Technology

Back to basics for basal rates?

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When insulin pump therapy was first introduced it offered the potential to vary basal insulin delivery in a way that could not be achieved with conventional subcutaneous injection. Now insulin pumps offer at least 24 basal rates over a 24-hour period, and some twice this number. Furthermore, all offer the pump user the potential to store several different basal rate profiles. Is the ability to vary basal rates through the day the key to optimising outcomes for insulin pump therapy, or is it perhaps the reliability of absorption of the much smaller insulin depot that is more important to the efficacy of pump therapy?

Two recent publications (summarised alongside) address different aspects of pump basal insulin delivery. Chow and colleagues reviewed insulin pump data in patients with either type 1 or type 2 diabetes who had been on pump therapy for over 3 months and had an HbA_{1c} ≤58 mmol/mol (7.5%). Their aim was to determine which method of determining a starting basal rate best approximated the stable basal rate achieved once pump therapy had been optimised. They concluded that the safest starting basal rate for those with type 1 diabetes was one calculated on the basis of the existing total daily dose of insulin, giving 75% of this dose as the pump total daily dose and 50% of this as the basal rate. Whist this was no better than a weight-based method (using 0.5 unit/kg/day) or an empirical 0.8 unit/hour, it was more likely to underestimate the final basal rate and therefore less likely to put the user at increased risk of hypoglycaemia. The authors did formulate an algorithm based on weight and total daily basal insulin dose pre-pump, which was significantly better at predicting the final basal rate, but not to the extent that we should be advocating a move away from the commonly used method for determining starting basal rates.

Laimer and colleagues report an observational study of data from 5545 adults with type 1 diabetes entered into a German–Austrian database between 1995 and 2014. The average age of the cohort was just over 33 years and the duration of diabetes over 17 years. The average total daily insulin dose was surprisingly high at 71.77 units. The authors devised a basal rate variability index and assessed the correlation between the basal rate variability and complications. By considering the hourly variation of the basal rate from the lowest hourly basal rate, the authors found that the mean variability in basal rate was 27.8±12.9%. After logistical regression analysis, greater basal rate variability was positively associated with an increased risk of severe hypoglycaemia and diabetic ketoacidosis. It is possible, as the authors discuss, that the basal rate variability reflects the difficulty of managing their diabetes for these particular pump users, and that basal rate changes have been made in response to episodes of hypoglycaemia or ketoacidosis, rather than predisposing the user to these acute complications. However, it seems reasonable to conclude that minimising unnecessary basal rate variability should be a consideration when optimising insulin pump therapy regimens.

Finally, though, a note of caution against over-simplification of basal rates. Ruan and colleagues (summarised alongside) report data from 1564 total days – and 1918 nights – of free-living closed-loop insulin delivery in 32 adults with type 1 diabetes. They found that the coefficient of variation of overnight insulin delivery was 31%, compared to 17% for total daily insulin requirements. The authors discuss the variety of factors that may contribute to this overnight variability, which include evening meal composition, activity levels the previous day and prior hypoglycaemia. Thus, we can conclude that whilst the standard basal insulin rate profile may need to be kept simple, pump users need to be cognisant of factors that alter their overnight insulin requirements and be prepared to make temporary basal rate adjustments to mitigate the effect of these factors. ■

BMJ Open Diabetes

Determining starting basal rates for CSII

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

1 This study aimed to evaluate the accuracy and risk of hypoglycaemia of currently available methods of estimating starting basal insulin rates, and to compare them with an empirically derived standard basal rate and a newly developed regression formula.

2 Retrospective data on 61 adults with T1D and 34 adults with T2D on continuous subcutaneous insulin infusion (CSII) therapy were collected. To be included, participants must have used CSII therapy for >3 months and those with T1D needed an HbA_{1c} ≤58 mmol/mol (7.5%).

3 Participant data were analysed for correlations between initial parameters and final basal rates. Starting basal rates for these individuals were then retrospectively calculated according to the weight-based method (WB-M), the total daily dose (TDD) of insulin method (TDD-M), a flat empiric value and a new formula developed by regression analysis.

4 Participant weight and TDD of long-acting insulin correlated with final titrated basal rates for T1D; only TDD correlated for T2D.

5 For T1D, the regression formula and the TDD-M were safer than the WB-M and empirical estimates. The regression formula was the most accurate in estimating T2D basal rates, but the TDD-M estimate was slightly safer.

6 The investigators conclude that the regression formula has potential use for CSII initiation in people with T2D.

Chow N, Shearer D, Tildesley HG et al (2016) Determining starting basal rates of insulin infusion for insulin pump users: a comparison between methods. *BMJ Open Diabetes Res Care* **4**: e000145

PLoS One

T1D complications: Basal rate variability

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

1 This study aimed to identify the associations between basal rate (BR) variability in continuous subcutaneous insulin infusion (CSII) therapy and acute or chronic complications in adult T1D.

2 Data from 5545 adults (3118 women, 2374 men) from the German–Austrian DPV registry were analysed. The registry documents diabetes care and clinical outcomes.

3 Acute (severe hypoglycaemia, hypoglycaemic coma and diabetic ketoacidosis [DKA]) and chronic (diabetic retinopathy, micro- and macroalbuminuria) complications were recorded 6 months before and after the most recently documented BR. The "variability index" (VI), which describes the excursions of the BR intervals from the median BR, was calculated as variation of BR intervals in percent.

4 The VI correlated positively with severe hypoglycaemia, hypoglycaemic coma and microalbuminuria. Furthermore, higher VI was associated with higher frequency of DKA. After logistic regression analysis, VI was found to be significantly correlated with severe hypoglycaemia and DKA.

5 The study illustrates an association between higher individual variability in daily basal rates and an increased frequency of acute complications in adults with T1D using CSII therapy. Further studies are required to establish whether this association is causal, however.

6 Such higher variability could identify individuals with T1D who are more difficult to treat regarding glycaemic goals.

Laimer M, Melmer A, Mader JK et al (2016) Variability of basal rate profiles in insulin pump therapy and association with complications in type 1 diabetes mellitus. *PLoS One* **11**: e0150604

Diabetes Care

Closed-loop insulin delivery: Variability of requirements

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

1 The authors of this article set out to quantify the variability of insulin requirements during closed-loop insulin delivery.

2 The multicentre, randomised crossover study involved 32 adults with T1D (17 female, 15 male). Participants underwent 4–6 weeks of insulin pump therapy optimisation using real-time continuous glucose monitoring before randomisation.

3 Participants then applied hybrid day-and-night closed-loop delivery in free-living home settings for 12 weeks.

4 For each individual, a coefficient of variation (COV) of overnight (2300–0700), daytime (0700–2300) and total daily (midnight–midnight) insulin requirements over 12 weeks was calculated.

5 Overnight insulin requirements were 14 percentage points higher than the COV of total daily requirements (31% vs 17%; $P<0.001$), and 9 percentage points higher than daytime requirements (31% vs 22%; $P<0.001$).

6 In males, the COV of overnight insulin requirements was 3.7% higher than in females ($P=0.03$). This result was unexpected and warrants further investigation.

7 A number of potential factors contributing to overnight variability are suggested, including evening meal composition and the prolonged effect of daytime exercise. The results may indicate why some people with T1D experience variability in morning glycaemia.

Ruan Y, Thabit H, Leelarathna L et al (2016) Variability of insulin requirements over 12 weeks of closed-loop insulin delivery in adults with type 1 diabetes. *Diabetes Care* **39**: 830–2

Diabet Med

Insulin pump use in labour and delivery

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

1 Although an increasing number of women with T1D are using continuous subcutaneous insulin infusion (CSII) therapy during pregnancy, little is known about the effects of continuing its use during labour and delivery.

2 The aim of this retrospective observational study was to assess the safety and efficacy of maintaining CSII therapy during this period. A cohort of 161 consecutive pregnancies delivered between 2000 and 2010 at a single Canadian hospital was studied.

3 Blood glucose levels during labour and delivery, and time spent in/out of target glycaemic range (4–6 mmol/L) were compared along with neonatal outcomes in three groups: women who remained on CSII during labour ($n=31$); women on CSII who switched to intravenous (IV) insulin infusion during labour ($n=25$); and women on multiple daily injections of insulin who switched to IV infusion during labour ($n=105$).

4 Analysis found no significant differences in glucose values during labour and delivery between the three groups, and no significant difference in time spent in hypoglycaemia. However, women who remained on CSII had significantly better glycaemic control compared with women who changed from CSII to IV infusion.

5 No adverse events occurred in the CSII group. There were no significant differences in neonatal outcomes between the three groups.

6 The findings suggest that allowing women to continue using CSII therapy in labour and delivery should be standard practice.

Drever E, Tomlinson G, Bai AD, Feig DS (2016) Insulin pump use compared with intravenous insulin during labour and delivery: the INSPIRED observational cohort study. *Diabet Med* **33**: 1253–9

"The results of this study may indicate why some people with type 1 diabetes experience variability in morning glycaemia."