Alcohol and diabetes

PAT PHILLIPS MB BS, MA(Oxon), FRACP, MRACMA, GradDipHealthEcon(UNE)
MELISSA CARAPETIS APD, BHSc, MND
CONNIE STANTON APD, BSc, MND, DipEd

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In people with diabetes, alcohol consumption can have particular adverse effects and is commonly associated with hypertriglyceridaemia, fatty liver and weight gain.

It has been said that alcohol '*…improves the lipid profile, is one of the few interventions to increase HDL cholesterol, improves quality of life and has been shown to reduce the risk of heart disease… Take two doses each night with your evening meal.*' It could be good medicine for people with diabetes who commonly have dyslipidaemia, a low HDL cholesterol and increased risk of cardiovascular disease.

It has also been said that alcohol '*…increases weight, triglyceride, blood pressure and the risk of hypoglycaemia… and is a major cause of marital disharmony and violent death.*' Perhaps not so good after all.

Both these statements are true. Alcohol consumption is associated with decreased cardiovascular risk – the so-called 'French paradox' of a lower risk of cardiovascular disease despite a high prevalence of smoking – and, when consumed in moderation, it is a great social lubricant. However, the drinking of alcohol has the potential for adverse metabolic effects and is a major contributor to motor vehicle accidents, domestic and other violence, morbidity and mortality.

Dr Phillips is Senior Director, Endocrinology, North Western Adelaide Health Service, The Queen Elizabeth Hospital, and Ms Carapetis and Ms Stanton are accredited practising dietitians, Diabetes Centre, The Queen Elizabeth Hospital, Adelaide, SA.

Like the general population, people with diabetes may derive some health benefits from a modest intake of ethanol, and are also likely to suffer from the well-known adverse effects of excess consumption. They are, however, more likely to experience particular adverse metabolic effects. This article focuses on the particular potential adverse effects of ethanol in patients with diabetes and provides information, in the form of a handout for patients, on sensible drinking.

Alcohol metabolism

Alcohol (ethanol) metabolism starts in the liver with conversion of alcohol to acetaldehyde by the enzyme alcohol dehydrogenase and then conversion of acetaldehyde to acetate by acetaldehyde dehydrogenase, with the production of energy via the co-enzyme NAD^+/NADH (see the box on page 68). Acetate can then be metabolised to energy (via NADH) and carbon dioxide, or converted to ketones and triglycerides and exported for metabolism or storage elsewhere in the body. Alcohol is not metabolised directly to glucose.

The NADH produced in the metabolism of alcohol can be converted back to its oxidised form (NAD^+) through the electron transport chain, generating energy that is stored as ATP (adenosine triphosphate).

If the acetyl CoA production from the metabolism of alcohol exceeds immediate liver demands, NADH accumulates and must be converted to NAD^+ by the reduction of other substrates, which are then exported for use elsewhere. Examples of such reactions are the conversion of pyruvic acid to lactic acid and the production of triglycerides (see the box on page 68). The conversion of pyruvic acid to lactic acid effectively inhibits the production of glucose by the liver, leading to hypoglycaemia when food sources and liver stores of glucose are used up.

The production of triglycerides leads to hypertriglyceridaemia and fatty liver.

Metabolic effects of alcohol

The apparently complex metabolic effects of alcohol are now more easily understood. These occur in both people with and without diabetes.

Common effects

- Hypertriglyceridaemia – from the conversion of acetyl CoA to triglycerides, which are secreted into the blood as very low density lipoproteins (VLDLs).
- Fatty liver – from excess triglyceride production and fat storage in the liver.
- Weight gain – from energy derived from alcohol (29 kJ or 7 cal per g alcohol, second only to fat [37 kJ/g or 9 cal/g]).

Less common effects

- Hypoglycaemia – from conversion of pyruvic acid, the substrate for glucose production, to lactic acid.

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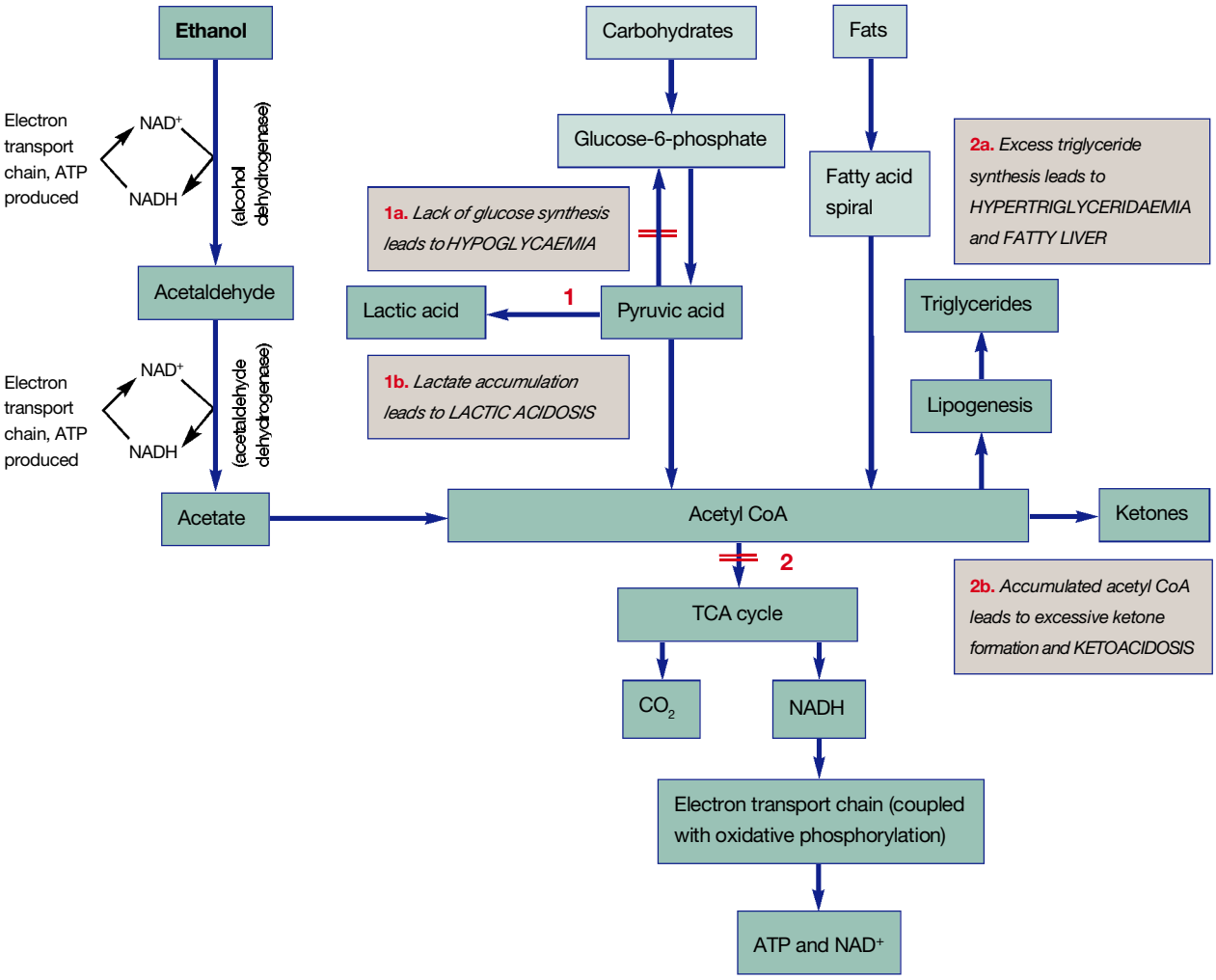
continued

A summary of ethanol metabolism



Ethanol metabolism and toxic effects

Alcohol (ethanol) is metabolised in the liver to acetaldehyde and then acetate, which then is metabolised via the TCA cycle (tricarboxylic acid cycle, also known as the citric acid or Krebs' cycle) to energy and carbon dioxide. The redox reactions involve the reduction of NAD^+ to NADH and conversion back to the oxidised state by the electron transport chain coupled with oxidative phosphorylation (with production of ATP). When acetyl CoA production exceeds immediate demands, acetyl CoA and NADH accumulate.

Several metabolic effects of alcohol are due to excess acetyl CoA and NADH.

Excess NADH is disposed of by conversion to NAD^+ by means other than the electron transport chain, i.e. reducing substrates of various metabolic pathways, such as reduction of pyruvic acid to lactic acid.

1. Excess NADH drives conversion of pyruvic acid to lactic acid. The resulting lack of pyruvic acid as a substrate for gluconeogenesis causes hypoglycaemia (1a). The build up of lactic acid may lead to lactic acidosis (1b).
2. Excess NADH produced by the electron transport chain inhibits the TCA cycle. The accumulated acetyl CoA can be used for lipogenesis, leading to excessive triglyceride production, hypertriglyceridaemia and fatty liver (2a). The excess acetyl CoA can also be converted to ketones, and this may lead to excessive ketone production (ketosis) and, in very high levels, ketoacidosis (2b).

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Rare effects

- Ketoacidosis – from excess production of ketones.
- Lactic acidosis – from excess production of lactic acid.
- The disulfiram reaction – from inhibition of acetaldehyde dehydrogenase by sulfonylureas, resulting in accumulation of acetaldehyde, which causes flushing of the skin, gastrointestinal upset and other ill effects.

Ketoacidosis is usually associated with another precipitant, such as insulin deficiency, which causes the excess acetyl CoA to be diverted from lipogenesis to ketone production (2a and 2b in the box on page 68). Lactic acidosis is also usually associated with another precipitant, such as hypoxia or metformin use, which themselves increase lactic acid production (1b in the box on page 68).

The disulfiram reaction is so named because the medication disulfiram (Antabuse), which is used to help manage alcohol dependence, inhibits acetaldehyde metabolism. The same reaction occurs in some people who are naturally deficient in acetaldehyde dehydrogenase (e.g. those of Asian extraction).

Table. Lifestyle changes and effects on hypertension[2]

Lifestyle change	Target	Benefit (systolic blood pressure reduction)
Increase activity	30 to 40 min, 3 to 4 times per week	4 mmHg
Lose weight	BMI: <25 kg/m^2 Waist circumference: <94 cm, men <80 cm, women	2 mmHg per kg loss
Limit sodium intake	<100 mmol/day	6 mmHg
Limit alcohol intake	<40 g/day, men* <20 g/day, women	3 to 4 mmHg
Limit saturated fat intake	<10% energy	2 to 3 mmHg

* One standard drink contains 10 grams of alcohol.

Alcohol and type 2 diabetes

Weight gain

Australia has one of the most overweight populations of all developed nations and Australians with diabetes are more overweight than the average Australian. Being overweight (particularly centrally overweight) underlies the disturbed metabolism of people with diabetes. Any excess energy intake, particularly of high-energy foods like alcohol, leads to further weight/waist gain and worsens the metabolic disturbance.

Dyslipidaemia

Apart from dyslipidaemic affects through worsening central overweight, alcohol metabolism directly increases triglyceride levels (see the box on page 68). Although moderate alcohol intake is associated epidemiologically with increased levels of high density lipoprotein cholesterol (HDL-C), this potential benefit can be outweighed by high triglyceride levels, which are associated with lower HDL-C levels.

Alcohol can, therefore, potentially worsen the lipid profile, particularly in those who already have high triglyceride or low HDL-C levels (as is the case with 20.5% and 11.9%, respectively, of Australians with type 2 diabetes).[1]

Hypertension

Moderating alcohol intake is one of the lifestyle changes that can reduce systolic hypertension (Table).[2]

Drug interactions

Polypharmacy is common in Australians with type 2 diabetes. Apart from their hypoglycaemic medication and medications for hypertension, dyslipidaemia and prothrombosis, individuals with type 2 diabetes may be taking the other prescription medications generally taken by the general population and an equal or greater number of complementary and OTC medications and health foods.

Alcohol has many drug interactions, including several related to hypoglycaemic medications. It interacts with sulfonylureas acutely or chronically. Acutely, there is competition for metabolism such that the action of sulfonylureas are augmented, thereby predisposing patients to hypoglycaemia, and also causing skin flushing, gastrointestinal upset and other adverse effects due to the disulfiram reaction. Chronically, alcohol induces the metabolism of sulfonylureas, reducing their therapeutic effect. Alcohol also interacts with metformin, increasing the risk of lactic acidosis.

Apart from interactions with hypoglycaemic agents, alcohol can reduce insulin secretion, predisposing patients to hyperglycaemia.[3] It can also increase the risk of, or worsen, hypoglycaemia by reducing hepatic glucose production.[3]

Impaired judgement

Alcohol is a valued contributor to the pleasure associated with food, friends and social activities but may impair judgement, predisposing individuals to less healthy food choices, less recognition of hyper- or hypoglycaemia and omission or misdosing of medication.

Alcohol and type 1 diabetes

Hypoglycaemia

Alcohol can affect all three of the factors predisposing to and protecting against hypoglycaemia – behaviour, awareness

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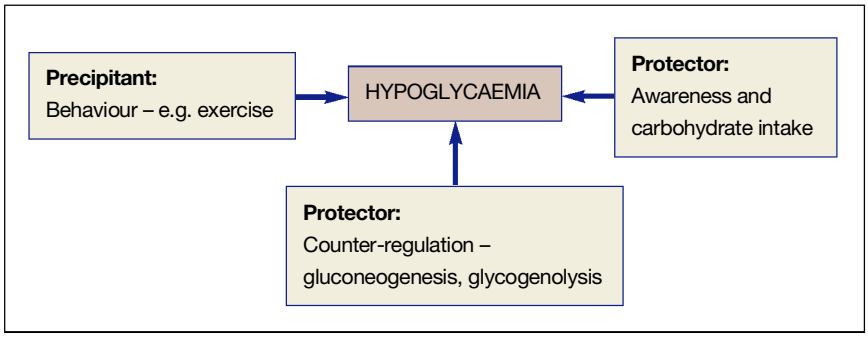

Figure. Hypoglycaemia – precipitants and protectors.

and counter-regulation (Figure). Impaired judgement may predispose to behaviours that cause hypoglycaemia and impair corrective responses. Alcohol can also reduce recognition of hypoglycaemic symptoms. As noted earlier, alcohol metabolism may divert glucose precursors to lactate synthesis, reducing gluconeogenesis and worsening hypoglycaemia.

The sedative effect of alcohol may mean that a person continues to sleep through hypoglycaemia that would otherwise have roused them and prompted corrective action.

Certain groups of people with diabetes are at particular risk of dangerous and potentially life threatening hypoglycaemia. These include:

- for those with type 1 diabetes – young men who get drunk
- for those with type 2 diabetes – older women taking sulfonylureas that have renally excreted active metabolites (glimepiride, glibenclamide)
- for all people with diabetes – when there is loss of hypoglycaemia awareness; participation in activities where mistakes may have fatal consequences; presence of comorbidities or use of medications that increase the depth or ill effects of hypoglycaemia; cold climate (which reduces the liver's capacity for gluconeogenesis); and sleeping alone (which increases the likelihood of not being found unconscious for a long time).

Ketoacidosis

In patients with ketoacidosis, insulin deficiency increases glucose and ketoacid production, causing an osmotic diuresis, dehydration, acidosis and the risk of life-threatening collapse.

As with hypoglycaemia, the combination of the metabolic, cognitive and sedative effects of alcohol may lead to dangerous and potentially life-threatening ketoacidosis.

Alcohol and diabetes – recommendations

Diabetes Australia and the RACGP have endorsed the NHMRC Australian Alcohol Guidelines, which are under review.[4-6] The current recommendations are up to four and two standard drinks (each 10 g of alcohol) per day for men and women, respectively, and one to two alcohol free days per week.[5] The American Diabetes Association recommends abstinence in those with high triglyceride levels.[7,8]

The patient information sheet accompanying this article is consistent with the Diabetes Australia, RACGP and NHMRC guidelines for alcohol use, which are the same as those for the general population. The information sheet suggests that people with diabetes and other individuals who are trying to lose weight or who have high triglyceride levels or high blood pressure should limit their alcohol intake to one or two drinks on special occasions only.

Generally beer, wine and spirits are low in carbohydrate (sugar) and are more likely to cause hypoglycaemia than hyperglycaemia when consumed on their own.

Key points for sensible drinking include:

- drink low alcohol rather than high alcohol drinks
- avoid alcoholic drinks high in sugar
- eat low fat, high carbohydrate foods when consuming alcohol. MT

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Ms Stanton and Ms Carapetis: None.

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