Hyperinsulinaemia

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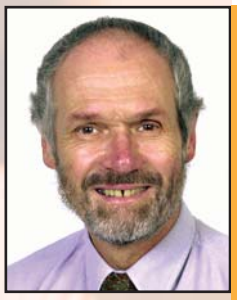
Case history

'...and this new diet is great. I've lost 4 kg in the past month, it is just falling off me'.

Jane is 35 years of age and has struggled with her weight since puberty. You think she has polycystic ovary syndrome. Jane has irregular periods, a fair amount of course facial hair, and has had terrible acne through her teenage years. She has two children, is happily married and works in the clothing department of a major department store.

You last saw her about 6 months ago when she complained that her dermatitis had worsened dramatically and was making it difficult for her to keep working. You referred her to a medical allergist for advice. Jane now tells you that there were 'lots of skin and blood tests' and she was told she had high insulin levels (hyperinsulinaemia). A high protein diet was prescribed to decrease insulin levels, help her lose weight and also help her dermatitis. She saw a dietitian who is very pleased with the result. She has lost weight and her dermatitis is better (Jane is also using a corticosteroid cream which may be helping). There is a family history of type 2 diabetes (mother and brother) and Jane had gestational diabetes with her second pregnancy. She is still overweight (height 158 cm and weight 70 kg*) and has marginal hypertension (145/90 mmHg). She takes ranitidine 150 mg twice per day for reflux, herbal tea to help her sleep and a multivitamin supplement.

* Body mass index (BMI)=weight (kg)÷height^2(metre^2)=70÷1.58^2=28. Healthy BMI 22–25, overweight 25–30, obese >30 kg/m^2



Question 1

What is the significance of Jane's hyperinsulinaemia?

Question 2

How likely is Jane to get diabetes?

Question 3

What other problems might Jane be predisposed to and how might they be managed?

Question 4

How long can Jane stay on a high protein diet?

FEEDBACK

Answer 1

Jane is progressing through the natural history of type 2 diabetes (*Figure 1, Table 1*) where as the years progress, insulin resistance increases and insulin secretion decreases. Initially both blood glucose and insulin levels are normal (zone A). As insulin resistance increases, insulin levels match the rise and exceed the normal range (hyperinsulinaemia). Glucose levels remain normal (zone B).

Interestingly, the variability of insulin levels is so high that the reference range quoted is + 1 standard deviation (SD: including 68% of the normal population) instead of the usual + 2 standard deviation (95%). This means that 16% of 'normal' people without any metabolic abnormality have hyperinsulinaemia!

It was probably while Jane was in 'zone B' that she got gestational diabetes with her second child. Higher levels of placental lactogen increased insulin resistance which exceeded her capacity to secrete insulin. She developed gestational diabetes which stopped when the placenta was delivered and placental lactogen fell. From where insulin resistance matches insulin secretion, glucose levels become progressively abnormal – first as impaired fasting glucose/impaired glucose tolerance, then as undiagnosed diabetes and then as diagnosed diabetes. Insulin levels still exceed the 'normal' range (zone C).

As insulin secretion decreases further, levels drop into the normal range (zone D). Paradoxically her diabetes is the worst to date, but she has 'normal' insulin levels.

Measuring Jane's insulin level is not likely to be helpful. Jane is likely to have insulin resistance and high insulin levels given her family history, polycystic ovary features, overweight and gestational diabetes. On the other hand, one in six people with normal metabolism will have 'hyperinsulinaemia 'because of test variability.

With rare exceptions the only indication for measuring insulin levels is in the investigation of hypoglycaemia looking for an insulinoma where hypoglycaemia does not

Table 1. Insulin resistance

Insulin resistance is genetically determined but it is:

Increased with:

- age
- central adiposity
- inactivity
- medications (eg. corticosteroids)

Decreased with:

- weight loss
- increased activity
- medications (eg. metformin, glitazones)

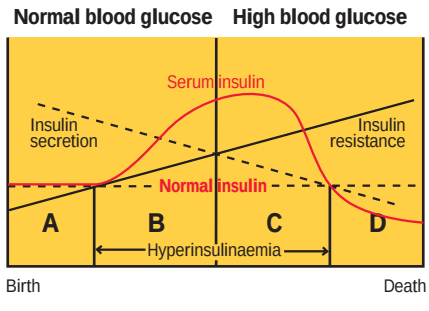


Figure 1. Insulin resistance

Figure 2. Syndrome X (metabolic syndrome)

suppress insulin secretion.

Answer 2

Very likely. Just having had gestational diabetes gives Jane a 50–80% chance over the next 10 years. Her strong family history and probable polycystic ovary syndrome are further indicators of high risk. Other members of her family are also at risk – her siblings who share half her genes and had a similar childhood environment to shape their lifestyle, and her children who also share half her genes (but who might benefit from a parental healthy lifestyle example).

Answer 3

Jane has at least two of the features of 'syndrome X' (*Figure 2*) otherwise known as the metabolic syndrome, the deadly quartet or the insulin resistance syndrome. The syndrome has been expanded to include the polycystic ovary syndrome (which Jane has) and hyperuricaemia. It would have been more useful to assess the other components of 'syndrome X' than to check her insulin levels (eg. lipid profile, blood pressure).

Jane's 'fat tummy' (central overweight – abdominal circumference men: overweight 94–102, obese >102cm; women: overweight 80–88, obese >88 cm) contributes to her metabolic syndrome by flooding the liver and peripheral tissues with fatty acids and hormones such as 'resistins'. These increase insulin resistance, triglyceride levels, blood glucose, blood pressure and thrombotic risk.

The lifestyle recipe is to 'eat less, walk more' but medications will probably be required at some stage, eg. metformin for glycaemia, angiotensin converting enzymes (ACE) inhibitors for hypertension, statins for cholesterol and aspirin for thrombosis. There are also medications that might help Jane reduce her central obesity such as xenical (Orlistat), and sibutramine (Reductil).

Answer 4

Fashions for high protein diets come and go and are always controversial. Some points seem quite established:

- equi-caloric diets with high protein or the more usual nutrient distribution result in equal weight loss
- high protein diets may be associated with high fat/saturated fat intake and inadequate intake of some nutrients
- high carbohydrate diets can cause hyperglycaemia and hypertrygliceridaemia in some individuals
- high protein diets may be more successful than more liberal diets partly because protein is more satiating and partly because food choices are more limited.

Jane is having great success and probably wouldn't change her diet even if you suggested she did. However, she may be prepared to consider modifications that would reduce fat and saturated fat intake and improve the nutrient profile. She also might be prepared to 'walk more' which would accelerate her weight loss and to gradually liberalise her diet to include a wider range of food groups. Although she is taking a multivitamin supplement, food groups such as fruit and vegetables have other benefits over and above their vitamin and mineral content (eg. soluble and insoluble fibre, antioxidants).

Resource

Syndrome X: problems associated with central obesity. Available from the author.

Reference

1. Executive summary of the third report of the National Cholesterol Education Program (NCEP) expert panel on detection, evaluation and treatment of high blood cholesterol in adults (Adult Treatment Panel III). JAMA 2001;285:2486–2497.

Conflict of interest: none declared.

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