## What happens to people with "brittle" diabetes?

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The key message of the rather bleak article by Cartwright et al (2011; summarised alongside) is that, of a cohort of 33 women with a diagnosis of brittle diabetes, survival rate at 20 years is very poor. Of those individuals who could be traced at this stage, the mortality rate was a shockingly 50%. This is in a group of women with a mean age of 42 years.

The original report from this group (Pickup et al, 1983), described the clinical features of a small group of individuals with a label of brittle diabetes. The main inclusion criterion at that time was life-disrupting glycaemic control. All the study participants had had multiple, prolonged admissions to hospital with primarily ketoacidosis. In the original article, the authors characterised the group and made the point that the problem is mainly psychological rather than physiological.

Since the original description, that cohort showed a gradual steady decline in the need for hospital admissions, but had, unfortunately, developed complications relating to poor glycaemic control, and the associated high rate of death.

The main purpose of the current article (Cartwright et al, 2011) was to describe what happened to this group of women. Frustratingly, it leaves a number of questions unanswered – specifically, what lessons have we learnt that would allow us to improve the care of this group in the future?

If we started the same study today, a major concern would be whether the outcome would be any different? Although there have been a number of technical advances in the management of diabetes with newer insulins, greater ease of monitoring and the development of safe and effective insulin pump therapy, none of these would particularly benefit this cohort. Intuitively, it is obvious that better communication is needed between the hospital diabetes care teams looking after people admitted repeatedly with ketoacidosis and the community team looking after them after discharge.

> *"... there needs to be a specific focus on intensive support for the person with 'brittle' diabetes around each hospital admission, and shortly after they return home."*

It appears to me that there needs to be a specific focus on intensive support for the person with "brittle" diabetes around each hospital admission, and shortly after they return home. Unfortunately, there is little published evidence to support this view.

Pickup J, Williams G, Johns P, Keen H (1983) Clinical features of brittle diabetic patients unresponsive to optimized subcutaneous insulin therapy (continuous subcutaneous insulin infusion). *Diabetes Care* **6**: 279–84

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## Insulin plus liraglutide improved $HbA_{1c}$ and weight

| | |
|---|---|
| Readability | ✓✓✓ |
| Applicability to practice | ✓✓ |
| WOW! factor | ✓✓✓✓ |

1 Participants ($n$=14) with T1D were treated with liraglutide for 1 week; eight continued treatment for 24 weeks.

2 In all participants, mean fasting and weekly glucose concentrations decreased significantly after 1 week compared with baseline (both $P$<0.01).

3 Those who continued therapy with liraglutide for 24 weeks saw a significant decrease in $HbA_{1c}$ level at 24 weeks compared with baseline (6.5% [48 mmol/mol] vs 6.1% [43 mmol/mol]) and a weight decrease of 4.5±1.5 kg (both $P$=0.02).

4 Liraglutide treatment in addition to insulin therapy was found to improve glycaemic control and weight in people with T1D.

Varanasi A, Bellini N, Rawal D et al (2011) Liraglutide as additional treatment for type 1 diabetes. *Eur J Endocrinol* **165**: 77–84

QJM

## High mortality rate in brittle diabetes

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|---|---|
| Readability | ✓✓✓✓ |
| Applicability to practice | ✓✓✓✓ |
| WOW! factor | ✓✓✓✓ |

1 The authors of this cohort study aimed to determine the long-term outcomes of people with brittle diabetes (a term used to describe people with T1D whose lives are disrupted by glycaemic instability and repeated hospital admissions).

2 A group of 33 people with brittle diabetes were identified between 1979 and 1985 and were traced, where possible, via their diabetes clinic or GP.

3 Participants were also compared with a matched case-control group of people with T1D, who had no history of brittle diabetes.

4 Participants were all female, had a mean age of 18±5 years at the start of the study, and a diabetes duration of 8±4 years. Thirteen were not traceable after a mean follow-up of 22 years.

5 Out of the remaining 20 participants that were traced, 10 had died during follow-up (50%). Causes were chronic renal failure (3), diabetic ketoacidosis (3), hypoglycaemia (2), subarachnoid haemorrhage (1) and uncertain (1).

6 The 10 survivors were substantially burdened with complications. Compared with the control group, those with brittle diabetes experienced significantly more nephropathy and autonomic neuropathy.

7 The authors concluded that people with brittle diabetes characterised by recurrent diabetic ketoacidosis have a high long-term mortality rate and substantial burden of complications.

Cartwright A, Wallymahmed M, Macfarlane IA et al (2011) The outcome of brittle type 1 diabetes – a 20 year study. *QJM* **104**: 575–9

# Type 1 diabetes

## LANCET

## $HbA_{1c}$ associated with heart failure

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|---|---|
| Readability | ✓✓✓✓ |
| Applicability to practice | ✓✓✓✓ |
| WOW! factor | ✓✓✓✓ |

1 The association between heart failure and glycaemic control was assessed in this Swedish cohort study.

2 Participants aged ≥18 years with T1D and no known heart failure were identified from the Swedish national diabetes registry from January 1998 to December 2003, and were followed-up until hospital admission for heart failure or death or end of follow-up on 31 December 2009.

3 The cohort consisted of 20 985 people with a mean age of 38.6±13.3 years. A total of 635 people (3%) were admitted to hospital with a primary or secondary diagnosis of heart failure during a median follow-up of 9 years. The incidence of events per 1000 person-years was 3.38 (95% confidence interval [CI], 3.12–3.65).

4 Incidence increased monotonically with $HbA_{1c}$, with a range of 1.42–5.20 per 1000 person-years between participants in the lowest (<6.5%; <48 mmol/mol) and highest (≥10.5%; ≥91 mmol/mo]) categories of $HbA_{1c}$.

5 Increased age and duration of diabetes were associated with an increasing risk of heart failure.

6 A subgroup analysis of data for blood lipids (18 281 participants) revealed that higher HDL-cholesterol levels were associated with a lower risk of heart failure. No association was identified with LDL-cholesterol.

7 The authors concluded that $HbA_{1c}$ and risk of heart failure were positively associated in this relatively young cohort, indicating that improved glycaemic control may reduce the risk of heart failure.

Lind M, Bounias I, Olsson M et al (2011) Glycaemic control and incidence of heart failure in 20,985 patients with type 1 diabetes: an observational study. *Lancet* **378**: 140–6

## DIABETOLOGIA

## Exposure to candesartan in first trimester in pregnant women with T1D

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|---|---|
| Readability | ✓✓✓ |
| Applicability to practice | ✓✓✓ |
| WOW! factor | ✓✓ |

1 The consequences of treatment with angiotensin-converting enzyme inhibitors angiotensin receptor blockers (ARBs) during the second and third trimesters of pregnancy are well-described.

2 The authors examined the effects of ARB treatment in the first trimester. These three placebo-controlled trials focused on the effects of candesartan on diabetic retinopathy (DIRECT [Diabetic Retinopathy and Candesartan Trials]).

3 A total of 178 normotensive women with T1D were randomised as part of the DIRECT trial to receive either candesartan 32 mg once-daily ($n$=86) or placebo ($n$=92). Over the 4-year trial period, there were 208 pregnancies.

4 Over half of the women who became pregnant were exposed to candesartan or placebo prior to or in early pregnancy, but all discontinued it at an estimated 8 weeks from the last menstrual period.

5 Outcomes were similar in those receiving candesartan versus placebo: full-term pregnancies (51 vs 50); premature deliveries (21 vs 27), spontaneous miscarriages (12 vs 15), elective terminations (15 vs 14), respectively.

6 The authors concluded that the risk for fetal complications due to ARBs may not be high if exposure is limited to the first trimester. The authors suggest that long-term trials of the effects of ARBs can be conducted in fertile women as long as the drug is stopped on planning or detection of pregnancy.

Porta M, Hainer JW, Jansson SO et al (2011) Exposure to candesartan during the first trimester of pregnancy in type 1 diabetes: experience from the placebo-controlled DIabetic REtinopathy Candesartan Trials. *Diabetologia* **54**: 1298–303