MedNut Mail

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

# Insulin resistance and pharmaconutrition

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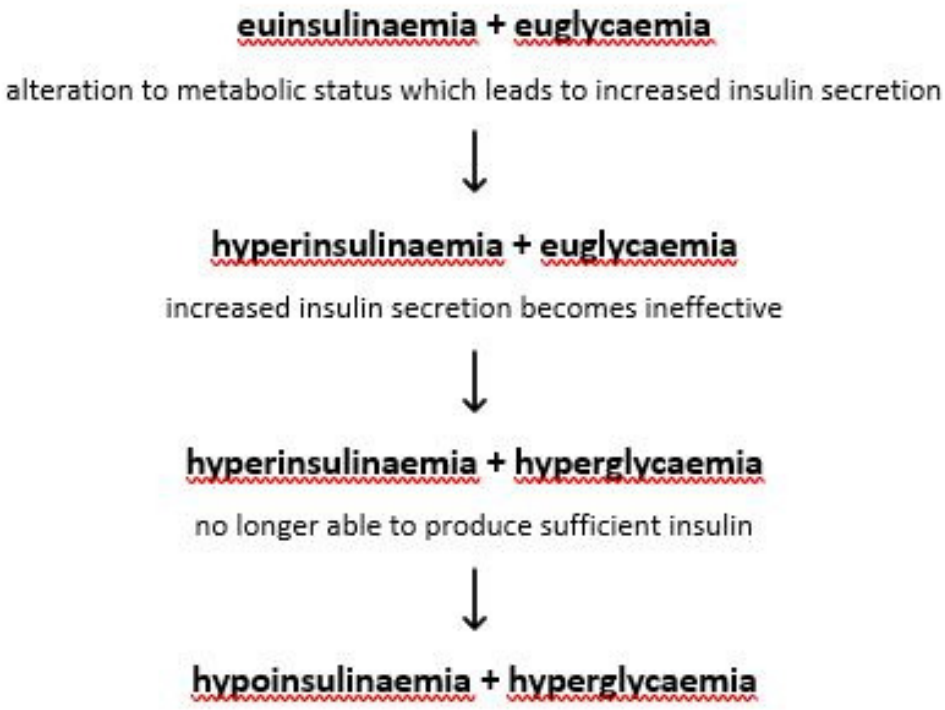
https://medicationsandnutrition.online

# Commentary

Insulin resistance is defined as a lack of cellular response to insulin – likely due to closed, damaged or insufficient insulin receptor sites, or some form of within-cell impairment. The lack of cellular response to insulin causes elevated blood glucose levels (hyperglycaemia). As a consequence of hyperglycaemia the pancreas increases the rate of insulin secretion which if sustained, results in both increased insulin levels (hyperinsulinaemia) and impaired pancreatic function. Both hyperinsulinaemia and hyperglycaemia, separately and together, are associated with a range of negative health outcomes.

**Summary of the sequence of events relating to insulin status**



Alterations to the status of a range of nutrients results in utilization of alternate pathways with consequent alteration to metabolic status, ultimately resulting in hyperinsulinaemia.

If the levels of nutrients are altered then alternate metabolic pathways are accessed and the outcome is hyperinsulinaema.

The following is a comprehensive, but not complete, list of nutrients associated with insulin resistance, and includes -

**Biotin** - modulates glucose-stimulated insulin secretion, insulin signalling pathway and insulin signal transduction in target tissues, glucose uptake in the liver, and glycogen synthesis;

**Boron** - modulates plasma insulin concentrations, and confers an antioxidant effect with pancreatic beta-cell preservation;

**Calcium** – important in β-cell function, and regulation of insulin secretion;

**Cholecalciferol** - maintains the normal resting levels of calcium in both pancreatic β-cells and insulin responsive tissues, important in insulin signalling, and prevention of epigenetic alterations associated with insulin resistance ie vitamin D deficiency is one of the factors that accelerates insulin resistance;

**Chromium** – participates in increased insulin binding, increased insulin receptor number, increased insulin receptor phosphorylation, enhanced insulin activity with consequent improved glucose disposal rates, and modulates various metabolic pathways such as insulin signalling pathway and the improvement of insulin signal transduction in target tissues.

HbA1c and serum chromium levels are inversely correlated;

**Cobalt** - enhances insulin action by activating insulin receptor sites;

**Copper** - enhances insulin action by activating insulin receptor sites;

**Iodine** - excessive iodine diminishes cell viability and compromises the function of insulin secretion in Islet β cells;

**Iron** - a bidirectional association exists between between glucose homeostasis and iron metabolism as impaired iron uptake may affect glucose metabolism;

**Magnesium** – is important as a cofactor for cellular uptake of glucose, for carbohydrate metabolism, for the cellular activity of insulin by alleviating insulin resistance, and downstream actions of the insulin cascade; decreased intracellular magnesium blocks insulin action within the cell;

**Molybdenum** - enhances insulin action by activating insulin receptor sites;

**Pantothenate** - modulation of CoA has a direct impact on glucose production;

**Pyridoxine** - enhances insulin sensitivity, antioxidant function can modify hyperglycaemic effects, is essential in the tryptophan-serotonin pathway which is crucial for β-cell proliferation ie inadequate B6 reduces β-cell proliferation;

**Retinols** – inadequate status associated with disruption to metabolic pathways and consequent insulin resistance;

**Riboflavin** - modulates the pro-inflammatory, pro-insulin resistance of adipocytes and macrophages;

**Sulfur** - enhances insulin action by activating insulin receptor sites;

**Thiamine** - is important in glucose metabolism – particularly the activities of transketolase, (pentose phosphate shunt), pyruvate-dehydrogenase (Krebs cycle), α-ketoglutarate-dehydrogenase (Krebs cycle). If there is inadequate thiamine then glucose is metabolised by alternate metabolic pathways that can stimulate insulin resistance.

Hyperglycaemia impairs within-cell thiamine transport and therefore availability;

**Zinc** - important in the processing, storage, secretion and action of insulin in pancreatic cells, and in activating insulin receptor sites; altered zinc status is associated with insulin resistance;

**Others** – there is some evidence, and many claims, of an association with insulin resistance with folate, B12, ascorbic acid, tocopherols, phylloquinones, potassium and selenium.

Given the increasing evidence of the negative impacts of pharmaceuticals on nutrition factors it seems a valid question is – are our prescribed medications causing more longterm harm than they heal or more importantly, why aren't the negative

impacts on nutrition factors part of the therapeutic intervention to optimize outcomes?

The increasing evidence of negative impacts that pharmaceuticals confer on nutrition factors prompts the questions -

- is the longterm (nutritional) harm caused by our prescribed medications greater than or less than the healing benefits they confer?

and/or,

- why aren't the negative impacts on nutrition addressed and integrated into the prescribed therapeutic intervention(s) to optimize outcomes?

What will you do when you see someone prescribed one or more pharmaceutical interventions that negatively impact any of the identified nutrients associated with insulin resistance, will you –

- identify each nutrient identified, and include how it contributes to insulin resistance in your clinical report?
- recommend interventions for each of the negatively impacted nutrients?
- recommend regular monitoring of negatively impacted nutrients?

**Conclusions**

Inadequate nutrient availability seems to be a significant contributor to the development of insulin resistance. A range of management strategies need to be developed and integrated into clinical practice in order to address the compromised nutrients in order to modify the development and progression of insulin resistance and its negative health impacts.

# 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: vit D def

## Biochemistry with Pharmaconutritional Consequences

| | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Na: | 141 | mmol/l | Hb: | 141 | g/L | Albumin: | 39 | g/L | BSL: | | mmol/l |
| K: | 4.1 | mmol/l | Lymph: | 2.4 | | Total Protein: | 69 | g/L | HbA1C: | 4.9 | |
| Urea: | 4.4 | mmol/l | MCV: | 89 | mmol/l | B12: | | pmol/L | INR: | | |
| Creatinine: | 0.076 | mmol/l | Zn: | | umol/l | Folate: | | nmol/L | TSH: | | mIU/L |

Other: eGFR > 90, eAG 5.2, vit D 57, chol 6.5, Tg 3.1, HDL 0.87, LDL 4.2, LDL:HDL 4.8, chol:HDL 7.5

## 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 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Baclofen | | ☐ | NV | CD | ↑ | ↓ | ☑ | | | | ☑ | ☐ | ☑ |
| Cholecalciferol | (1000 IU/day) | ☐ | | | | | ☐ | | | | ☐ | ☐ | ☐ |
| COLOXYL WITH S | | ☐ | | D | | | ☐ | | | | ☐ | ☐ | ☐ |
| LIPITOR | | ☑ | NV | CD | ↑ | ↓ | ☑ | | | | ☐ | ☐ | ☐ |
| MOVICOL | | ☐ | N | D | | | ☐ | | | | ☐ | ☐ | ☐ |
| Sertraline | Na | ☑ | NV | CD | ↑ | ↑ | ☐ | | | | ☑ | ☐ | ☐ |
| | | ▩ | | | | | ▩ | | | | ▩ | ▩ | ▩ |

Extra drug: clexane, cranberry , microlax enema

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

| Organ (transporter) | Thiamine | Choline | Carnitine |
|---|---|---|---|
| **Inhibitor function** | | | |
| From gut | sertraline | | |
| Liver (OCT1 inhibitor) | sertraline | sertraline | sertraline |
| Kidneys (OCT2 inhibitor) | sertraline | Sertraline | Sertraline |
| **Substrate function** | | | |
| Skeletal muscle | sertraline | Sertraline | Sertraline |

Organ uptake of 2 key nutrients is inhibited by one of the prescribed medicines therefore it remains in the blood.

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

**Biochemistry comments**

Recent relevant available biochemistry indicates -

- marginal vitamin D - currently prescribed vitamin D 1000 IU/day (1 tab/s) therefore advisable to review current vitamin D management strategy;
- elevated cholesterol – recently commenced Lipitor.

**Glycaemia comments**

Currently prescribed 3 medications that may alter glycaemia, being baclofen, atorvastatin and Lipitor.

**Bowel management comments**

- regular interventions prescribed
- no PRN interventions prescribed
- no Nurse Initiated interventions administered

**Staff comments**

Staff advise commencement of poor appetite due to mouth infection - ceased antibiotic intervention yesterday and today is saying mouth is still painful.

**Observations**

Mr ACA is a tall, well-built lovely young man with thyroidy eyes and who was sitting in the Day Room when I went to speak to him - he told me the food has an unacceptable taste.

**Pharmaconutrition comments**

Currently 3 prescribed medications that include nausea, vomiting, constipation, diarrhoea and reduced appetite as side effects.

Currently 2 prescribed medications that include altered taste as a side effect.

Meta-analysis of statin therapy on plasma CoQ10 concentrations found statins significantly reduced plasma CoQ10 status.

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

Regular monitoring sodium levels recommended whilst sertraline prescribed.

Statins interfere early in the cholesterol metabolic pathway and consequently decrease -

- conversion of sunlight 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.

The Scottish Lipid Study shows that a 5-year prescription of atorvastatin confers 20 years of benefit.

Mr ACA's diagnoses include depression, and as he is losing weight advisable to clarify effectiveness of current intervention.

Mr ACA is prescribed 3 medications that both directly and indirectly negatively impact appetite therefore advisable to review necessity for currently prescribed interventions and also consider alternative strategies to modify expression of the side effects.

Mr ACA's diagnoses include arthritis however currently no interventions prescribed for pain management.

Mr ACA's diagnoses include Multiple Sclerosis – relatively recent evidence indicates both Multiple Sclerosis and diabetes are considered to be part of the dysfunctional mitochondria spectrum - and statins are contra-indicated if the mitochondria are dysfunctional. Given Mr ACA's poor appetite which is likely due to multiple factors, and also given the negative impact of Lipitor on mitochondrial function in the presence of Multiple Sclerosis, it may be worthwhile clarifying the duration of Mr ACA's statin intervention and if greater than 5 years then consider a "statin holiday" for 3-6 months and monitor for both improving appetite and changing lipid status.

What else would you include?

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