformin can be a cause of significant weight loss and yet it is rarely considered as a cause when options are being considered.

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: cardiomyopathy, chronic pain

Other: IDA, B12 def, GORD, hypercholesterolaemia, ABI

Biochemistry with Pharmaconutritional Consequences

Na:	144	mmol/l	Hb:	133	g/L	Albumin:	39	g/L	BSL:		mmol/l
K:	4.0	mmol/l	Lymph:	1.1		Total Protein:	69	g/L	HbA1C:		
Urea:	6.5	mmol/l	MCV:	101	mmol/l	B12:		pmol/L	INR:		
Creatinine:	0.054	mmol/l	Zn:		umol/l	Folate:		nmol/L	TSH:	1.81	mIU/L

Other: eGFR > 90, Ca 2.32, Ca corr 2.34, phos 0.89, Mg 0.75, Fe 18, TRF 2.1, satn 34%, ferritin 107, vit D 53

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
ASTRIX	C, Fe	☑	NV				☐				☐	☐	☑
Carvedilol		☑	NV	CD	↑	↓	☐				☑	☐	☑
COLOXYL WITH S		☐		D			☐				☐	☐	☐
CRESTOR		☑	N	C			☑				☐	☐	☐
DIABEX	XR (08:00) B12, B1	☐	NV	D	↓	↓	☑				☐	☐	☑
DIAMICRON MR	(08:00)	☑	NV	CD	↑	↕	☑				☐	☐	☑
ENDEP	B2	☑	NV	CD	↑	↑	☑		↓		☑	☐	☑
ENDONE		☐	NV	CD		↕	☑	↓			☑	☑	☐
FERRO-F	Ca, Mg, Zn	☐					☐				☐	☐	☐
LASIX	(40 mg/day) Ca, Cl, K, Mg, Na,	☑	NV	CD		↓	☐				☑	☐	☑
NEXIUM	(40 mg/day) B1, B12, Ca, Fe,	☑	NV	CD	↑		☑				☑	☐	☐
OSTELIN	(1/day)	☐					☐				☐	☐	☐
Perindopril		☐	NV	D			☑				☑	☐	☐
Risperidone		☑	NV	C	↑		☐		↑		☐	☐	☐
		▩					▩				▩	▩	▩

Extra drug: norspan

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

Advisable to check plasma proteins (albumin, total proteins) as markers of nutritional status. The plasma proteins are the primary transporters for 8 of the prescribed drugs and hypoproteinaemia may alter their effects.

"Old" biochemistry indicates

- elevated MCV - advisable to check B12 levels. There is disagreement between pathology ranges and research findings with regard to appropriate B12 levels - neuro-imaging research shows a direct causal link between B12 status, damage to the brain, and consequent memory impairment; they also found increasing memory impairment as B12 levels dropped even whilst within currently defined acceptable ranges. The authors recommend B12 interventions once levels are less than 300 pmol/L.

- low magnesium - and prescribed frusemide and nexium. There is now a recommendation that 0.80 mmol/L be the lower acceptable limit for magnesium therefore intervention recommended. Men require 420 mg magnesium per day; the Upper Limit for magnesium from non-food sources is 350 mg elemental magnesium per day therefore advisable to consider an intervention for 90-120 days that provides about 300 mg elemental magnesium/day.

- marginal vit D - currently no intervention and prescribed rosuvastatin. Evidence indicates 50 mcg vitamin D per day is a maintenance dose; ostelin provides 25 mcg vitamin D per tab (25 mcg vitamin D is equivalent to 1000 IU vitamin D). Increasingly the evidence is indicating vitamin D levels should be > 100 nmol/L to minimise non-bone health impacts. In fact a meta-analysis found that vitamin D levels need to be > 160 nmol/L to remove low vitamin D's contribution to diabetes. Evidence found that 10,000 IU/day, 5 days/week for 12 weeks did not cause harm; whilst this level of intervention may not be considered at this stage it does show that short-term high-dose interventions do not confer harm. Advisable to check vitamin D levels and if still low then review current vitamin D management strategy.

BSLs (Dec-Jan)

- before breakfast - 7.3-9.5; recommended range 4-6

- daily range - 7.3-9.5; recommended range 4-10

- tested twice-weekly

- reportable limits: < 3 and > 20

- advisable to check HbA1c and clarify adequacy of glycaemic control

Diabetes drugs

- diabex XR has a duration of 24 hours,

- diamicron MR has a duration of 24 hours.

Diabetes drugs coverage

- before breakfast BSLs - minimal, if any, coverage from previous morning's diabex XR or diamicron MR;

- before evening meal BSLs - covered by current morning's diabex XR and diamicron MR.

Vitamin C (960 mg/day) attenuates aspirin-induced gastric injury.

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

Diabex XR decreases B12 absorption and thiamine availability - regular monitoring B12 status now recommended, and possibly regular monitoring thiamine status.

Phenothiazine derivatives such as endep are similar in structure to riboflavin and may reduce riboflavin availability.

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

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

Mr AAS is prescribed the daily double ie two drugs that decrease magnesium availability - being frusemide and nexium. Magnesium is an intracellular ion therefore serum levels are unlikely to detect early depletion of status. Cellular magnesium status is unknown whilst magnesium levels within acceptable range however if magnesium levels are low then typically indicates significant cellular depletion and intervention recommended.

Statins interfere early in the cholesterol metabolic pathway and consequently decrease

- conversion of sun to vitamin D - vitamin D intervention recommended,

- production of CoQ10 - important in cellular energy production; CoQ10 intervention recommended,

- DHEA production - low DHEA associated with increased risk of metabolic syndrome; intervention recommended.

Mr AAS pulled a face when we asked if the food had a bitter, metallic or no taste, and told us the food has a bitter taste. Zinc is important in a range of body functions, including sense of taste, release of the hunger hormone Neuropeptide Y, and insulin production amongst other functions. Loss of weight is associated with depletion of zinc status, and both frusemide and nexium also decrease zinc availability. Advisable to check zinc levels and if low then short term

(90-120 days) interventions recommended however effectiveness of intervention is questionable whilst both frusemide and a proton pump inhibitor are prescribed.

Staff advise Mr AAS has food in his room and that he has been observed eating at times other than mealtimes and snacktimes. Mr AAS's diabetes management includes 2 drugs administered before breakfast, and both have durations of about 24 hours and should be fully effective before midday. Mr AAS's afternoon glycaemia is not being monitored however 2 very powerful drugs are fully effective at that time therefore advisable to check afternoon glycaemia for 3 days and ascertain status. If Mr AAS has elevated afternoon glycaemia then one has to ask why and there are 5 possible causes

1. the hyperglycaemic effects of the afternoon tea snack food, caffeine, and chlorogenic acid in the caffeine are sufficient to offset the hypoglycaemic effects of the drugs;

2. current medication management strategy is undermedicating glycaemic control;

3. current medication management strategy is overmedicating glycaemic control and causing the liver to release stored glucose as a hypoglycaemia management strategy;

4. current medication management strategy is overmedicating glycaemic control and Mr AAS is grazing to offset the hypoglycaemic effect;

5. current medication management strategy is overmedicating glycaemic control and causing both the liver to release stored glucose and Mr AAS to graze.

Mr AAS's diagnoses include chronic pain - pharmaconutrition issues include:-

- vitamin D - current intervention may not be adequate to attain adequate range especially since a statin is prescribed. Evidence indicates increasingly brittle pain control with decreasing vitamin D levels.

- vitamin C - pain increases the reactive substances (formerly Reactive Oxygen Species) within cells. Vitamin C is important in quenching reactive substances and if there is insufficient vitamin C then cell status becomes compromised and the cells typically die which also causes pain. Advisable to consider a vitamin C intervention - the optimal intervention is 500 mg vitamin C/day (if more than 500 mg vitamin C administered at a time then the excess above 500 mg is not absorbed as the vitamin C transporters are overloaded). Vitamin C is not considered part of the pain management armament however it won't cause harm and evidence suggests it may confer benefit. Currently prescribed nexium which decreases conversion of vitamin C to its active form.

- low B12 exacerbates elevated TNF- α which is an inflammatory response marker; elevation of the inflammatory response can include a pain response and currently prescribed metformin XR and nexium therefore advisable to check B12 status. There is disagreement between pathology ranges and research findings with regard to appropriate B12 levels - neuro-imaging research shows a direct causal link between B12 status and memory impairment, and recommend B12 interventions once levels are less than 300 pmol/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 and consequent exacerbation of pain.

Currently prescribed frusemide and a proton pump inhibitor both of which decrease magnesium availability.

Mr AAS is in the difficult position of having chronic pain whilst a proton pump inhibitor is prescribed. Advisable to consider

- whether proton pump inhibitor 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 proton pump inhibitors.

What else would you include?

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