Management of type 1 diabetes

Recurrent ketoacidosis is still associated with a high risk of death

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Recurrent diabetic ketoacidosis (DKA) is still associated with an unacceptably high risk of death despite modern treatment. The rate of death associated with admission to hospital with DKA has historically been high. For clinicians managing this condition in hospital, such findings may perhaps be surprising as, intuitively, the mortality rate associated with DKA during the acute hospital stay feels low. This is not a reflection of particularly high standards of care during the hospital stay, however, as a survey by Dhatariya et al (2016) suggests. Seventy-two hospitals responded to the survey, and low potassium levels were reported in 55% of inpatients. Their study relates to the hour-by-hour management of the acute condition, and they conclude that this area of care could be significantly improved.

The article by Gibb and colleagues (summarised alongside) would perhaps suggest that this is missing the point. The authors conclude that recurrent DKA is still associated with a high mortality rate and that the deaths occur not in hospital but at home. We can predict who is at risk, as recurrent DKA tended to affect young, socially disadvantaged adults with very high HbA_{1c} levels. This in itself is not a novel finding; this is the group of individuals who would previously have been labelled as having brittle diabetes. Our understanding of this condition is that it does not represent an organic disease of insulin action but rather is the result of psychosocial problems (Gill et al, 1996).

A number of approaches have been described to try and address this issue, and many diabetes centres have programmes in place to try and help this at-risk cohort of individuals. The importance of this paper is that it shows us they are still not working. We can and should continue to improve the day-to-day management of DKA in hospital, but to reduce deaths we need better strategies to engage this troubled group of patients. Hospital-based diabetes services have traditionally focused on the technical aspects of insulin delivery. These data would suggest that this approach is not appropriate. The authors' conclusion is that a combined medical, psychological and social approach is required. ■

Dhatariya KK, Nunney I, Higgins K et al (2016) National survey of the management of diabetic ketoacidosis (DKA) in the UK in 2014. *Diabet Med* **33**: 252–60

Gill GV, Lucas S, Kent LA (1996) Prevalence and characteristics of brittle diabetes in Britain. *QJM* **89**: 839–43

Diabetologia

Recurrent DKA and subsequent mortality

Readability	✓✓✓✓
Applicability to practice	✓✓✓✓
WOW! Factor	✓✓✓✓✓

1 In this retrospective cohort study, the authors evaluated the subsequent risk of death in all people admitted to the Royal Infirmary of Edinburgh with diabetic ketoacidosis (DKA) between 2007 and 2012.

2 The cohort included 628 admissions in 298 individuals, and the median follow-up was 4.9 years.

3 Among these people, 44 deaths occurred, 19 of which were of uncertain cause and potentially attributable to acute metabolic decompensation. No death occurred during the admission for DKA itself.

4 Mortality rates were significantly associated with the number of DKA admissions over the 6-year study period, with rates of 29.6% (8/27) in those with four or more admissions, 18.3% (15/82) in those with two to four admissions, and 10.6% (20/189) in those with a single admission (P=0.016 for trend).

5 Overall, 52.3% of deaths occurred at home, at a median age of 38 years, in comparison to a median age of 57.7 years in those who died in hospital. Ten deaths (eight at home) occurred within 2 months of a DKA admission.

6 Recurrent DKA admissions were associated with longer diabetes duration and earlier age at diagnosis, greater social deprivation and higher HbA_{1c} levels (103 vs 79 mmol/mol [11.6% vs 9.4%]).

7 Recurrent DKA admissions were also associated with a history of psychiatric admission and previous antidepressant use, with 47.5% of people with more than five admissions having received antidepressants.

Gibb FW, Teoh WL, Graham J, Lockman KA (2016) Risk of death following admission to a UK hospital with diabetic ketoacidosis. *Diabetologia* **59**: 2082–7

Diabetologia

Increased risk of epilepsy in people with T1D

Readability	✓✓✓
Applicability to practice	✓✓
WOW! Factor	✓✓

1 A number of epidemiological studies from different countries suggest that T1D and epilepsy are linked; however, the evidence is conflicting. Therefore, these authors sought to determine the relationship between the two conditions in a large cohort from the UK.

2 In a retrospective, open-cohort study using data from The Health Improvement Network, people newly diagnosed with T1D aged ≤40 years between 1990 and 2015, with no pre-existing epilepsy, were evaluated.

3 This cohort (n=4922; mean age, 17.9 years) was matched according to age, gender and general practice with up to four control subjects (n=19 688).

4 Over a mean follow-up of 5.4 years, 35 people in the T1D cohort and 46 in the control cohort were diagnosed with epilepsy, an incidence rate of 132 vs 44 per 100 000 person-years.

5 After adjustment for social deprivation scores, cerebral palsy, head injury and learning disability, the hazard ratio for epilepsy in the T1D cohort was 3.01 (95% confidence interval, 1.93–4.68).

6 These findings appear to validate the observed association between T1D and epilepsy. While a prospective study would be ideal to confirm the findings, the authors suggest that healthcare professionals should seriously consider epilepsy, alongside hypoglycaemia, in the differential diagnosis of seizure-related disorders in people with T1D.

Dafoulas GE, Toulis KA, Mccorry D et al (2017) Type 1 diabetes mellitus and risk of incident epilepsy: a population-based, open-cohort study. *Diabetologia* **60**: 258–61

Diabetes Care

Liraglutide added to insulin in T1D

Readability	✓✓✓
Applicability to practice	✓✓✓
WOW! Factor	✓✓✓

1 This 52-week, double-blind, phase III, randomised controlled trial was conducted to assess the effects of adding liraglutide to insulin therapy in a treat-to-target approach in people with T1D.

2 The cohort had broad selection criteria, designed to reflect the general T1D population at large. In total, 1398 participants were randomised to receive liraglutide 1.8, 1.2 or 0.6 mg, or the same volumes of placebo.

3 HbA_{1c} fell quickly in all four groups in the first 8 weeks but subsequently increased, leaving small but significant reductions in the liraglutide 1.8 mg and 1.2 mg groups compared with placebo (estimated treatment difference, 2.2 mmol/mol and 1.6 mmol/mol [0.20% and 0.15%], respectively).

4 All doses of liraglutide significantly reduced weight in a dose-dependent manner, with losses of 4.0, 2.7 and 1.3 kg, respectively, compared to an increase of 0.9 kg with placebo.

5 In addition to the expected gastrointestinal adverse events, the rate of symptomatic hypoglycaemia was higher with the three liraglutide doses than placebo, at 16.5, 16.1, 15.7 and 12.3 events per person-year of exposure (PYE), respectively.

6 The rate of hyperglycaemia with ketones was also higher with liraglutide, at 0.28, 0.15 and 0.17 vs 0.12 events per PYE.

7 While the effects on weight loss may be appealing in certain individuals, generally the small effect on HbA_{1c} and the increased rates of hypo- and hyperglycaemia may limit the clinical use of liraglutide in people with T1D.

Mathieu C, Zinman B, Hemmingsson JU et al (2016) Efficacy and safety of liraglutide added to insulin treatment in type 1 diabetes: the ADJUNCT ONE treat-to-target randomized trial. *Diabetes Care* **39**: 1702–10

Diabetes Res Clin Pract

The relationship between severe fatigue and T1D

Readability	✓✓
Applicability to practice	✓✓✓✓
WOW! Factor	✓✓

1 Cross-sectional studies have often shown a higher rate of severe fatigue in people with T1D compared with the general population; however, there have been few prospective studies and it is unclear whether this is a persistent or short-lived symptom.

2 Therefore, this prospective study was conducted to explore the natural course of severe fatigue, and to determine the factors associated with it, in people with T1D.

3 A total of 214 adults with T1D (mean duration, 33 years) filled in questionnaires on fatigue and related factors. After 43 months, 194 returned to fill in the questionnaires again.

4 Severe fatigue was present in 40% of participants at baseline and in 42% at follow-up. Of those with severe fatigue at baseline, 75% still had it at follow-up.

5 Baseline factors associated with severe fatigue at follow-up included depressive symptoms, more pain, sleep disturbances, lower self-efficacy concerning fatigue, less confidence in diabetes self-care, more diabetes complications and greater fatigue severity at baseline.

6 The authors conclude that severe fatigue is not only common in people with T1D but also persistent over time.

7 Almost 40% of the predicted variance was explained by cognitive–behavioural factors such as such as sleep disturbance and physical inactivity. Therefore, addressing these factors may be effective in people with T1D who have severe fatigue.

Menting J, Nikolaus S, van der Veld WM et al (2016) Severe fatigue in type 1 diabetes: exploring its course, predictors and relationship with HbA_{1c} in a prospective study. *Diabetes Res Clin Pract* **121**: 127–34

> ***"The authors suggest that healthcare professionals should seriously consider epilepsy, alongside hypoglycaemia, in the differential diagnosis of seizure-related disorders in people with T1D."***