MedNut Mail

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

AcetylCoA and aspirin

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https://medicationsandnutrition.online

Commentary

Pantothenate is important in many basic physiological functions, and especially as a precursor for Coenzyme A also known as CoA and CoA-SH; CoA is the precursor for the formation of acetylCoA; acetylCoA is an important metabolic intermediary.

Acetyl-CoA is the substrate, intermediary, or product of various energy systems as well as being -

- the actual molecule through which glycolytic pyruvate enters the tricarboxylic acid (TCA) cycle ie necessary for energy generation,
- a signal transducer,
- a precursor of anabolic reactions,
- an allosteric regulator of enzymatic activities,
- a key precursor of lipid synthesis,
- important in the activity of a wide panel of processes (including gene expression) via (de)acetylation reactions,
- a key determinant of protein acetylation,
- the sole donor of the acetyl groups for acetylation.

A range of pharmaceutical agents that focus on various aspects of acetyl-CoA metabolism in health disorders such as diabetes and obesity, are in are in various stages of development. Given the importance of acetylCoA in so many aspects of metabolism, perhaps we need to be aware of the consequences of inadequate acetylCoA and/or it's precursors.

Acetyl-CoA is transported by Acetyl-coenzyme A transporter 1 which is also known as ACATN, AT1, AT-1; SPG42; CCHLND.

Aspirin (acetylsalicylic acid) is absorbed from both the stomach and proximal small intestine. Ideal absorption of salicylate occurs in the pH range of -

- stomach - 2.15 - 4.10, unabsorbed at pH 6.5;
- intestinal - 3.5 or 6.5.

Aspirin is transported from blood into kidneys by OAT1/3.

The paper *Aspirin impairs acetyl-coenzyme A metabolism in redox-compromised yeast cells* (https://doi.org/10.1038/s41598-019-39489-4) found that aspirin impaired both the synthesis and transport of acetyl-coenzyme A (acetyl-CoA) into the mitochondria of manganese superoxide dismutase (MnSOD)-deficient Saccharomyces cerevisiae EG110 yeast cells, but not of the wild-type cells; the effect was at both gene and protein levels. Proposed mechanism of actions -

- impairment of the carnitine shuttle pathway via impairment carnitine acetyltransferases,
- impairment of the glyoxylate pathway via impairment of peroxisomal citrate synthase.

Both these mechanisms are important in the transfer of acetyl-CoA into the mitochondria.

Should we, as busy clinicians, be concerned about negative impacts on acetylCoA? There is very limited evidence on this subject so I suggest we need to be very cautious and not be influenced by the hype surrounding diabetes and body size; perhaps as a precaution, we should be clarifying carnitine status and effectiveness.

Next time you see someone prescribed aspirin will you –

- request clarification of carnitine status?
- monitor triglyceride and cholesterol levels for an impact via acetylCoA?

Conclusions

There is limited evidence in relation to the negative impact of aspirin on acetylCoA function, however what is available is concerning.

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: asthma

Biochemistry with Pharmaconutritional Consequences

No recent relevant biochemistry 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
ARICEPT		☑	NV	CD	↓	↓	☐				☑	☐	☐
COLOXYL WITH S		☐		D			☐				☐	☐	☐
PANADOL		☐	NV	CD			☐				☐	☐	☐
Risperidone		☑	NV	C	↑		☐		↑		☐	☐	☐
Warfarin	D	☑	NV	D			☑				☐	☐	☐
		▩					▩				▩	▩	▩

Extra drug: enprocal (100 ml tds)

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

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 three of the prescribed drugs and hypoproteinaemia may alter their effects.

Risperidone associated with increased risk of diabetes therefore advisable to monitor on a regular basis.

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

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

Concurrent ingestion of Panadol 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.

Bowels –

- regular aperient prescribed,
- oral PRN aperients prescribed: administered 1 x Nov,
- no Nurse Initiated interventions administered.

Staff advise Mrs ABT mostly eats well and agree she could probably manage more.

Mrs ABT is a pale, rubinesque lady who was sitting in the Day Room watching TV - she responded to some of my questions and told me she eats well.

The side effects of all five of the prescribed medications includes nausea.

The side effects of four of the prescribed medications includes nausea and diarrhoea.

Advisable to review daily food and fluid intake for 3 days and ensure a stable and adequate daily intake of vitamin K – women require a minimum 90 mcg/day.

Mrs ABT's diagnoses include chronic pain - nutritional factors that may be useful to consider in pain management include -

- **vitamin D** - current intervention may not be adequate to attain adequate range and currently prescribed warfarin. Evidence indicates increasingly brittle pain control with decreasing vitamin D levels. Advisable to check vitamin D levels and if low then review current vitamin D management strategy;
- **vitamin K** - has been found to suppress the inflammatory cytokines and NF-kappaB and prevent oxidative, hypoxic, ischemic injury to oligodendrocytes and neurons – vitamin K deficiency therefore results in classic expression of the inflammatory response and consequently pain, and currently prescribed warfarin.

Both liver and kidney uptake of thiamine are inhibited by risperidone and Aricept, therefore there is increased of serum thiamine levels and likely altered within-organ metabolism.

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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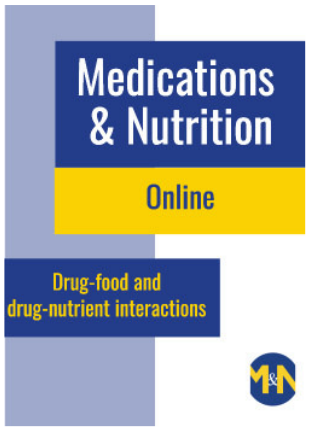

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