

Management of type 1 diabetes



Treating hypothyroidism in people with type 1 diabetes

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There are some areas of the diagnosis and treatment of thyroid disease that remain highly controversial. Looking at some of the contributions on the web, one would get the impression that there is a conspiracy amongst health professionals to deny people the available treatments. The management of hypothyroidism is one of these difficult areas.

Current guidance would suggest that maintaining a thyroid-stimulating hormone (TSH) concentration within the normal range (usually defined at around 0.4–4.5 mU/L) is associated with normal health and normal life expectancy. However, there are some situations in which it is accepted that an increased levothyroxine dose may be required. Most women with hypothyroidism who become pregnant will require an increased dose of levothyroxine. Suboptimal thyroid function in this situation is associated with an increased risk of miscarriage and premature delivery. Some guidelines are now suggesting that thyroid hormone replacement therapy should be adjusted to achieve TSH levels of 0.2–2.5 mU/L in pregnancy (Taylor et al, 2014).

Thyroid function may also contribute to the risk of diabetes-related complications. A number of studies have suggested an association between raised TSH levels and both microvascular and macrovascular complications in type 2 diabetes (Yang et al, 2010). It must be acknowledged, however, that there is less evidence that increasing thyroid hormone replacement and lowering TSH

levels will reduce the risk. At present, there are no recommendations that individuals with type 2 diabetes should maintain a lower TSH concentration than the rest of the population.

Adding to this controversy is the recent article by Rodacki and colleagues (summarised alongside). In this multicentre study from Brazil, the authors examined the records of a large population of people with established type 1 diabetes. Approximately 1200 people with type 1 diabetes and no previous diagnosis of thyroid disease were invited to participate. Of these, 822 were found to have TSH levels of 0.5–2.4 mU/L, 304 had levels of 2.5–4.4 mU/L and 72 had levels of ≥ 4.5 mU/L. Participants with TSH levels in the lowest range were found to have a lower risk of developing retinopathy and renal dysfunction independently of glycaemic control or duration of diabetes.

Although this study supports similar findings in other patient groups, it is the first to suggest a link between TSH levels and diabetes-related complications in type 1 diabetes. This does not determine that we should immediately change practice, but clinicians should perhaps be careful in explaining to patients what we mean by a normal range when discussing thyroid function. ■

Taylor PN, Minassian C, Rehman A et al (2014) TSH levels and risk of miscarriage in women on long-term levothyroxine: a community-based study. *J Clin Endocrinol Metab* **99**: 3895–902

Yang JK, Liu W, Shi J, Li YB (2010) An association between subclinical hypothyroidism and sight-threatening diabetic retinopathy in type 2 diabetic patients. *Diabetes Care* **33**: 1018–20

Diabet Med

TSH levels and risk of diabetes-related complications

Readability ////

Applicability to practice ///

WOW! Factor ///

1 This observational, cross-sectional, multicentre study was performed to determine whether thyroid-stimulating hormone (TSH) levels of < 4.5 mU/L were associated with diabetes-related complications in people with T1D.

2 A total of 1205 people with T1D of ≥ 5 years' duration were categorised according to TSH levels of 0.5–2.4 mU/L ($n=822$), 2.5–4.4 mU/L ($n=304$) or ≥ 4.5 mU/L ($n=72$). Those with TSH levels below 0.5 mU/L were excluded, as these levels can indicate hyperthyroidism, which has its own effects on diabetes complications.

3 The groups were similar in terms of age, diabetes duration, gender and glycaemic variables such as HbA_{1c}.

4 Diabetic retinopathy (DR) occurred in 16.8% of participants, nephropathy occurred in 19.2% and a glomerular filtration rate (GFR) of < 60 mL/min/1.73 m² occurred in 6.9%.

5 Compared with those in the lowest TSH range, there was a higher risk of DR and low GFR not only in participants with a TSH level of ≥ 4.5 mU/L (odds ratios [ORs], 1.9 and 2.3, respectively) but also in those with a TSH level of 2.5–4.4 mU/L (ORs, 1.5 and 2.3).

6 This study has some limitations, including the cross-sectional design and, in particular, the fact that most participants had HbA_{1c} levels of ≥ 53 mmol/mol ($\geq 7\%$). The association between TSH levels and diabetes complications was not observed in those with lower HbA_{1c} levels, but this may have been because that group was too small to detect any differences.

Rodacki M, Zajdenverg L, Dantas JR et al (2014) Should thyroid-stimulating hormone goals be reviewed in patients with type 1 diabetes mellitus? Results from The Brazilian Type 1 Diabetes Study Group. *Diabet Med* **31**: 1665–72

“Closed-loop, unsupervised, day-and-night insulin delivery appeared to achieve superior glycaemic control to sensor-augmented pump therapy, the current best treatment, although the authors admit that this was a small study with a short follow-up.”

Diabetes Care

Closed-loop insulin delivery at home in people with T1D

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

- The authors evaluated a closed-loop insulin delivery system through the day and night over a 1-week period at home in 17 adults with T1D.
- In a prospective, open-label, crossover study, the closed-loop system was compared with sensor-augmented pump (SAP) therapy. Participants began both treatment periods with a 1-day stay in a clinical research facility, and then spent 1 week under free-living conditions at home. There was a 1–4-week washout period between the two treatment periods.
- At home, the primary outcome, percentage of time spent in the target blood glucose range of 3.9–10.0 mmol/L, was achieved in 74.5% of people in the closed-loop group and 61.8% of those in the SAP group ($P=0.005$). The closed-loop system resulted in a lower mean glucose level and less time spent above the target level, without increasing the time spent in hypoglycaemia.
- The closed-loop system achieved superior glycaemic control in both the day and the night, and also during the clinic stay, compared with SAP.
- Severe hypoglycaemia occurred once in the washout period and once in the closed-loop arm; the latter occurred when sensor data were unavailable and the system reverted to the user’s default pump settings.
- Closed-loop, unsupervised, day-and-night insulin delivery appeared to achieve superior glycaemic control to SAP, the current best therapy, although the authors admit that this was a small study with a short follow-up.

Leelarathna L, Dellweg S, Mader JK et al (2014) Day and night home closed-loop insulin delivery in adults with type 1 diabetes: three-center randomized crossover study. *Diabetes Care* **37**: 1931–7

Diabetes Care

Depression in T1D

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

- Most studies of depression in diabetes either include only people with T2D or combine data from people with T1D or T2D; therefore, these authors sought to evaluate the frequency of depression in people with T1D only, and to determine the association between depression and diabetes-related clinical characteristics.
- A total of 6172 participants in the American T1DX (Type 1 Diabetes Exchange) registry who completed the eight-item Patient Health Questionnaire (PHQ-8) at 1 year’s follow-up were evaluated.
- A cut-off score of ≥ 10 points out of a possible 24 on the PHQ-8 was used to define probable major depression. Use of a higher cut-off to account for symptoms that could reflect hypoglycaemia rather than depression yielded similar results.
- Of the 6172 participants, 638 (10.3%) met the criterion for depression. Multivariate analysis showed that female gender, non-white ethnicity, lower household income, lower education level, unemployment and having one or more diabetes-related complications were associated with depression.
- People with depression had a higher mean HbA_{1c}, were more likely to miss injections and exercise less, and were more likely to have episodes of diabetic ketoacidosis and severe hypoglycaemia.
- The frequency of probable major depression of 10.3% in this cohort contrasts to a prevalence of 4.1% in the general population. The authors state that better identification and treatment of depression is needed in people with T1D, and that the relationship between depression and poor metabolic control should be evaluated.

Trief PM, Xing D, Foster NC et al (2014) Depression in adults in the T1D Exchange Clinic registry. *Diabetes Care* **37**: 1563–72

Diabetes Obes Metab

Direct comparison of two CGM systems

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

- The authors compared the two most widely used continuous glucose monitoring (CGM) systems – the Dexcom G4[®] Platinum (Dexcom, San Diego, CA, USA) and the Medtronic Paradigm[®] Veo Enlite (Medtronic, Northridge, CA, USA) – in terms of accuracy during routine daily living.
- The participants ($n=24$; mean age, 40 years) had T1D with a mean duration of 23.5 years. They wore both sensors simultaneously for 6 days of home use, including one 6-hour visit to a clinical research centre halfway through the study.
- During home use, the CGM measurements were compared with capillary finger stick measurements, and during the clinic visit they were compared with venous measurements. The primary outcome was the mean absolute relative difference (MARD) between the CGM and reference readings.
- With home readings, the G4 system was more accurate than the Enlite system (MARD, $12.2 \pm 12.0\%$ vs $19.9 \pm 20.5\%$; $P < 0.001$). It was also more accurate in the clinic.
- Both systems were less accurate during hypoglycaemia than during euglycaemia, but the G4 was more accurate than the Enlite at this time, both at home and in the clinic.
- The difference in accuracy did not translate into differences in clinical outcomes; however, the study was not powered to detect the latter, and the follow-up was very short. The authors note that an updated version of the Enlite has since been released but was not evaluated here.

Kropff J, Bruttomesso D, Doll W et al (2014) Accuracy of two continuous glucose monitoring systems: a head-to-head comparison under clinical research centre and daily life conditions. *Diabetes Obes Metab* **11** Aug [Epub ahead of print]