The Hoechst Sweet & Deadly Challenge Case Study

Round One Questions

A 52 year old male consults you for the first time. The history is one of tiredness, slight weight-gain and intermittent blurring of vision. His mass is 78 kg and his height 168 cm. His blood-pressure is a persistent 160/105. Urinalysis shows 1% glucosuria but no ketonuria or proteinuria. His blood-glucose is 14,8 mmol/ℓ, serum cholesterol 8,4 mmol/ℓ and serum triglycerides 6,7 mmol/ℓ. Everything else is normal.

In order to confirm your diagnostic impression of diabetes you would do the following investigation:

1. a. A fasting blood-glucose.
   b. An oral glucose-tolerance test.
   c. A 2 hour post-prandial glucose.
   d. A fasting blood-glucose followed by another taken 2 hours after a glucose load of 75 gm.
   e. None of the above.

Round One Answers

Answer 1. When the diagnosis of diabetes mellitus is suspected because of symptoms, a single immediate random blood glucose measurement may reveal a concentration so high that it establishes the diagnosis. The likelihood of the diagnosis depends on the type of sample used, whether whole blood or plasma, or venous or capillary, the whole blood levels being 10,0 mmol/ℓ for a venous sample and 11,1 mmol/ℓ for a capillary sample, with the corresponding plasma levels 1,1 mmol/ℓ higher in each case. Note that the fingerprick samples you obtain for your reflectance meters are capillary. In this case the random-level is so high that no further tests are necessary as the diagnosis is established.

Your results firmly indicate the diagnosis of NIDDM. What are your patient's chances of having detectable micro-vascular disease at the time of diagnosis?

2. a. 20%
   b. 2%
   c. 15%
   d. 5%
   e. 30%

Answer 2. We are becoming increasingly aware that Type 2 or non-insulin-dependent-diabetes is particularly malignant in respect of many of the so-called "late" complications, and that our South Africans of Indian descent are particularly prone. In addition, many of these patients have already got serious complications at the time of diagnosis. No fewer than 30% of NIDDM patients have detectable micro-angiopathy at the time of diagnosis.

After two months of dietary management he loses 5 kg but is still symptomatic and has a fasting blood-glucose of 13,1 mmol/ℓ so you start him on glibenclamide ("DAONIL" — Hoechst), at a dose of 2,5 mg. There is a marked improvement in well-being and his fasting blood-glucose drops to under 8 mmol/ℓ.

With regard to the raised blood-pressure you detected at the first consultation your initial approach to control of hypertension should be:

3. a. A cardio-selective Beta-blocker.
   b. Diuretics.
   c. Non-pharmacological.
   d. ACE-inhibitors.
   e. Calcium-channel blockers.

Answer 3. Our attitude to hypertension in diabetics is becoming more and more aggressive as we realise that hypertension increases the risk of small- and large-vessel disease. This factor notwithstanding, however, the same principles apply to the diabetic with hypertension detected for the first time as for the non-diabetic. Thus, your initial management is non-pharmacological, with a low sodium diet, weight reduction and exhortations to stop smoking and increase leisure time physical activity.

With regard to the presence of both diabetes and hypertension in this patient:

4. a. Both are caused by his being overweight.
   b. The diabetes caused the hypertension.
   c. The hypertension caused the diabetes.

Answer 4. There is no doubt that hypertension is commoner in patients with diabetes, but there is no evidence that diabetes CAUSES hypertension. Obesity is an environmental factor which increases the risk of the emergence of diabetes in one who is genetically prone to the disorder, and we have all observed the drop in

d. Hypertension is commoner in diabetic patients.
e. Their occurrence in the same patient is purely coincidental.

blood pressure in hypertensives who manage to lose weight. However, there is nothing to suggest that obesity causes either of these disorders.

The hyperlipidaemia noted in your patient:

5. a. Will improve with improved glycaemic control.
   b. Will improve with adequate weight reduction.
   c. Does not require a specific diet.
   d. Requires the immediate addition of a lipid-lowering agent.
   e. Is of no importance as it is a common finding in South Africans.

Answer 5. The hypertriglyceridaemia and hypercholesterolaemia noted in our NIDDM patient will respond to improved glycaemic control and, probably even more so, to adequate weight reduction. You will note that when first seen our patient had a Body Mass Index (Mass in kg/Height in metres^2) of over 27 which indicates he is obese. Lipid-lowering agents are certainly not indicated at this stage.

Two years have passed and for the last 5 months of this time there has been a steady decrease in diabetic control with rising fasting blood-glucose estimations despite repeated dietary reinforcement and increasing the dose of Daonil to 10 mg at breakfast and 5 mg at supper. With his mass 70 kg and his fasting blood-glucose 15 mmol/ℓ you decide that the following therapeutic intervention would be the *most likely way* to achieve improved diabetic control.

6. a. Stress diet again and increase to a total dose of Daonil 25 mg.
   b. Add a biguanide.
   c. Commence insulin therapy.
   d. Continue the Daonil and start on insulin in addition.
   e. Start insulin together with a biguanide.

Answer 6. Our patient is now entering the phase of what is generally termed "secondary sulphonylurea failure". About 10% of our NIDDM population will do this per annum. Adding a biguanide (ie metformin) is not unreasonable, but, in our experience, is seldom successful. Whilst peripheral insulin insensitivity is part of the problem, it is more likely that increasing impairment of the pancreatic ß-cells to release insulin is the dominant factor, and the most appropriate treatment is to commence insulin in the form of one of the long- or intermediate-acting insulins, the latter used either once or twice a day. In many centres this will be combined with a small single daily dose of a sulphonylurea, preferably glibenclamide. Note that the dose of daonil used in our patient is excessive. It is highly unlikely that any diabetic not responding to 5 mg a day will respond to a higher dose. The drug is a potent one and the average dose used in our clinic (in conjunction with a prudent and appropriate diet) is 2,5 mg daily.

Eventually this patient is controlled on a single daily dose of 54 iu of intermediate-acting insulin. However, within a few weeks, he starts complaining again of tiredness and you find his mass has increased to 76 kg. A random blood-glucose is 17,3 mmol/ℓ. The most likely problem now is:

7. a. Too little insulin.
   b. Too much insulin.
   c. Overeating and cheating on diet.
   d. An infection.
   e. None of the above.

The correct therapeutic approach would be to:

8. a. Increase the insulin.
   b. Split the insulin dose to twice daily.
   c. Stress diet once more.
   d. Reduce the insulin.
   e. Recommend more exercises.

Answers 7 and 8. A useful maxim in diabetes management is "more is not necessarily better" as we have seen in the case of the sulphonylureas. Similarly, with the use of insulin in the NIDDM patient with secondary failure, one needs to be aware that loss of glycaemic control, particularly when associated with an increase in mass, is more likely to be due to too much insulin, with a consequent inability to control the appetite, and that an appropriate reduction in the dose often has the desired effect.

Once this patient has been started on insulin:

9. a. He will need to stay on insulin for ever.
   b. The insulin requirement will rise progressively.
   c. He may be able to get back onto oral hypoglycaemic agents.

Answer 9. The chances of a diabetic with secondary failure putting on weight when insulin has been added to his management are about as great as those of a SAA flight being delayed. Occasionally, it may, after a while, be possible to stop the insulin and maintain reasonable control on diet and oral agents again. It is remarkable