The impact of empagliflozin dose on HbA1c and weight outcomes at 6 and 12 months: updated analysis from the ABCD empagliflozin audit programme

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Introduction

Following the launch of Association of British Clinical Diabetologists (ABCD) audit programmes for dapagliflozin and canagliflozin, the ABCD nationwide empagliflozin audit was launched in March 2017..

What we know so far

Previously, phase IIb trials demonstrated dose-dependent reductions in HbA1c[1]. In contrast, changes in weight were significant across all doses assessed but not dose-dependent. The aim of this analysis is to establish how exposure to the 25mg empagliflozin dose vs 10mg dose impacts HbA1c and weight outcomes in a real-world cohort of patients.

Methods

Datasets were extracted from the ABCD audit and included providing the had a minimum of baseline and relevant follow-up data for HbA1c and weight and stratified into groups by exposure to high-dose empagliflozin as follows:

- Group 1 - 10mg from commencement
- Group 2 - 25mg from commencement
- Group 3 - increased from 10mg to 25mg at 6-months

Changes from baseline were assessed using paired t-tests (within groups and across the entire population) and ANOVA with Bonferroni corrections (between groups) in Stata 16 SE.

Results

9,371 datasets were included (Group 1, n=5,765; Group 2, n=1,887; Group 3, n=1,719) with baseline characteristics as demonstrated in **table 1.**

At 6-months and 12-months HbA1c decreased by 11.1mmol/mol (P<0.001, 95% CI 10.8, 11.5) and 11.4mmol/mol (P<0.001, 95% CI 11.1, 11.8) respectively and weight by 3.6kg (P<0.001, 95% CI 3.4, 3.7) and 3.8kg (P<0.001, 95% CI 3.6, 3.9) respectively.

No significant difference was found between groups at 6-months for weight or HbA1c change. At 12-months, group 2 and 3 had greater HbA1c reductions versus group 1 (P=0.01 and P<0.001 respectively) but no difference between each other (P=0.51).

Results (cont.)

At 12 months there was no significant difference in the weight changes between group 1 and groups 2 or 3; group 3 lost more weight (4.4kg, 95% CI 4.1, 4.7) versus group 2 (3.4kg, 95% CI 3.1, 3.7) (P=0.02).

These results are shown below in **Figures 2 and 3.**

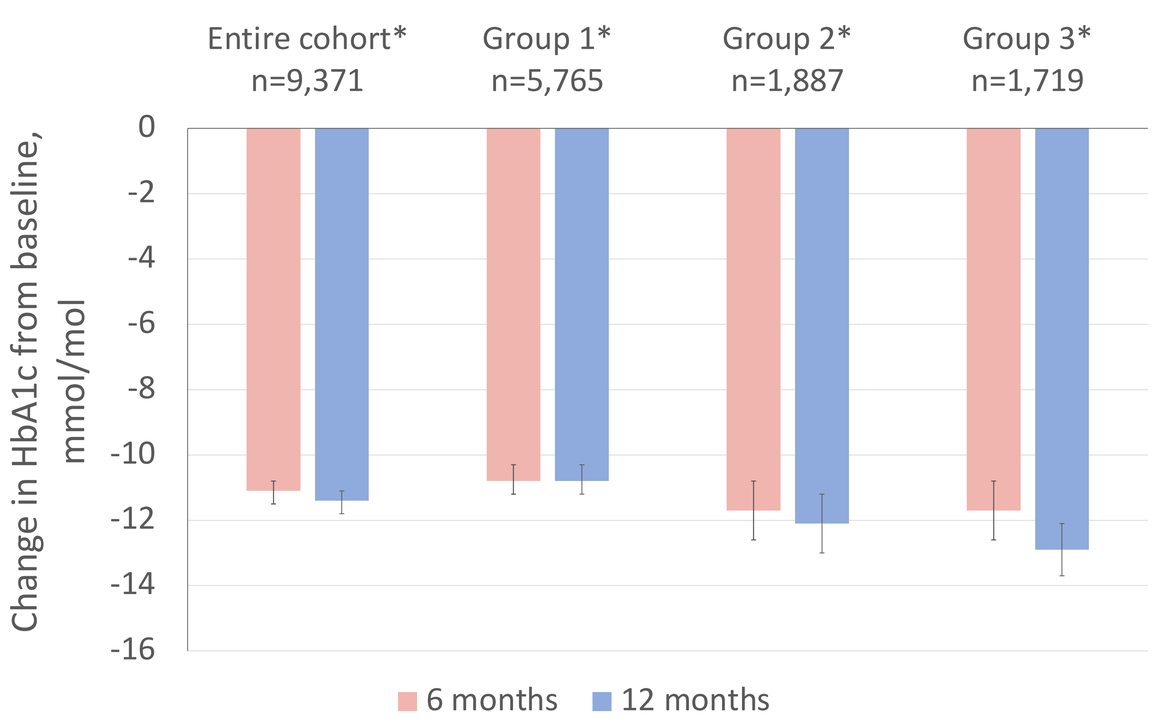

Figure 2. (above) Bar chart showing change in HbA1c (mmol/mol) from baseline at 6- and 12-months

Figure 3. (below) Bar chart showing change in weight (kg) from baseline at 6- and 12-months

***** Indicating statistical significance P<0.05

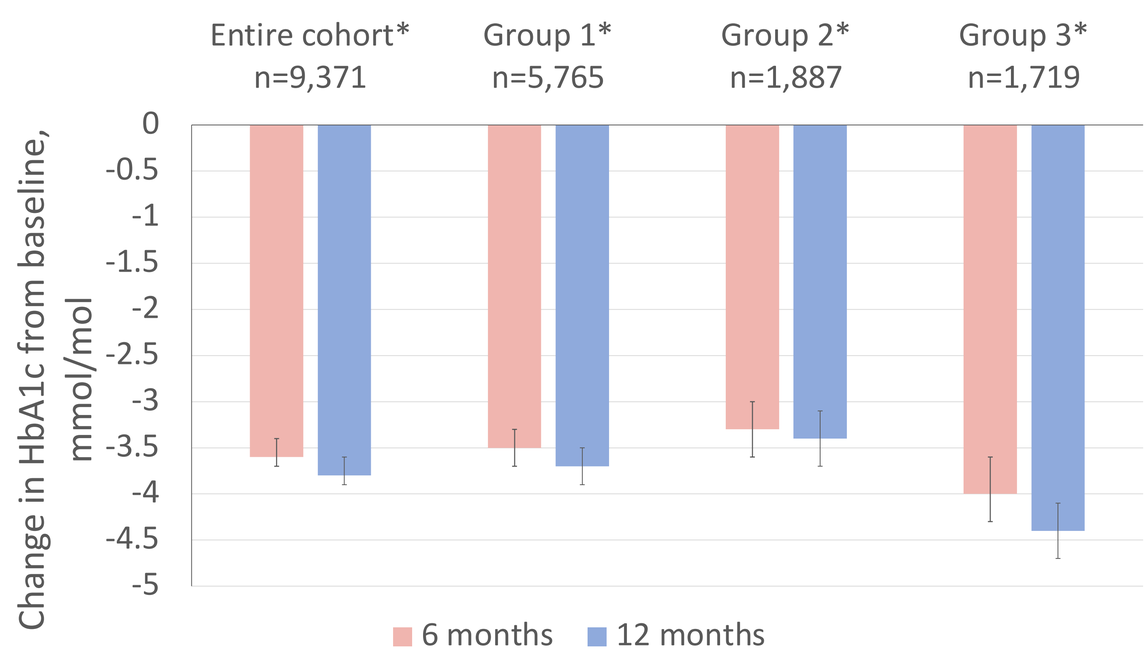

Table 1. Table showing the baseline characteristics of those included in this analysis of the ABCD empagliflozin audit

Characteristic	Entire cohort n=9,371	Group 1* n=5,765	Group 2* n=1,887	Group 3* n=1,719
Age, years ± SD	60.3 ± 10.3	60.5 ± 10.5	59.7 ± 10.0	60.1 ± 10.1
Male, %	61.5	61.6	62.5	60.3
Median diabetes duration, year (IQR)	8.3 (4.5-12.6)	8.3 (4.6-12.6)	8.5 (4.5-12.7)	8.2 (4.4-12.2)
Mean HbA1c, % ± SD	9.07 ± 1.54	9.00 ± 1.5	9.16 ± 1.62	9.21 ± 1.51
mmol/mol ± SD	75.7 ± 16.8	74.9 ± 16.6	76.5 ± 17.6	77.4 ± 16.6
Mean BMI, kg/m2 ± SD	33.7 ± 6.7	33.5 ± 6.7	33.9 ± 6.8	33.9 ± 6.8
Mean weight, kg ± SD	96.9 ± 22.1	96.5 ± 22.3	97.4 ± 21.9	97.5 ± 21.5
Mean serum creatinine, umol/L ± SD	73.1 ± 15.9	73.3 ± 15.9	73.3 ± 16.7	72.3 ± 15.2
Mean eGFR, H ± SD	82.1 ± 13.8	82.1 ± 15.1	81.9 ± 11.6	82.1 ± 11.7
Mean systolic BP, mmHg ± SD	128.2 ± 20.1	127.5 ± 20.6	130.7 ± 17.0	127.5 ± 21.1
Mean diastolic BP, mmHg ± SD	78.2 ± 9.1	78.0 ± 9.1	78.5 ± 9.1	78.4 ± 9.0
Insulin use, %	13.6	12.8	16.1	13.3
Thiazolidinediones (TZD) use, %	3.4	2.4	6.5	3.1
DPP4 inhibitor, %	18.8	19.7	18.4	16.5
Metformin use, %	82	81.3	85.2	80
Sulphonylurea use, %	30.8	30.5	31.7	31

Conclusion

HbA1c reductions appears to be greatest amongst taking higher doses of empagliflozin by 12-months, but no difference was noted between those commenced immediately on high dose and those titrated up by 6-months.

Weight reductions were greater in group 3 compared to those who were started immediately on high dose (group 2). Reasons for this are unclear and further work should explore how high dose empagliflozin impacts other important parameters.

References

1. Ferrannini, E., et al., *A Phase IIb, randomized, placebo-controlled study of the SGLT2 inhibitor empagliflozin in patients with type 2 diabetes.* Diabetes, Obesity and Metabolism, 2013. **15**(8): p. 721-728.