

# Type I diabetes, dialysis and insulin pump therapy

Gillian Atherton

## Introduction

**Diabetic nephropathy is a major cause of end-stage renal failure. People with type I diabetes who are on insulin and require renal replacement therapy can experience several problems in the control of glycaemia. They are at risk of hypoglycaemia from the effect of haemodialysis, particularly when glucose-free dialysate is used. Insulin regimens based on multiple dose injections can help to minimise this problem. Many patients have a basal bolus regimen and many can learn carbohydrate counting to maximise flexibility, but even this may not always prevent severe hypoglycaemia. This case history shows how continuous subcutaneous insulin infusion can help prevent life-threatening hypoglycaemia.**

**M**ary developed type I diabetes in 1975, at 12 years of age. She was referred to the hospital in 1992 when she was 29 years old and 20 weeks pregnant. The pregnancy was uneventful, but her glycaemic control deteriorated over the next few years with glycosylated haemoglobin (HbA<sub>1c</sub>) levels averaging 10%.

By 1993 Mary had developed retinopathy and proteinuria, a marker for diabetic nephropathy. Mary also smoked 20 cigarettes a day.

The Diabetes Control and Complications Trial Research Group (1993) showed that poor glycaemic control is a predisposing factor for the development of microvascular disease, and that intensive insulin therapy to improve glycaemic control effectively delays the onset, and slows the progression, of retinopathy, nephropathy and neuropathy. However, as Hasslacher (2001) points out:

*'There are reports that some apparently well-controlled patients will develop proteinuria, whereas other poorly controlled patients will not. These findings lead to the assumption that there is variable individual susceptibility to develop renal complications'.*

Smoking is implicated in the development of persistent microalbuminuria, an early indicator of renal disease. Salahudeen (2002) concluded that 'smoking remains a clearly modifiable risk factor in patients with renal failure'.

Mary was on a basal bolus regimen of Actrapid (soluble insulin) and Insulatard (isophane insulin), but her HbA<sub>1c</sub> levels remained high at around 11%. Unfortunately, Mary failed to attend hospital appointments and was admitted in 2000 with diabetic ketoacidosis. Her renal function was declining, with creatinine levels rising, now 208 µmol/L (normal range 70–110 µmol/L).

Mary was not taking an angiotensin-converting enzyme (ACE) inhibitor and was hypertensive, with blood pressure readings above 150/100 mm/Hg. She also had hyperlipidaemia. Clinical trials have shown that ACE inhibition slows the rate of progression to end-stage renal failure (ESRF) (Lewis et al, 1993). Mary was prescribed ramipril (Tritace), an ACE inhibitor, 2.5 mg once daily, and simvastatin (Zocor) 20 mg at night to reduce cholesterol levels.

In June 2001, Mary was admitted to hospital with diabetic ketoacidosis, but had also had two 'seizures' of unknown cause. At that time, there was no evidence that hypoglycaemia could cause

## ARTICLE POINTS

**1** People with type I diabetes on insulin who require renal replacement therapy are at risk of hypoglycaemia from haemodialysis.

**2** Mary had poor glycaemic control smoked, was hypertensive and had hyperlipidaemia.

**3** She was admitted to hospital with diabetic ketoacidosis. Her insulin regimen was changed to NovoRapid and Insulatard before starting haemodialysis.

**4** She experienced severe hypos while on dialysis and had a left-sided hemiparesis after a severe hypo. Insulatard was replaced with Lantus and carbohydrate counting started.

**5** As severe hypos continued, Mary started continuous subcutaneous insulin infusion. Her HbA<sub>1c</sub> is now 6.5–7.6% and hypoglycaemic events are rare.

## KEY WORDS

- Type 1 diabetes
- Hypoglycaemia
- Dialysis
- End-stage renal failure
- CSII

Gillian Atherton is a Diabetes Nurse Specialist at Bradford Royal Infirmary, Bradford

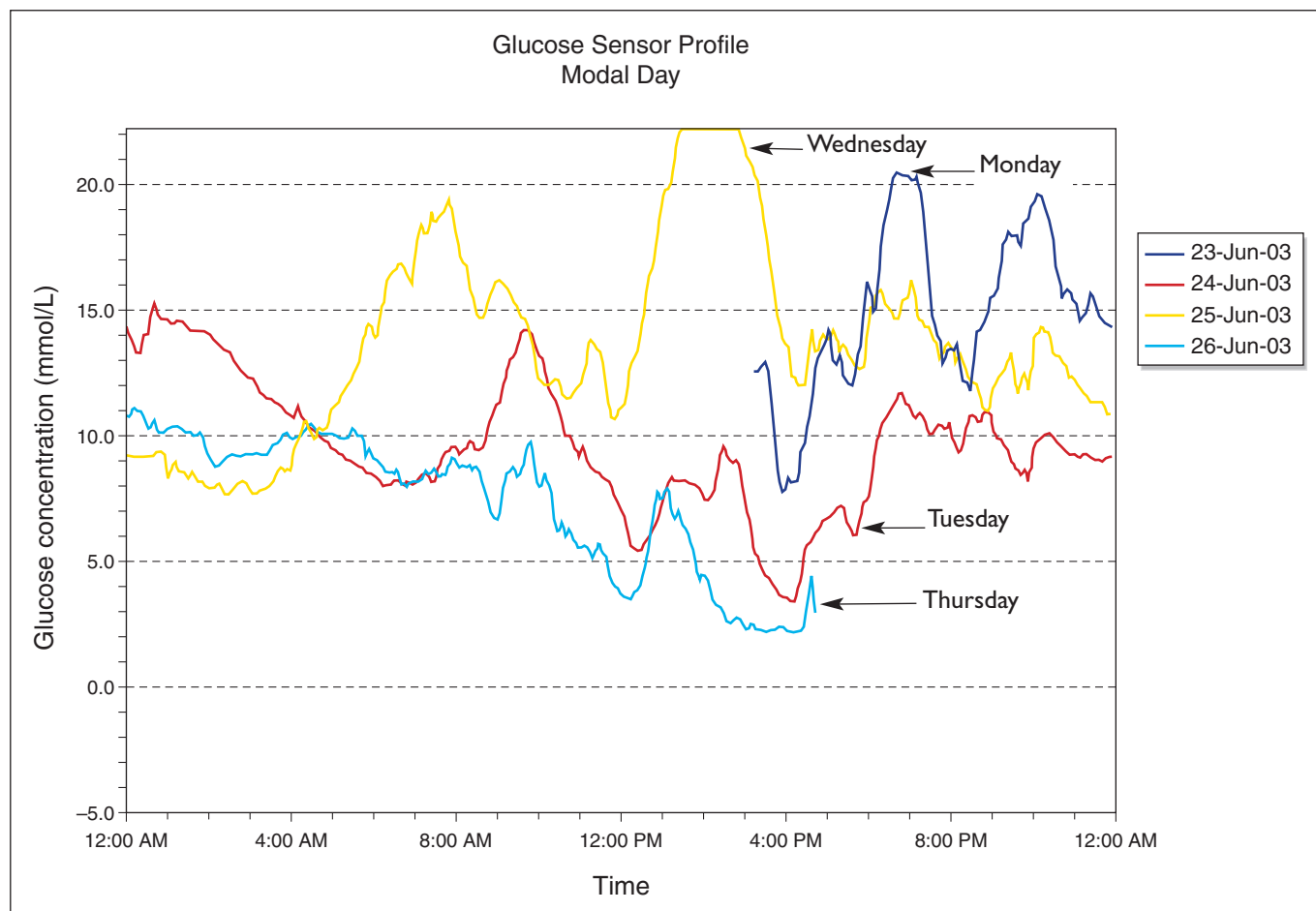


Figure 1. Mary's glucose sensor profile: modal day.

**PAGE POINTS**

**1** Haemodialysis predisposes people with diabetes to hypoglycaemia, particularly when non-glucose dialysate is used.

**2** The kidney usually metabolises 30–40% of insulin, and provides approximately 45% of endogenous glucose through gluconeogenesis during prolonged fasting, thus people with end-stage renal failure are predisposed to hypoglycaemia.

seizures. Her glycaemic control had improved, with an HbA<sub>1c</sub> of 7.9%. Mary had stopped taking ramipril as she was not sure why she was taking it and did not know about the detrimental effects on renal function of not taking it. She continued to take simvastatin, however, and her cholesterol levels showed improvement, now 4.5 mmol/l.

In July 2001, Mary's basal bolus regimen was changed to NovoRapid (insulin aspart) and Insulatard (isophane insulin) before starting haemodialysis. Haemodialysis predisposes people with diabetes to hypoglycaemia, particularly when non-glucose dialysate is used, and many dialysis units recommend glucose/dextrose dialysate to prevent this (Smith, 1997). Our unit uses glucose-free dialysate.

We hoped to minimise hypoglycaemia by using a quick-acting insulin analogue rather than soluble insulin, and adjusting the dose pre-dialysis to take into account

the effect of haemodialysis.

ESRF also predisposes people with diabetes to hypoglycaemia, as the kidney usually metabolises 30–40% of insulin and provides approximately 45% of endogenous glucose through gluconeogenesis during prolonged fasting (Weinrauch et al, 1978). In renal failure, metabolism is reduced, thus increasing the risk of hypoglycaemia. It is estimated that approximately 60–70% of people with diabetes and renal failure have experienced hypoglycaemia (Parmar, 2004).

Mary's dialysis sessions took place on Monday, Wednesday and Friday afternoons. Initially her insulin aspart dose taken with lunch was reduced, but this had to be omitted when she experienced severe hypoglycaemic events while on dialysis. Mary was depressed, her appetite was poor and she had a left-sided hemiparesis after a severe hypoglycaemic event. Continuous

blood glucose monitoring showed significant change in diurnal blood glucose levels on dialysis days compared with non-dialysis days (Figure 1).

Insulatard insulin was stopped and insulin glargine (Lantus) – a long-acting insulin analogue – was started in the hope of reducing these problems. Mary also saw the dietitian and started carbohydrate counting and dose adjusting the insulin aspart to allow flexibility in her eating pattern and to improve glycaemic control.

Unfortunately, the hypoglycaemic events continued. Hypoglycaemia is a frequent and common problem, affecting 10–25% of people with diabetes and resulting in death in 3–4% (Parmar, 2004). There has been considerable research and debate about the long-term effects of hypoglycaemia on cognitive function. Lincoln et al (1996) concluded:

***‘Results support previous work that suggests that major hypoglycaemic attacks have a significant effect on some aspects of cognitive function, but the clinical importance of this finding remains to be determined.’***

As Mary was now having recurrent life-threatening episodes of hypoglycaemia, she was given a trial of continuous subcutaneous insulin infusion (CSII) or ‘insulin pump’ therapy, which is given at basal rate, removing the need for a basal insulin. This follows the recommendations of the National Institute for Clinical Excellence (NICE, 2002) in its appraisal consultation document on CSII.

NICE recommend CSII for people:

***‘... for whom multiple dose injection therapy has failed [...] for whom it has been impossible to maintain an HbA<sub>1c</sub> level no greater than 7.5% (or 6.5% in the presence of microalbuminuria or adverse features of the metabolic syndrome) without disabling hypoglycaemia occurring, despite a high level of self-care of their diabetes’.***

Evidence of ‘disabling hypoglycaemia’

includes:

- hypoglycaemia resulting in continuing anxiety over recurrence, associated with significant adverse effect on quality of life
- the repeated and unpredictable occurrence of hypoglycaemia requiring third-party assistance
- lack of awareness of the onset of hypoglycaemia
- hypoglycaemia significantly interfering with normal activities.

CSII is delivered by an electromechanical pump. It allows insulin – now mainly fast-acting analogue insulin – to be delivered continuously (basal rate) over 24 hours, with a bolus or boosting dose activated by the patient with meals. The basal rate can be adjusted every 30 minutes to give 48 different rates in 24 hours if necessary.

The pump can be suspended to stop insulin delivery, to help prevent hypoglycaemia when exercising, or to assist in treating a hypoglycaemic event. It allows a far more predictable rate of absorption of insulin compared with injection regimens, and physiologically acts more like a ‘healthy pancreas’ than do other insulin regimens (Raskin and Strowig, 1995).

CSII is not suitable for everybody with diabetes – patients should be aware that it is not an easy option and that they need to be highly motivated to succeed. They must be able to carbohydrate count, check blood glucose levels four to six times a day, respond quickly to problems with the pump, follow protocols for treating hypoglycaemia and hyperglycaemia, and have realistic expectations of what CSII can achieve.

Mary and her mother attended education sessions on CSII. Her mother was also taught how to use the pump, change the pump catheters, treat hypoglycaemic events (including the administration of glucagon) and react to emergency situations, such as diabetic ketoacidosis.

They attended the hospital daily for four days when pump therapy was initiated, and had access to a diabetes specialist nurse via an on-call system.

## PAGE POINTS

**1** As Mary experienced significant hypoglycaemic events while on dialysis, her insulin was changed to insulin glargine.

**2** Unfortunately, using insulin glargine, carbohydrate counting and dose adjusting insulin aspart did not prevent the hypoglycaemic events.

**3** Because of recurrent hypoglycaemia, Mary was then given a trial of continuous subcutaneous insulin infusion (CSII).

**4** CSII basal rate can be adjusted every 30 minutes, with a bolus dose at meal times, and basal insulin can be suspended when exercising to prevent hypoglycaemia.

**5** Patients must be highly motivated, able to count carbohydrates, check blood glucose levels four times a day, follow protocols and respond quickly to pump problems to succeed with CSII.

**6** Mary and her mother attended education sessions on CSII and attended the hospital daily for four days after therapy was initiated.

PAGE POINTS

1 Mary now suspends CSII about an hour before dialysis and recommences it as soon as dialysis has finished.

2 Mary's glycaemic control on CSII is satisfactory and hypoglycaemic episodes are now rare.

Basal rates were adjusted on home blood glucose readings initially, but regular use of a continuous blood glucose monitoring device was invaluable for checking overall glycaemic control.

Mary now suspends the CSII approximately one hour before dialysis and recommences it immediately dialysis has finished. Her glycaemic control is satisfactory, with HbA<sub>1c</sub> levels 6.5–7.6%, but, more importantly, the episodes of hypoglycaemia are very rare.

CSII was first invented in the 1960s, and, with the considerable advances in technology, now offers a significant alternative to standard insulin therapy in controlling diabetes. Unfortunately, financial constraints and misunderstandings about the safety of insulin pumps mean that many patients who would benefit from this treatment are still denied access to this service.

Keen and Pickup (2001) suggest that:

**'Reluctance to fund pump therapy may also stem from the erroneous belief that this would prove costly. In fact, CSII is not indicated in most people with type 1 diabetes, who can achieve good control with intensified insulin therapy. Real benefits are obtained in 1–2% of those with type 1.'**

Mary is definitely benefiting from CSII: not only are there reduced hospital admissions, but she also has greater flexibility allowing choice and amount of food taken, resulting in improved quality of life. ■

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