Audit of the outcomes of adding an SGLT2 inhibitor to insulin in suboptimally controlled type 2 diabetic patients

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Introduction

Type 2 diabetes mellitus is a prevalent, progressive disease in need of new therapeutic agents to continue to advance disease management.

Sodium-glucose cotransporter 2 (SGLT2) inhibitors are the latest therapeutic class of oral agents available to physicians and patients. Besides the significant reduction in blood glucose, SGLT2 inhibitors have the additional advantage of promoting weight loss when combined with other oral agents or insulin. All three SGLT2 inhibitors available on the market (Dapagliflozin, Canagliflozin, Empagliflozin) are approved by NICE and have got licences for use in combination with insulin *(https://www.nice.org.uk/guidance).*

Objectives

To review the outcomes of adding an SGLT2 inhibitor (dapagliflozin or canagliflozin) to insulin, in type 2 diabetic patients, in a secondary care setting. To assess which patients benefited most from the combination and identify baseline predictors of response.

Materials & Methods

Subjects deemed suitable by a consultant diabetologist (LC and SB), were commenced on dapagliflozin or canagliflozin if they were obese (BMI ≥30), suboptimally controlled (HbA1c ≥7.5%) and stable on insulin. The intention was to promote weight loss, spare the insulin usage and optimise diabetes control with further up-titration of insulin deemed counterproductive in view of continuing weight gain.

23 subjects were started on Dapagliflozin and 9 on Canagliflozin. Pre-existent medications were continued with the exeption of the DPP-4 inhibitors and GLP-1 agonists which were stopped when initiating the SGLT2 inhibitor.

Following initiation, patients were seen by the DSN-s at 5-6 and 12-14 weeks and by the consultant diabetologist at 24-28 weeks. Total daily insulin doses and insulin regimens remained unchanged at the initiation visit but could be adjusted in a discretionary manner at subsequent visits.

Results

We analysed 32 patients (21 male, 11 female), on the combination for at least 12 weeks, with full data at baseline and follow-up. Age at baseline (mean ± SD) was 56.3 ± 7.6 years and diabetes duration was 13.9 ± 7.4 years.

In three subjects, the response was deemed unsatisfactory and the SGLT2 inhibitor was discontinued at the follow-up visit (after 3.9, 4.8 and 6.4 months of treatment). Two other patients experienced side effects (recurrent thrush, recurrent urinary tract infections) and stopped the drug after 5.5 and 6.9 months of treatment respectively. All 5 patients who came off the SGLT2 inhibitor were on Dapagliflozin. Table 1 displays the main parameters at baseline and follow-up.

	Baseline	Last visit
n (male/ female)	32 (21/ 11)	32
Follow-up (months)	-	6.7 ± 3.4
Weight (kg)	113.4 ± 18.9	111.1 ± 17.7†
BMI (kg/m²)	38.9 ± 5.5	38.2 ± 4.9†
25th percentile	*35.2*	*34.9*
75th percentile	*41.9*	*41.1*
HbA1c (%)	9.6 ± 1.5	8.4 ± 1.5††
25th percentile	*8.6*	*7.3*
75th percentile	*10.6*	*8.9*
Daily insulin dose (U) (median)	140 ± 72 (128)	131 ± 65 (110)§
Insulin dose/kg (U/kg) (median)	1.24 ± 0.64 (1.04)	1.18 ± 0.59 (0.95)
Insulin injections/day, n (%)		
0	*0 (0)*	*0 (0)*
1	*5 (15.6)*	*4 (12.5)*
2	*13 (40.6)*	*14 (43.8)*
3	*8 (25.0)*	*8 (25.0)*
4 or 5	*6 (18.7)*	*6 (18.7)*
Metformin, n (%)	29 (91.0)	28(87.5)
Sulphonylurea, n (%)	3 (9.0)	2 (6.3)
DPP-4 inhibitors, n (%)	3 (9.0)	0 (0)
GLP-1 agonists, n (%)	2 (6.3)	0 (0)

Data given as means ± SD unless specified *†P<0.05, ††P<0.001: Paired-Samples T Test. §P<0.05: Wilcoxson test*

Table 1: Baseline and follow-up variables

Total daily insulin dose decreased by 9 ± 31 units (median 0U, maximum -96U, minimum +78U)

9 (28%) patients lost over 3% of body weight and 20 (62.5%) improved their HbA1c by over 1%. Only 6 (19%) subjects achieved both parameters. 9 (28%) patients actually gained weight.

Frequency of insulin injections remained unchanged.

A scatter plot of the change in HbA1c vs. %change in weight at follow up compared to baseline, is shown in Figure 1.

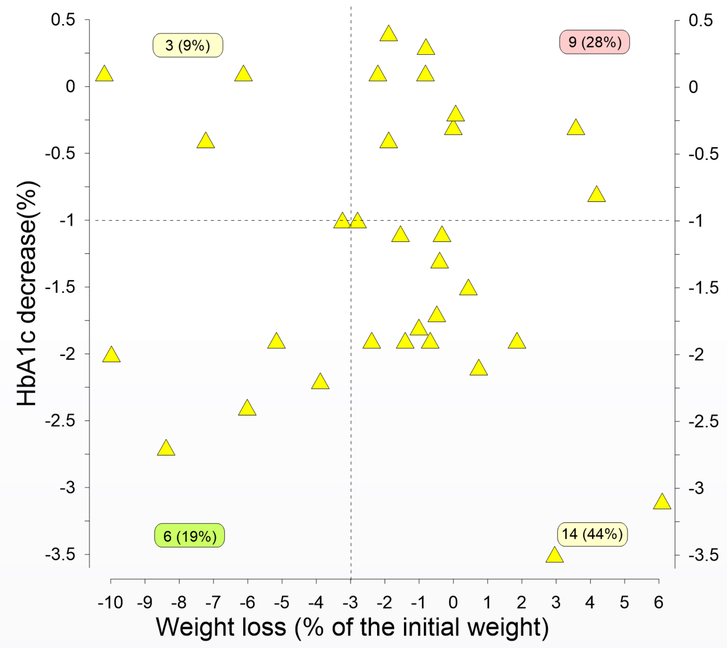

Figure 1: HbA1c and %weight change vs baseline

A higher baseline HbA1c predicted a larger decline in HbA1c but did not predict the change in weight or reduction in insulin dose. Baseline weight did not predict any parameters at follow-up.

Conclusions

Because of their insulin independent mechanism of action, the SGLT2 inhibitors should be an effective treatment choice at all stages of the disease and when used in combination with most other glucose lowering therapies. The combination with insulin in particular may offer some advantages compared with the combination of insulin and other oral agents because of the potential weight loss expected with the SGLT2 inhibitors.

We found that adding dapagliflozin or canagliflozin to insulin in our obese type 2 diabetic population led to significant improvements in HbA1c in the majority of patients with an associated weight loss of around 1.8%. However, around a third of our patients gained weight suggesting the response to the combination needs to be monitored and the drug discontinued early in unresponsive subjects.