Predictors of glycaemic and weight response to empagliflozin treatment: the Association of British Clinical Diabetologists (ABCD) Nationwide Empagliflozin Audit

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INTRODUCTION

- Empagliflozin, an inhibitor of sodium-glucose cotransporter 2, improves glycaemia and weight in patients with type 2 diabetes.
- We explored potential factors which may be associated with improved glycaemia or weight response to empagliflozin treatment.

METHODS

The ABCD Nationwide Empagliflozin Audit

•The Association of British Clinical Diabetologists (ABCD) conducted a large scale audit of the use of empagliflozin routinely initiated clinical practice in the UK.
•Participating diabetes centres provided anonymised information of patient initiated on empagliflozin including patient demographics, baseline metabolic control and diabetes treatment, and outcomes and adverse events after starting empagliflozin.
•Data was collected between December 2014 to September 2018.

Outcomes

•We analysed the association between patients' baseline age, HbA1c, weight, duration of diabetes, alanine aminotransferase (ALT), sex, chronic kidney disease (CKD) stage, empagliflozin dose (25 vs 10mg), use of GLP-1 receptor agonist (GLP-1RA) and use of insulin with HbA1c and weight changes.
•The latest HbA1c and weight at 26 weeks of treatment (minimum 12 weeks) were used for analyses.

Statistical analyses

- Univariate analyses were performed using correlation statistics, t-tests or ANOVA.
- Variables with association p-value <0.05 were included in linear regression analysis.
- Interval to HbA1c and weight data and empagliflozin dose were covariates in multivariate analyses.
- ALT levels were logarithm transformed for linear regression analyses

Subjects

- Data on 2081 patients with diabetes with at least one follow-up visit after empagliflozin initiation was received.
- 134 patients were excluded (type 1 diabetes = 13, switched from dapagliflozin = 3, baseline HbA1c < 7.0% = 118).
- Among remaining 1947 patients, there were 1436 and 1381 patients with relevant follow-up HbA1c and weight data, respectively.

RESULTS

HbA1c results

•HbA1c reduced by, mean [95%CI] 1.35%[1.27,1.42] (p<0.0001) from a baseline of mean ± SD, 9.41 ± 1.41%.
•In univariate analysis, greater HbA1 reduction was seen among patients with higher baseline HbA1c, younger patients, higher weight, higher ALT levels, better renal function, and being on GLP-1RA.
•In the final multivariate model, greater HbA1c reduction was seen among patients with higher baseline HbA1 (p<0.001), better renal function (p=0.002), higher ALT (p=0.042) and higher weight (p=0.047).

Table 1: Association of baseline age, HbA1c, weight, BMI, diabetes duration and ALT with subsequent HbA1c and weight reduction

	HbA1c reduction		Weight reduction	
Pearson correlation	**R**	**P value**	**R**	**P value**
Age	-0.14	<0.0001	0.003	0.90
HbA1c	0.63	<0.0001	-0.05	0.15
Weight	0.06	0.035	0.32	<0.0001
BMI	0.05	0.09	0.03	0.21
Spearman correlation	***r***	**P value**	***r***	**P value**
Diabetes duration	-0.04	0.30	-0.05	0.27
ALT	0.08	0.006	0.01	0.85

Table 2: Association between gender, CKD stage, empagliflozin dose, use of GLP-1RA, and use of insulin with subsequent HbA1c and weight reduction

	HbA1c reduction		Weight reduction	
T-test or ANOVA	**Mean [95%CI]**	**P value**	**Mean [95%CI]**	**P value**
Male vs Female	1.34%[1.24,1.44] vs 1.35% [1.23,1.47]	0.95	3.7kg[3.4,4.1] vs 3.5kg[3.0,3.9]	0.35
CKD stage 1 vs 2 vs 3A	1.60%[1.48,1.73] vs 1.15%[1.04,1.25] vs 1.04%[0.72,1.36]	<0.0001	3.6kg[3.2,4.0] vs 3.8kg[3.4,4.2] vs 3.1kg[0.9,5.2]	0.50
Empagliflozin dose 25mg vs 10mg	1.36%[1.27,1.45] vs 1.31%[1.17,1.45]	0.59	3.7kg[3.3,4.1] vs 3.5kg[3.1,3.8]	0.43
GLP-1RA use vs non-GLP-1 RA use	1.69%[1.47,1.90] vs 1.29%[1.20,1.37]	0.0003	4.2kg[3.2,5.2] vs 3.5kg[3.3,3.8]	0.09
Insulin use vs non-insulin use	1.34%[1.17,1.50] vs 1.35%[1.26,1.43]	0.90	2.8kg[2.1,3.5] vs 3.8kg[3.5,4.1]	0.003

CKD group 1: eGFR>90 ml/min/1.73m^2
CKD group 2: eGFR 60-89 ml/min/1.73m^2
CKD group 3A: eGFR 45-59 ml/min/1.73m^2

Weight results

•Weight reduced by 3.6kg [3.3,3.9] (p<0.0001) from a baseline of 100.2 ± 20.7kg.
•In both univariate and multivariate analyses, greater weight reduction was seen among patients with higher baseline weight (p<0.001) and patients not on insulin (p<0.001).
•Renal function did not seem to impact on the degree of weight reduction

CONCLUSION

- As expected, patients with higher baseline HbA1c or baseline weight achieve greater reduction of HbA1c and weight, respectively.
- In the range of renal function analysed, better renal function appears to predict better HbA1c improvement, but not greater weight loss.
- While it appeared that patients on GLP-1RA obtained greater HbA1c reduction, this effect was not seen in multivariate analysis, possibly due to the adjustment for renal function.
- The interactions between HbA1c reduction and ALT levels and weight reduction with insulin treatment status warrant further investigations.

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