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DIABETIC Medicine

LETTER

Implementation of dapagliflozin as adjunctive therapy in type 1 diabetes: A single centre real-world experience

In 2019, the National Institute for Health and Care Excellence (NICE) approved sodium-glucose transport protein 2 inhibitor (SGLT2i) dapagliflozin 5 mg as an adjuvant to insulin therapy for adults with type 1 diabetes (T1D), a body mass index (BMI) of ≥27 kg/m^2 where insulin therapy fails to provide optimal glycaemic control.[1] NICE recommends its use in those with an insulin dose ≥0.5 units/kg who have completed structured education including information about ketoacidosis. We aimed to evaluate real-world clinical outcomes following initiation of dapagliflozin adjunctive therapy in a single tertiary diabetes centre in England.

We conducted a retrospective analysis reviewing the electronic patient records (EPRs) of adults (≥18 years) with T1D prescribed adjunctive dapagliflozin at a single diabetes clinic between August 2019 and June 2021. This period included three national Covid-19 lockdowns (23 March to 23 June 2020, 5 November to 2 December 2020 and 6 January to 8 March 2021) when there was increased attention on ketone monitoring and ketosis in those with T1D. The audit received local approval. Demographic and biomedical (height, weight, blood pressure, glycated haemoglobin [HbA_{1c}], creatinine and total daily insulin dose) data were collected from electronic health records and diabetes data management platforms. Episodes of DKA and severe hypoglycaemia or other side effects occurring during dapagliflozin therapy were recorded, and whether dapagliflozin was discontinued. As this was a retrospective analysis, biomedical values were not systematically collected at pre-specified time-points. If multiple data points for a single outcome were available the value closest to 6 months was used. Data from within the first 3 months of starting dapagliflozin were not included.

Glycaemic and other biomedical data before and after initiation of dapagliflozin were compared using a paired samples *t* test for normally distributed data and Wilcoxon matched-pairs signed rank test for non-normally distributed data; statistical analyses were performed using SPSS, version 27 (IBM Software, Hursley, UK). Data are reported as mean ± SD or median (IQR) and *p*-values of <0.05 were considered statistically significant.

Eighteen adults with T1D were prescribed adjunctive dapagliflozin between August 2019 and June 2021 (mean age 40.6 ± 12.7 years, diabetes duration 24.0 ± 9.4 years, baseline HbA_{1c} 74 ± 11 mmol/mol (8.9 ± 1.0%), BMI 35 ± 5 kg/m^2, insulin dose 0.9 ± 0.3 units/kg) and 61% were using insulin pump therapy. Ninety-four per cent (17/18) met NICE criteria for initiating dapagliflozin. The mean duration of adjunctive dapagliflozin was 12.7 months (range 1.0 to 23.4 months).

In those using dapagliflozin for ≥6 months (n = 14), dapagliflozin significantly improved mean HbA_{1c} from 76 ± 12 mmol/mol to 64 ± 12 mmol/mol (9.1 ± 1.1% to 8.1 ± 1.1%), a mean difference of 11 mmol/mol (95% CI 7 to 16 mmol/mol [1.0%]; 95% CI 0.6 to 1.4%; $p < 0.001$)

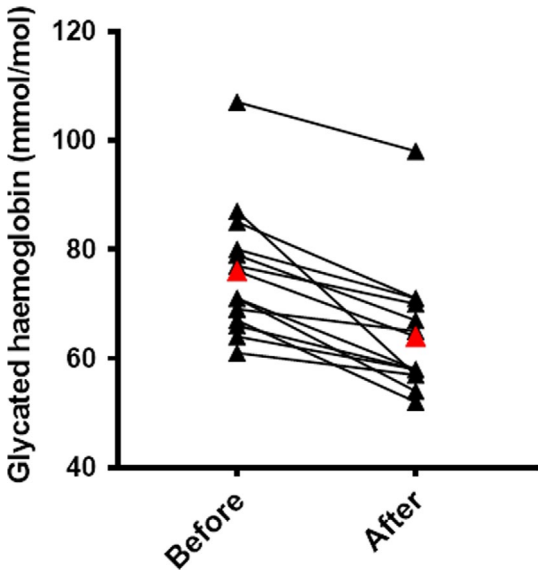

FIGURE 1 Change in glycated haemoglobin (HbA_{1c}) following initiation of adjunctive dapagliflozin in adults with type 1 diabetes. Black triangles represent individual people and the red triangles indicate the cohort mean

(Figure 1). Everyone who started dapagliflozin had ≥0.3 mmol/mol (0.3%) reduction in HbA_{1c} at 6 months supporting continuation of therapy. Although there was a numerical reduction in bodyweight (98.3 ± 14.2 kg before to 95.5 ± 9.6 kg after; mean difference −2.8 kg 95% CI −1.3 to 6.8 kg; $p = 0.15$) and BMI (34.3 ± 2.9 before to 34.0 ± 2.9 kg/m^2 after; $p = 0.51$), this was not statistically significant, although the number of people with data available for paired comparisons was relatively small ($n = 9$ for bodyweight and $n = 8$ for BMI). Baseline bodyweight and percentage change in bodyweight at 6 months were correlated with greater reductions in bodyweight in those with highest baseline bodyweight ($p = 0.002$). Initiation of dapagliflozin was associated with a significant reduction in the median total daily insulin dose ($n = 13$) from 82.5 (67.6, 110.0) units/day to 72.3 (62.0, 84.0) units/day ($p = 0.023$). There was no effect of dapagliflozin on blood pressure in our cohort ($n = 6$). There was a small but significant increase in mean creatinine ($n = 11$) following introduction of dapagliflozin from 58.5 ± 18.3 to 64.2 ± 20.7 μmol/L ($p = 0.022$).

There were no reported episodes of ketoacidosis or severe hypoglycaemia. One person (6%) developed a urogenital infection requiring antibiotics. One person (6%) prescribed dapagliflozin discontinued treatment 2 weeks after starting as they preferred to continue with previously prescribed metformin.

In this retrospective analysis of adults with T1D prescribed adjunctive dapagliflozin following NICE TA597, we report real-world data from a single tertiary diabetes clinic over a period which included Covid-19 related lockdowns. Initiation of dapagliflozin was associated with a clinically and statistically significant reduction in HbA_{1c} and total daily insulin dose. Our real-world glycaemic data compare favourably with the DEPICT trial data with a greater reduction in HbA_{1c} (1.0% compared with 0.4%) although baseline HbA_{1c} was higher in our cohort.[2,3] Although we observed a clinically relevant weight reduction in our cohort (−2.8 kg), this was not statistically significant and numbers for comparison were small. Importantly there were no reported cases of ketoacidosis or severe hypoglycaemia and tolerability was high with one urinary tract infection and one discontinuation during the follow-up period.

To our knowledge this is the only real-world evaluation of dapagliflozin as an adjuvant to insulin therapy for adults with T1D in England following NICE TA597. Our audit was limited by a relatively small, single centre dataset, in part due to remote consultations during Covid-19, and the retrospective nature of the analysis.

In a real-world setting of a specialised care centre, with support from trained type 1 diabetes educators, adjunctive dapagliflozin was associated with significant glycaemic benefits and clinically relevant weight loss without significant safety issues, supporting increased use of this therapy in routine clinical practice to improve outcomes for selected adults with T1D and sub-optimal glycaemic control. It is therefore disappointing that the licence for adjunctive dapagliflozin for people with T1D has recently been withdrawn for reasons unrelated to safety or efficacy, denying people with T1D access to a treatment with important glycaemic and weight-related benefits.[4]

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