MedNut Mail

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

Insulin and pharmaconutrition

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https://medicationsandnutrition.online

Commentary

Insulin is a highly effective anabolic hormone that is primarily produced in the pancreas, and small amounts are also produced in some neurons.

Increased plasma glucose levels trigger insulin's release into the portal blood circulation and so it is transported to the liver which retains 50% of the insulin, the remaining 50% is released into the hepatic vein and transported to the heart, where it enters the arterial circulatory system and is distributed throughout the body ands bind onto insulin receptors in target cell membranes; the remaining insulin is ultimately delivered to the kidneys and excreted.

Functions

Insulin's primary functions include -

- regulating blood glucose levels and cellular uptake of glucose for energy production;
- inhibiting gluconeogenesis;
- stimulating the synthesis of glycogen in the liver (glycogenesis), and the storage of glycogen in the liver, muscle, and fat cells;
- regulating the synthesis of lipids (lipogenesis) and lipid metabolism;
- regulating skeletal muscle protein synthesis and its degradation;
- regulating cell growth and survival;
- maintaining metabolic and functional regulation of epithelial cells;
- maintaining immune cell metabolism and/or function;
- aiding bone formation and inhibiting osteoporosis-related inflammation;
- acting on the central nervous system, especially the memory and learning capabilities;
- performing pro- and anti-atherogenic functions in the vascular system;
- facilitating uptake of amino acids and potassium into cells;
- regulating the excretion of sodium and fluid volume in the urine.

Deficiency

Insulin deficiency means it is impossible for cells to use glucose as an energy source and so they become dependent upon fat stores for energy – which may ultimately cause ketone production and ketoacidosis.

Sustained insulin deficiency results in hyperglycaemia and resultant health complications such as diabetes and damaged peripheral neurons, kidneys and eyes.

Insulin resistance

Occurs when cells are unable to respond to an insulin signal, or when there are insufficient functional insulin receptors – both result in glucose not being able to be transported into cells, and consequent hyperglycaemia; the pancreas responds by increasing insulin production to try and reduce glucose levels to normal.

Exogenous insulin is administered when insufficient effective insulin is produced endogenously. Until exogenous insulin was discovered 100 years ago, those with Insulin Dependent Diabetes, mostly children, died - slowly - it must have been awful for the staff and families knowing hospital admission was a one-way street.

There is now a range of exogenous insulin products available – all with varying durations of effectiveness. There seems to be a move away from insulin administration once or twice a day to a small dose of long-duration insulin administered daily plus a rapid-acting insulin administered at mealtimes ie trying to emulate physiological response; service providers offer a broad range of preferred diabetes management practices which do not always seem to be congruent with this century.

I have developed, and made available, a Human Insulin Preparations Chart that outlines the various insulins, their times to peak, and their durations of action; it can be accessed by **clicking here**. I suggest it is important to know both time to peak, and duration of action especially when a combination of oral and exogenous interventions are administered, either at the same time or throughout the day, so that maximum intervention periods can be identified. I also suggest qid BSLs for 3 days is adequate for identifying maximum intervention periods.

If the BSLs are elevated at an identified maximum intervention period then one should ask – are the BSLs elevated because the person is overmedicated or undermedicated?

What will you do when you see someone whose prescribed medications include an insulin intervention, will you –

- clarify duration of the insulin intervention, identify the maximum intervention periods, chart BSLs, and include in your clinical report?
- develop management strategies for maximum intervention periods such as checking BSLs, offering alternate grazing snacks, and try and clarify whether overmedication is occurring during these periods?
- recommend review of the current diabetes management strategy if there are high BSLs during a maximum intervention period?

Conclusions

Insulin availability is a literal life and death issue, and our understanding of the importance of insulin and how to manage diabetes has increased profoundly since insulin was discovered 100 years ago.

However, there is still room for improvement in our management strategies such as identifying maximum intervention periods, and duration of the intervention, so that we can further optimise outcomes.

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:

Other: hypercholesterolaemia

Biochemistry with Pharmaconutritional Consequences

Na:	136	mmol/l	Hb:	128	g/L	Albumin:		g/L	BSL:		mmol/l
K:	5.0	mmol/l	Lymph:	2.0		Total Protein:		g/L	HbA1C:	8.0	
Urea:	8.4	mmol/l	MCV:	92	mmol/l	B12:		pmol/L	INR:		
Creatinine:	0.069	mmol/l	Zn:		umol/l	Folate:		nmol/L	TSH:		mIU/L

Other: eGFR > 90

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
Clopidogrel		☑	N	CD	↓		☑				☐	☐	☐
COLOXYL WITH S		☐		D			☐				☐	☐	☐
DIABEX XR	(08:00) B12	☐	NV	D	↓	↓	☑				☐	☐	☑
LIPITOR		☑	NV	CD	↑	↓	☑				☐	☐	☐
Metoprolol		☐	NV	CD	↑		☑				☑	☐	☑
OSTELIN	(2/day)	☐					☐				☐	☐	☐
PANAMAX		☐	NV	CD			☐				☐	☐	☐
Perindopril		☐	NV	D			☑				☑	☐	☐
Risperidone		☑	NV	C	↑		☐		↑		☐	☐	☐
SOMAC	(40 mg/day) B1, B12, Ca, Fe,	☑	NV	CD		↓	☑				☑	☐	☐

Extra drug: lantus, actrapid

Summary of organs and some transporters, relevant prescribed medications, and impacted nutrients

Organ (transporter) - inhibitors	Thiamine	Choline	Carnitine	Pyridoxine
From gut	metformin (THTR1)	metformin (THTR1)		metformin (THTR1)
Liver	clopidogrel (OCT1) metformin (OCT1) risperidone (OCT1) pantoprazole (OCT1)	clopidogrel (OCT1) metformin (OCT1) risperidone (OCT1) pantoprazole (OCT1)	pantoprazole (OCT1)	
Into kidneys	clopidogrel (OCT2) metformin (THTR2) metformin (OCT2) metoprolol (OCT2) risperidone (OCT2) pantoprazole (OCT2)	clopidogrel (OCT2) metformin (THTR2) metformin (OCT2) metoprolol (OCT2) risperidone (OCT2) pantoprazole (OCT2)	pantoprazole (OCT2)	
Into urinary system	metformin (MATE)	metformin (MATE)		
Skeletal muscle	metformin (OCT3) pantoprazole (OCT3)	metformin (OCT3) pantoprazole (OCT3)	pantoprazole (OCT3)	
Brain - inhibitors	metformin (THTR2)			
Organ (transporter) substrates	**Thiamine**	**Choline**	**Carnitine**	**Pyridoxine**
Liver	metformin (OCT1)	metformin (OCT1)		
Into kidneys	metformin (OCT2)	metformin (OCT2)		
Skeletal muscles	metformin (OCT3)	metformin (OCT3)		
OCTN1			metformin	

It is likely blood test results will reveal high-normal or elevated nutrient levels; duration of inhibition is currently unknown therefore fasting results are likely to be more reliable. Except for pyridoxine (B6) we don't know how elevated blood nutrients are expressed in the body so we don't know what factors to monitor.

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

Biochemistry comments

Relatively recent biochemistry indicates -
- low Hb - associated with increased risk of falls, and poor appetite.

Advisable to check plasma proteins (albumin, total proteins) as they are the primary transporters for four of the prescribed drugs and hypoproteinaemia may alter their effects.

Glycaemia comments

BSLs
- daily range 2.8-15.8, mostly 4-9; recommended range 4-10,
- reportable limits: < 2 and > 20,
- tested daily bd,
- last HbA1c indicates poor glycaemic control however this is not supported by current BSL monitoring therefore advisable to recheck status.

Diabetes drugs administration times

- 08:00 - diabex XR, lantus 40U, actrapid 6U,
- 12:00 - actrapid 6U,
- 17:00 - actrapid 6U.

Diabetes drugs

- lantus has a time to onset of 1hour, minimal peak and duration of 20-26 hours,
- actrapid has a time to onset of < 30 minutes, time to peak of 1.5 - 3.5 hours, and duration of 7-8 hours,
- diabex XR has a duration of 24 hours.

Diabetes drugs coverage

- before breakfast BSLs - minimal, if any, coverage from previous morning's lantus or diabex XR; no coverage from previous evening's actrapid;
- before midday BSLs - covered by current morning's lantus and diabex XR; some coverage from current mornings actrapid;
- before evening meal BSLs - covered by current morning's lantus and diabex XR, and midday's actrapid.

Currently prescribed 5 medications that may alter glycaemia, being atorvastatin, metoprolol, perindopril, risperidone, and of course metformin.

Bowel management comments
- regular aperient prescribed,
- oral + anal PRN interventions prescribed; oral administered 1 x Oct, 2 x Aug; anal administered 1 x Aug,
- Nurse Initiated anal intervention administered 1 x Jul.

Staff comments
Staff advise Mr ABZ eats well.

Observations
Mr ABZ is a tall, slender man with a lovely smile - he responded to my presence but not always to my questions.

Pharmaconutrition comments
Currently prescribed 9 medications that include nausea as a side effect.

Currently prescribed 8 medications that include diarrhoea as a side effect.

Currently prescribed 6 medications that include constipation as a side effect.

Currently prescribed 6 medications that include altered sense of taste as a side effect.

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

Diabex decreases B12 absorption - there is now a recommendation for regular B12 monitoring whilst metformin prescribed.

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

Two drugs that decrease B12 absorption, being diabex and somac, have been prescribed since admission and likely before then, therefore advisable to clarify B12 status.

Currently prescribed ostelin therefore advisable to check vitamin D levels and clarify current vitamin D status; if levels are still low then advisable to review current management strategy.

Dietary levels of caffeine intake in conjunction with paracetamol inhibit antinocieception.

Concurrent ingestion of panamax and iron resulted increased rate of iron absorption and decreased extent of drug absorption; the authors advise drug and iron to be administered at different times from each other.

Perindopril impairs zinc status.

Statins interfere early in the cholesterol metabolic pathway and consequently decrease -
- conversion of sun to vitamin D – currently prescribed a vitamin D intervention,
- production of CoQ10 - important in cellular energy production therefore advisable to clarify CoQ10 status,
- DHEA production - low DHEA associated with increased risk of metabolic syndrome therefore advisable to clarify status.

Currently prescribed a statin therefore advisable to check lipid levels and clarify current status.

There is increasing evidence that proton pump inhibitors such as somac significantly impair magnesium absorption - magnesium is important in muscle function, especially cardiac muscle, and glycaemic control amongst other functions. Magnesium deficiency manifests as confusion, disorientation, personality changes, loss of appetite, depression, muscle cramps, tingling, numbness, hypertension, cardiac dysrhythmia, seizures. 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.

Mr ABZ has been prescribed a proton pump inhibitor since admission ie 4 years ago, and likely before then. There is increasing evidence that longterm (3+ years) proton pump inhibitor 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;
- generalised malnutrition due to impaired absorption of a range of nutrients such as B12, vitamin C, magnesium, zinc, iron, etc;
- 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 reconsider reviewing current proton pump inhibitor prescription and 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).

As can be seen from the table, many of the prescribed medications alter nutrient availability to some of the key organs for an unknown duration via a plethora of transporter substrate and inhibiter mechanisms.

What else would you include?

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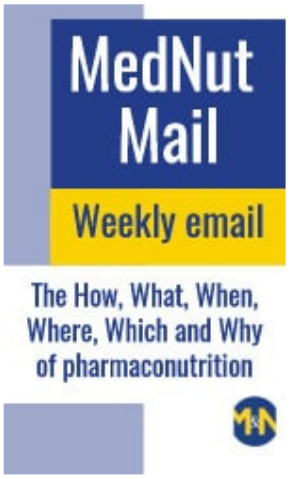

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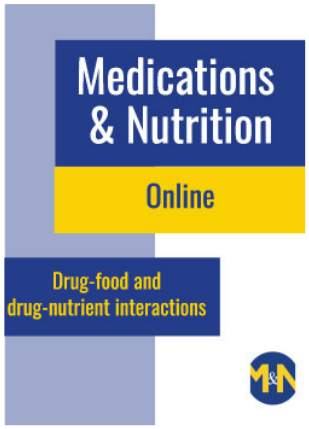

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