ORIGINAL RESEARCH

Assessment of role of SGLT2 inhibitors in elderly obese uncomplicated DM patients

[1]Shaheen Saeed, [2]Parvez SaeedAnsari

[1]Associate Professor, Pharmacology, AL Falah School of Medical Science and Research Center, Haryana, India
[2]Assistant Professor, Internal Medicine, Integral Institute of Medical Sciences & Research, Lucknow, Uttar Pradesh, India

Correspondence:
Dr ParvezSaeed Ansari
Assistant Professor, Internal Medicine, Integral Institute of Medical Sciences & Research, Lucknow, Uttar Pradesh, India

ABSTRACT

Background:SGLT2 inhibitor treatment has been shown to have additional benefits such as weight loss, renoprotective and cardioprotective effects. The present study was conducted to assess role of SGLT2 inhibitors in elderly obese uncomplicated DM patients.

Materials & Methods:84type II DM patients of both genders were prescribed empagliflozin or dapagliflozin. FBG, PPBG, HbA1c, liverenzymes and kidney function tests, complete urinalysis,serum lipids, protein excretion in spot urine were recordedbefore and after the initiation of SGLT2 inhibitor.

Results: Out of 84 patients, males were 50 and 34 were females. SGLT2 inhibitor used wereEmpagliflozin in 40 and Dapagliflozin in 44. Comorbidities were hyperlipidemia in 57, hypertension in 62, CAD in 12 and heart failure in 7 patients. Complications were diabetic nephropathy in 15, diabetic retinopathy in 10 and diabetic neuropathy in 22 patients. The difference was significant (P< 0.05). Laboratory findings before and after treatment in FBG (mg/dl) was 198.2 and 154.3, PPBG (mg/dl) was 276.2 and 235.9, HbA1c (%) was 9.5 and 7.1, hemoglobin (g/dl) was 13.5 and 14.2, hematocrit (%) was 43.2 and 45.0, urea (mg/dl) was 36.4 and 38.7, creatinine (mg/dl) was 0.8 and 0.9 and eGFR (mL/min/1.73 m2) was 84.2 and 79.5 respectively. The difference was significant (P< 0.05).

Conclusion: Glycemic control was successfully achieved with SGLT2 inhibitor treatment in type II DM patients.

Key words:Diabetes Mellitus, empagliflozin, SGLT2 inhibitor

INTRODUCTION

Type 2 Diabetes Mellitus (DM) is a chronic disease with an increasing prevalence worldwide which causes significant mortality and morbidity especially in the elderly population.[1]According to the International Diabetes Federation, about 415million people were suffering from diabetes worldwide, and this number is expected to exceed 640million by the year 2040. It is estimated that half of patients with diabetes are unaware of their disease and are thus more prone to developing diabetic complications. Type II DM has become an observably global public health problem.[2]

The treatment and follow-up of diabetes in the elderly is more difficult due to accompanying comorbidities, cognitive impairment, polypharmacy, side effects and interactions of

medicines. Besides, the risk of hypoglycemia is higher in the elderly.[3]Sodium-glucose co-transporter-2 inhibitors work by inhibiting SGLT2 in the PCT, to prevent reabsorption of glucose and facilitate its excretion in urine. As glucose is excreted, its plasma levels fall leading to an improvement in all glycemic parameters. This mechanism of action is dependent on blood glucose levels and, unlike the actions of thiazolidinediones (mediated through GLUTs), is independent of the actions of insulin.[4] Thus, there is minimal potential for hypoglycemia and no risk of overstimulation or fatigue of the beta cells. Because their mode of action relies upon normal renal glomerular-tubular function, SGLT2i efficacy is reduced in persons with renal impairment.SGLT2 inhibitor treatment has been shown to have additional benefits such as weight loss, renoprotective and cardioprotective effects.[5]The present study was conducted to assess role of SGLT2 inhibitors in elderly obese uncomplicated DM patients.

MATERIALS & METHODS

The present study comprised of 84type II DM patients of both genders. The consent was obtained from all enrolled patients.

Data such as name, age, gender etc. was recorded. All patients were prescribed empagliflozin or dapagliflozin. A thorough clinical examination was carried out. Estimated glomerular filtration rate (eGFR) wascalculated. Renal failure was defined as >30%decrease in eGFR value and/or eGFR<60 mL/min/1.73 m2. Severe hypoglycemia; hypoglycemia requiring help or aserum glucose reading of 54 mg/dl and severe hyponatremia; was defined as hyponatremia with Na<125 mEq/L andclinical finding.FBG, PPBG, HbA1c, liverenzymes and kidney function tests, complete urinalysis,serum lipids, protein excretion in spot urine were recordedbefore and after the initiation of SGLT2 inhibitor. Data thus obtained were subjected to statistical analysis. P value < 0.05 was considered significant.

RESULTS

Table I Distribution of patients

Total- 84		
Gender	**Males**	**Females**
Number	50	34

Table I shows thatout of 84 patients, males were 50 and 34 were females.

Table II Demographic characteristics

Parameters	Variables	Number	P value
SGLT2 inhibitor	Empagliflozin	40	0.94
	Dapagliflozin	44	
Comorbidities	Hyperlipidemia	57	0.05
	Hypertension	62	
	CAD	12	
	Heart failure	7	
Complications	Diabetic nephropathy	15	0.12
	Diabetic retinopathy	10	
	Diabetic neuropathy	22	

Table II, graph I shows that SGLT2 inhibitor used were Empagliflozin in 40 and Dapagliflozin in 44. Comorbidities were hyperlipidemia in 57, hypertension in 62, CAD in 12 and heart failure in 7 patients. Complications were diabetic nephropathy in 15, diabetic retinopathy in 10 and diabetic neuropathyin 22 patients. The difference was significant (P< 0.05).

Graph IDemographic characteristics

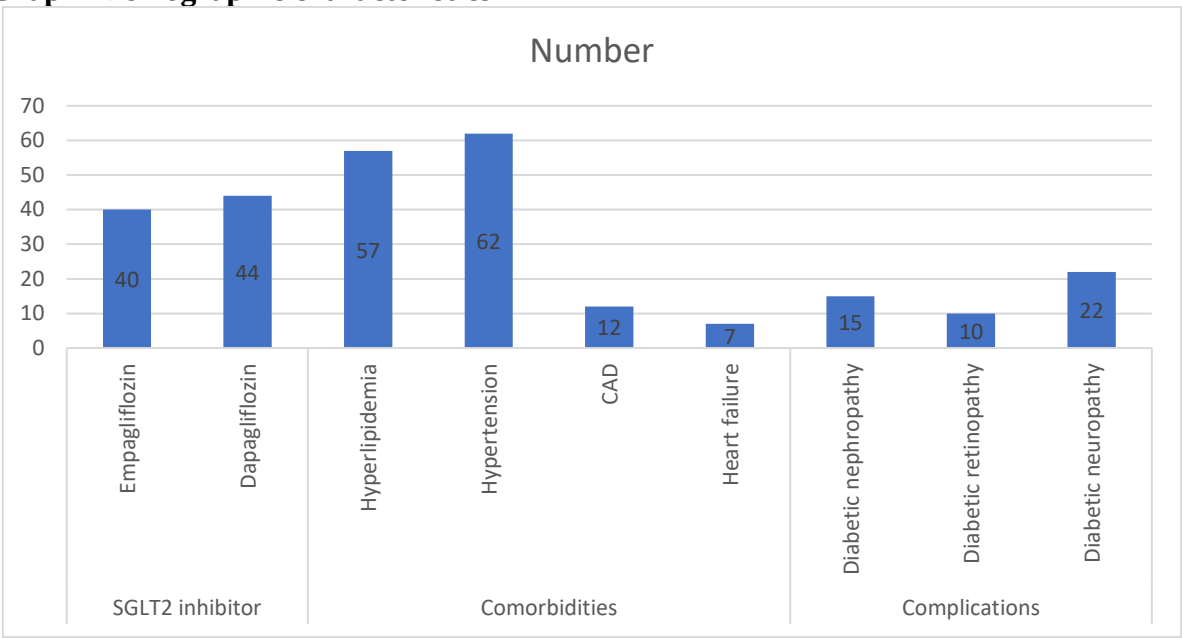

Table III Laboratory changes before and after SGLT2 inhibitor therapy

Laboratory findings	Before	After	P value
FBG (mg/dl)	198.2	154.3	0.04
PPBG (mg/dl)	276.2	235.9	0.05
HbA1c (%)	9.5	7.1	0.01
Hemoglobin (g/dl)	13.5	14.2	0.05
Hematocrit (%)	43.2	45.0	0.12
Urea (mg/dl)	36.4	38.7	0.81
Creatinine(mg/dl)	0.8	0.9	0.05
eGFR (mL/min/1.73 m2)	84.2	79.5	0.02

Table III, shows that laboratory findings before and after treatment in FBG (mg/dl) was 198.2 and 154.3, PPBG (mg/dl) was 276.2 and 235.9, HbA1c (%) was 9.5 and 7.1, hemoglobin (g/dl) was 13.5 and 14.2, hematocrit (%) was 43.2 and 45.0, urea (mg/dl) was 36.4 and 38.7, creatinine (mg/dl) was 0.8 and 0.9 and eGFR (mL/min/1.73 m2) was 84.2 and 79.5 respectively. The difference was significant (P< 0.05).

DISCUSSION

Sodium-glucose co-transporter-2 inhibitors use leads to a reduction in body weight, ranging from about 1 to 5 kg. A greater fall is seen in patients with long-standing diabetes and in those with a higher baseline weight.[6] This weight loss is sustained after up to 2 years of use of dapagliflozin, and may be linked to a reduction in insulin dose requirements of patients with long-standing diabetes.SGLT2i is a novel class of medication that decreases plasma glucose concentration. The pharmacological action shows that a healthy individual will approximately filter 160–180g glucose daily from the glomerulus with almost 100% reabsorption via the proximal convoluted tubule (PCT), hence leaving almost no urinary glucose.[7] Diabetic patients' glomerular filtration of glucose increased significantly to 180–240g daily above renal glucose threshold, leading to glycosuria.[8] SGLT2i bind to SGLT2 receptors with an insulin-independent mechanism of action, further increasing glycosuria and consequently lowering plasma glucose concentration (1), leading to cardiovascular and renal

benefit.[9]The present study was conducted to assess role of t SGLT2 inhibitors in elderly obese uncomplicated DM patients.

We found that out of 84 patients, males were 50 and 34 were females. Taşkaldiranet al[10]evaluated the effect and tolerability of using SGLT2 inhibitors in geriatric patients. Patients over 65 years of age with a diagnosis of type 2 DM who were started on empagliflozin or dapagliflozin. A statistically significant decrease was observed in the fasting blood glucose (FBG), postprandial blood glucose (PPBG), and HbA1c values of the patients after the SGLT2 inhibitor was started. While the urea and creatinine values of the patients increased after the treatment, a decrease was observed in the eGFR value. After treatment, a decrease in albumin/creatinine ratio in spot urine and an increase in hemoglobin and hematocrit values were observed. No complaints were reported in 31 patients (59.6%) and no side effects were detected. Side effects associated with SGLT2 inhibitor were observed in 21 patients (40.3%). In total, treatment was continued in 41 patients (78.8%) out of 52 patients, while treatment was discontinued in 11 patients (21.2%).

We found that SGLT2 inhibitor used were Empagliflozin in 40 and Dapagliflozin in 44. Comorbidities were hyperlipidemia in 57, hypertension in 62, CAD in 12 and heart failure in 7 patients. Complications were diabetic nephropathy in 15, diabetic retinopathy in 10 and diabetic neuropathy in 22 patients. Rosenstock J et al[11] assessed efficacy and safety of empagliflozin. Patients with type 2 diabetes mellitus (T2DM) were randomized to receive empagliflozin 10 or 25 mg once daily or placebo; the basal insulin regimen was kept constant for the first 18 weeks, after which the treating investigator could adjust the regimen at their discretion for the following 60 weeks. As well as significant improvements in HbA1c, patients in both of the empagliflozin groups had significant reductions in their insulin doses at week 78, and also registered weight loss versus a small weight gain in those receiving placebo.

We found that laboratory findings before and after treatment in FBG (mg/dl) was 198.2 and 154.3, PPBG (mg/dl) was 276.2 and 235.9, HbA1c (%) was 9.5 and 7.1, hemoglobin (g/dl) was 13.5 and 14.2, hematocrit (%) was 43.2 and 45.0, urea (mg/dl) was 36.4 and 38.7, creatinine (mg/dl) was 0.8 and 0.9 and eGFR (mL/min/1.73 m2) was 84.2 and 79.5 respectively. In the United States of America, the Food and Drug Administration (FDA) has authorised the use of four SGLT2 inhibitors including canagliflozin, dapagliflozin, empagliflozin and ertugliflozin in treating T2DM patients. Recent guidelines by American Diabetes Association state that patients with high-risk or pre-existing atherosclerotic cardiovascular disease, or pre-existing kidney disease, or heart failure, we recommended SGLT2i as part of the glucose-reducing regimen irrespective of HbA1c control.[12]

CONCLUSION

Diabetes treatment and follow-up is more difficult and sensitive in the elderly. Authors found that glycemic control was successfully achieved with SGLT2 inhibitor treatment in type II DM patients.Side effectsand drug withdrawal rates are within acceptable limits. SGLT inhibitors endureto be an imperativeantidiabetic agent that might bepreferred also in the elderly population

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