EASD European Association for the Study of Diabetes

825

Tirzepatide as an adjunctive therapy in type 1 diabetes: real-world experience from a large UK centre

S.A. Berry[1,2], E. McNally[2], I. Goodman[1], J. Elliott[1,2], A. Iqbal[1,2];

[1]Division of Clinical Medicine, University of Sheffield, Sheffield, UK,[2]Sheffield Teaching Hospitals NHS Foundation Trust, Sheffield, UK.

Background and aims: Tirzepatide is increasingly used for the management of type 2 diabetes and for weight reduction. Obesity is prevalent in people with type 1 diabetes (T1D), exacerbating insulin resistance, thereby augmenting cardiometabolic risk. We aimed to assess the safety, tolerability and efficacy of tirzepatide when used in people with T1D and obesity. We hypothesised that tirzepatide would improve glycaemia, promote weight loss and reduce insulin requirements.

Materials and methods: A longitudinal, retrospective study was conducted, including all people with T1D started on tirzepatide at a large tertiary centre. Case notes were reviewed for current dose, side effects, clinic weights, and hospital attendances. Glycaemic metrics were obtained from the respective CGM cloud applications. Where data were missing, paired data were excluded from analysis. Two-tailed paired t-tests were conducted to compare variables measured before and after six months of tirzepatide treatment. Data are presented as median (IQR) and mean (95%CI). Pearson's rank test was used to analyse for correlations.

Results: Fifty-seven participants were identified (66.7% female). Prior to initiating tirzepatide, the median age was 39 years (26-52), weight 101.6 kg (92.5-123.8), body mass index 36.3 kg/m^2 (33.2-40.6) and HbA1c 60 mmol/mol (52-67.) At 6 months, the dose of tirzepatide was 2.5mg once weekly in 9 participants (18%), 5mg in 37 (74%), 7.5mg in two, and there was one participant each on 10mg and 15mg. Mean weight significantly reduced by 9.8 kg (9.3%) after 6 months of tirzepatide use (7.7-11.9, p<0.001, n=42.) Mean total daily insulin dose decreased by 25.2% from 74.4 units to 57.3 units (8.2-26.1, p<0.001, n=27), with a mean reduction in total daily bolus dose of 11 units (4.5-17.5, p=0.002, n=26) and basal dose of 10.8 units (4.5-17.1, p=0.001, n=39). Mean HbA1c decreased by 3.7 mmol/mol (n=33, 1.0-6.4, p=0.008). Glycaemic metrics from CGM are presented in the table below. There was no significant correlation between percentage weight change and increase in time in range (r -0.218, p=0.239, n=31) nor improvement in the glucose management indicator (GMI) (r 0.099, p=0.597). Side effects were reported by 21 participants (36.8%), with nausea or vomiting the most common (26.3%) and abdominal pain the second most common (14.0%), but 50 participants (87.7%) continued on tirzepatide at 6 months. There were three unplanned admissions related to tirzepatide (median one day length of stay) - all were due to abdominal pain, one of which was found to be caused by gallstones. There were no cases of pancreatitis.

Conclusion: In real-world use in people with T1D, tirzepatide was safe and generally well tolerated, with significant clinical benefits including weight loss, reduced insulin requirements, and improvement of glycaemic metrics, without increasing hypoglycaemia. Definitive data from RCTs in T1D are required to confirm these findings.

Table. Continuous glucose monitor glycaemic metrics at baseline and at 6 months (n=35). Data presented as means. CI – Confidence Interval, TBR – Time Below Range, TIR – Time in Range, TITR – Time in Tight Range, TAR – Time Above Range, SG – Sensor Glucose, GMI – Glucose Management Indicator, CV – Coefficient of Variation, SD – Standard Deviation. *p<0.05, **p<0.01

	Baseline	6 months	Absolute Difference	95% CI	p value
% TBR <3.0 mmol/L	0.2	0.1	-0.1	-0.3, 0.1	0.373
% TBR 3-3.8 mmol/L	1.1	1.1	0	-0.4, 0.4	0.891
% TIR (3.9-10 mmol/L)	55.1	62.3	+7.3	1.1, 13.4	**0.022***
% TITR (3.9-7.8 mmol/L)	31.9	38.2	+6.3	2.2, 10.4	**0.004****
% TAR (>10 mmol/L)	42.8	36.3	-6.6	-12.9, -0.3	**0.042***
Mean SG (mmol/L)	10.3	9.6	-0.8	-1.4, -0.2	**0.011***
GMI (mmol/mol)	60.9	57.6	-3.3	-6.4, -0.2	**0.041***
CV (%)	35.6	33.3	-2.3	-4.3, -0.4	**0.019***
SD	3.7	3.2	-0.5	-0.7, -0.2	**0.002****

Clinical Trial Registration Number: N/A

Supported by: none

Disclosure: **S.A. Berry:** None.