The impact of dapagliflozin on HbA1c, systolic blood pressure and weight: a review of dapagliflozin use in a Scottish city

Abstract
We aimed to determine the efficacy of dapagliflozin in the management of type 2 diabetes in a Scottish population through measurements of glycaemic control, blood pressure and weight.

Dapagliflozin was effective in improving HbA1c by 10mmol/mol (SE 1.8, p<0.001), systolic blood pressure by 9.8mmHg (SE 2.2, p<0.001) and weight by 3.2kg (SE 0.6, p<0.001). There was a significant proportion of people with diabetes who reported side effects with dapagliflozin relating to genital and urinary tract infections.

Dapagliflozin appears to be an effective drug in improving HbA1c, systolic blood pressure and weight in people with type 2 diabetes. However, in this cohort a substantial proportion of people with diabetes did not tolerate this drug due to side effects. Copyright © 2017 John Wiley & Sons.

Key words
dapagliflozin; diabetes; SGLT2 inhibitor; Scotland; Glasgow

Introduction
Sodium glucose co-transporter 2 receptor (SGLT2) inhibitors are the newest class of oral hypoglycaemic agents to enter the market for the treatment of type 2 diabetes. These drugs inhibit glucose reabsorption in the proximal tubules of the kidneys, thereby increasing urinary glucose excretion and lowering blood glucose levels in an insulin-independent manner.1 In type 2 diabetes, SGLT2 inhibitors have been shown to improve glycaemic control, blood pressure and weight.2 Dapagliflozin was the first SGLT2 inhibitor licensed for the treatment of type 2 diabetes. In accordance with NICE guidelines, dapagliflozin can be used in combination with metformin in people with diabetes intolerant of sulphonylureas or at significant risk of hypoglycaemia. This SGLT2 inhibitor can also be used in combination with insulin therapy.3

Aims
We aimed to determine the effects of dapagliflozin on glycaemic control, systolic blood pressure and weight in people with type 2 diabetes who attend our secondary care clinic in Glasgow, UK.

Methods
A total number of 3292 people with type 2 diabetes attend our secondary care diabetes clinic based in Stobhill Hospital, Glasgow. This secondary care clinic covers the population of Glasgow living in the north-eastern side of the city.

We identified a study population of people with type 2 diabetes who attended our secondary care clinic in Stobhill Hospital. This population was cross-referenced with a database of prescriptions issued by community pharmacies to obtain our study population of people who had been prescribed dapagliflozin. Biometric parameters of HbA1c, blood pressure and weight were obtained from the clinical records on the SCI-Diabetes database at the time of commencement of dapagliflozin. Post-treatment parameters were also obtained through the SCI-Diabetes database.

Statistical analysis was performed with Stata version 10.1 program (Stata, San Antonio, TX). Paired t-tests were used to assess the effect of dapagliflozin upon participants’ HbA1c, weight and systolic blood pressure following six months of treatment. P-values <0.05 were considered to be statistically significant.
Results
Through the SCI-Diabetes database we identified 103 people who had been on dapagliflozin between its initial release in the UK in 2013 until February 2015, to ensure we had sufficient length of follow up.

Of all those with diabetes who were initiated on dapagliflozin, 57% were female (n=59) and 43% male (n=44). Of these people with diabetes, 28% (n=29) were already on insulin therapy. The average and median age of people with diabetes on dapagliflozin was 56 years.

Of the 103 people with diabetes identified, 24 had less than three months of treatment with dapagliflozin due to side effects or to non-concordance with therapy. This cohort of people with diabetes (n=24) were excluded in the post-treatment analysis.

Glycaemic control
Mean pre-treatment HbA1c was 83.6mmol/mol with the follow-up HbA1c improving to 73.6mmol/mol (p<0.001; SE 1.8; 95% CI 6.5–13.6).

Blood pressure
There was also an improvement in systolic blood pressure from a mean baseline of 136.4mmHg to 126.6mmHg (p<0.001; SE 2.2; 95% CI 5.3–14.2).

Weight
Mean weight (101.9kg) also improved with an average weight loss of 3.2kg across the treatment group (p<0.001; SE 0.6; 95% CI 1.9–4.5).

Side effects
There were 20 people with diabetes who had developed side effects due to dapagliflozin, with 19 having to stop as a consequence. The most common symptoms from dapagliflozin were lower urinary tract in origin with increased frequency of micturition (n=6), thrush (n=6), itch (n=2), urinary tract infection (n=1), vulval vaginitis (n=1), incontinence (n=1), nocturia (n=1), and dysuria (n=1). There was also a reported case of arthralgia (n=1).

Discussion
This review demonstrates that dapagliflozin is an effective oral hypoglycaemic agent in our Scottish population and was able to achieve an improvement in HbA1c of 10mmol/mol. This is comparable with other oral hypoglycaemic agent classes and potentially more efficacious than the randomised control trial data available for the drug. Furthermore, the weight reduction of 3.2kg is favourable compared to the weight gains usually associated with sulphonylureas. This study does not measure directly the impact of dapagliflozin upon clinical outcomes relating to the complications of type 2 diabetes. However, a reduction in HbA1c, blood pressure and weight would be highly advantageous in the long-term management of this condition. Recently, the EMPA-REG OUTCOME trial demonstrated that the SGLT2 inhibitor empagliflozin reduces cardiovascular mortality. A similar study, the DECLARE-TIMI trial, is ongoing and will determine if improvements in cardiovascular outcomes extend to dapagliflozin as well.

Interestingly, almost 20% of our cohort with diabetes developed side effects relating to genital or urinary tract infections. SGLT2 inhibitor-induced glycosuria is reported to be associated with these infections which are typically mild to moderate in severity, respond to standard treatment, and rarely recur. As these adverse effects are not severe and are highly treatable, we should advocate the continuation of dapagliflozin and avoid the high attrition rate evident in this study. Conversely, clinicians must be vigilant regarding the risk of SGLT2 inhibitors and the risk of developing diabetic ketoacidosis (DKA). The risk of SGLT2 inhibitor-associated DKA is exceptionally rare (<0.1%); however, it can occur in euglycaemic individuals, making this potentially fatal condition difficult to detect.

To conclude, this study demonstrates the effectiveness of dapagliflozin in improving glycaemic control, systolic blood pressure and weight in a Scottish population with type 2 diabetes mellitus. Limitations of this study include its retrospective nature, lack of a control group, short follow-up period and the potential for HbA1c to fall on repeat testing reflecting a regression to the mean. As this was an observational study, there was also an inability to correct for other factors that may have influenced the measured biometric parameters and HbA1c. Nevertheless, this study offers insight into the ‘real world’ use of dapagliflozin, and its potential benefits in the treatment of type 2 diabetes.

Declarations of interests
Christopher JL Kueh has received honoraria from AstraZeneca. Christopher Smith and James G Boyle have both received speaker fees from AstraZeneca.

References