

Dapagliflozin is more effective in the patients with most poorly controlled diabetes

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INTRODUCTION

- Dapagliflozin is a sodium-glucose cotransporter-2 (SGLT-2) inhibitor that inhibits renal glucose reabsorption in an insulin-independent manner, thereby increasing urinary glucose excretion.
- Dapagliflozin can be used as monotherapy or in combination with other antidiabetic medications, including insulin therapy in type 2 diabetes.
- Dapagliflozin reduces HbA1c, body weight and blood pressure in type 2 diabetes.
- Trials have mostly recruited patients with modest elevations of HbA1c: mean baseline HbA1c range (7.92%- 8.08%).
- In the analysis of five phase 3 trials (n=139), the efficacy of dapagliflozin 10mg was higher in patients with baseline HbA1c \geq 9% than in the overall cohort.

AIM

- To investigate the efficacy of dapagliflozin in patients with most poor glycaemic control in routine clinical practice.

METHOD

- A prospective observational trial was conducted in secondary care hospital clinics in Wrexham and Swansea.
- Dapagliflozin was added to concomitant medications including insulin and glucagon like peptide -1 (GLP-1) agonists.
- Results in patients with baseline HbA1c \geq 9.5% were compared with those with baseline HbA1c <9.5%.

RESULTS

Whole Group analysis

- We identified 146 patients who had their first follow-up visit. 13 patients did not continue for non-specific reasons, and hence only 133 (65% male) were included in analysis.
- Mean age was 57.6 \pm 9.4 years, mean duration of diabetes was 11.12 \pm 6.56 years & mean duration of treatment was 6.0 \pm 2.6 months.
- Pre and post treatment mean HbA1c were 10.03 \pm 1.43 % & 8.76 \pm 1.45 % (p <0.001), respectively.
- Mean body weight reduced from 104.1 \pm 17.9 kg to 101.5 \pm 17.8 kg (p <0.001).
- Insulin total daily dose (TDD) reduced from 96.9 \pm 56.8 IU to 86.6 \pm 47.6 IU (p<0.001).

Patients with baseline HbA1c \geq 9.5% versus patients with baseline HbA1c<9.5%

- Mean change from baseline in HbA1c, body weight, blood pressure and insulin total daily dose in patients with HbA1c \geq 9.5 and those with HbA1c<9.5% are shown in Table 1.
- In poor control group, HbA1c reduced from 10.84% to 9.19% (p<0.001). In those with moderate impairment, HbA1c reduced from 8.56 to 8.00% (p<0.001). Using linear modelling there was an interaction (p<0.001) indicating significantly greater response in patients with poor glycaemic control. (Figure 1)

Table 1. Mean change in efficacy parameters in all patients, those with baseline HbA1c \geq 9.5% & those with baseline HbA1c <9.5%

	All patients n=133	Patients with HbA1c \geq 9.5 n=85	Patients with HbA1c<9.5 n=48
HbA1c (%)			
Baseline \pm SD	10.03 \pm 1.43	10.84 \pm 1.10	8.59 \pm 0.55
Change (95% CI)	-1.27 (-1.04,-1.51)	-1.65(-1.35,-1.96)	-0.59 (-0.31,-0.88)
p	<0.001	<0.001	<0.001
Weight (kg)			
Baseline \pm SD	104.1 \pm 17.9	103.7 \pm 18.4	104.0 \pm 17.3
Change (95% CI)	-2.3(-1.7,-2.9)	-1.9(-1.2, -2.6)	-3.1(-1.9,- 4.2)
p	<0.001	<0.001	<0.001
SBP (mmHg)			
Baseline \pm SD	138.80 \pm 17.50	139.79 \pm 17.88	136.37 \pm 17.00
Change (95% CI)	-3.72(-0.81,-6.62)	-3.15(0.52,-6.82)	-4.72(0.20,-9.64)
p	0.013	0.092	0.06
DBP (mmHg)			
Baseline \pm SD	78.34 \pm 10.98	78.16 \pm 10.84	78.63 \pm 11.16
Change (95% CI)	-2.61(-0.86,-4.37)	-2.33(-0.35,-4.32)	-3.11(0.36,-6.57)
p	0.004	0.022	0.077
Insulin (IU)	n=85	n=57	n=28
Baseline \pm SD	96.9 \pm 56.8	92.4 \pm 61.8	105.9 \pm 44.5
Change(95%CI)	-10.3(-4.7,-15.8)	-7.4(-0.7,-14.2)	-16.0(-6.2,-25.8)
p	<0.001	0.032	0.002

Table 2. Demographics & Baseline Characteristics grouped by degree of glycaemic control

	Patients with HbA1c \geq 9.5%	Patients with HbA1c<9.5%
n	85	48
Gender (M/F)	50/35	35/13
Age (years)	57.5 \pm 8.3	57.6 \pm 11.2
Duration of diabetes (years)	10.7 \pm 6.0	11.9 \pm 7.5
Weight (kg)	103.7 \pm 18.4	104.0 \pm 17.3
BMI (kg/m ²)	36.3 \pm 6.3	34.14 \pm 5.63
HbA1c (%)	10.84 \pm 1.10	8.59 \pm 0.55
SBP (mmHg)	139.79 \pm 17.88	136.37 \pm 17.00
DBP (mmHg)	78.16 \pm 10.84	78.63 \pm 11.16
Insulin (n)	57	28
Insulin TDD (IU)	92.4 \pm 61.8	105.9 \pm 44.5
GLP-1 Therapy	19	10
Metformin (n)	64	34
Metformin TDD (mg)	2044.8 \pm 606.4	1973.5 \pm 687.4

Data are mean \pm SD

Figure 1. Mean change in HbA1c, Body weight, BMI and Insulin TDD in between group comparison (General linear model)



SUMMARY

- For the whole group, dapagliflozin reduced HbA1c by 1.27%, body weight by 2.3 kg and daily insulin requirement by 10.3 IU.
- Baseline characteristics for patients with HbA1c \geq 9.5% and those with HbA1c<9.5% are similar. However, significantly greater HbA1c reduction was seen in the most poorly controlled patients.
- There was no statistically significant difference in reduction in body weight and daily insulin requirement between two groups.

CONCLUSION

- The effect of dapagliflozin on HbA1c is greatest in patients with the worst glycaemic control.

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