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Title of project: Assessing Appropriate Utilization of SGLT2 Inhibitors in Type II Diabetic Patients

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ABSTRACT

Specific Aims: To determine if SGLT2 inhibitors were used appropriately in type II diabetic patients at El Rio Health Center given their estimated glomerular filtration rate (eGFR).

Subjects: El Rio Health Patients with a formal diagnosis of type II diabetes prescribed an SGLT2 inhibitor.

Methods: In this retrospective analysis, informatic specialists provided a de-identified report of type II diabetic patients on SGLT2 inhibitors with renal function labs available. The data was retrieved from July 2019-July 2020. Evaluation of appropriate use of SGLT2 inhibitors was assessed by comparing the patient's eGFR to current dosing guidelines for each individual SGLT2 inhibitor.

Main Results: Of the 234 patients evaluated, the average age of the subjects was 69 years old with 54% being of Caucasian descent. An average eGFR of 85 mL/min./1.73m^2 in patients with included comorbidities of 94% hyperlipidemia, 87% hypertension, and 15% cardiovascular disease. In the observed population, nearly 95% of patients were appropriately prescribed SGLT2 inhibitors based on current eGFR and current dosing guidelines.

Conclusions: Based on the analyzed data, a majority of type II diabetic patients at El Rio Health Center were appropriately prescribed an SGLT2 inhibitor for their eGFR based on current guideline recommendations.

Assessing Appropriate Utilization of SGLT2 Inhibitors in Type II Diabetic Patients

INTRODUCTION

Type 2 diabetes mellitus (T2DM) is the leading cause of kidney failure.[1] According to the Centers for Disease Control and Prevention (CDC) as well as the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), 1 in 3 adults with diabetes has chronic kidney disease.[1,2] Glomerular filtration rate (GFR) determines how your kidneys are filtering functionally. Creatinine, a waste product from muscle breakdown, is removed by the kidneys and is a marker for estimating one's GFR. As creatinine increases, GFR decreases indicating kidney disease declined. Defined by NIDDK: an eGFR of 60 mL/min/1.73m^2 or greater is considered in the *normal* range, eGFR less than 60 mL/min/1.73m^2 but greater than 15 mL/min/1.73m^2 is considered *chronic kidney disease* (CKD), and eGFR less than 15 mL/min/1.73m^2 is considered *kidney failure.*[1] Another indicator of kidney disease is the urine albumin-to-creatinine ratio (UACR) that measures the amount of albumin to the amount of creatinine in a urine sample where 30mg/g or less is normal and greater than 30 mg/g may indicate kidney disease.[1] Sodium-glucose cotransporter 2 inhibitors (SGLT2i) improve glycemic control in type 2 diabetics by inhibiting glucose reuptake in the proximal tubule of the kidney, which induces urinary glucose secretion. [3]

Cardiovascular trials of SGLT2 inhibitors have suggested they may improve renal outcomes in type 2 diabetics by increasing renal vascular resistance, which normalizes the measure glomerular filtration rate (mGFR).[3] The ADA recommends patients w/ heart failure or chronic kidney disease with an eGFR of 30-60 ml/min/1.73 m^2 to be started on an SGLT2 inhibitors because it has been shown to have cardiovascular and renal protective properties.[6] The issue becomes the use of SGLT2 inhibitors in patients with eGFR < 30 ml/min/1.73^2 at the time this is not recommended due to concerns that it will worsen kidney function as evidenced by increased serum creatinine and decreased eGFR.[7]
Studies are being conducted to establish safe use of SGLT2 inhibitors past this eGFR cutoff, if these are successful in showing benefit they will prove to be crucial in providing renal protection while also

offering means to control diabetes and prevent complications related to poorly controlled diabetes. As these studies are ongoing the purpose of this study is to determine given current guidelines if SGLT2 inhibitors were used appropriately in type II diabetic patients at El Rio Health Center.

METHODS

Design: This retrospective cohort study, in which a de-identified list of patients with type II diabetes on SGLT2 inhibitors was evaluated. The design allowed the project to be qualified as non-human research by the University of Arizona Human Subjects Protection Program.

Subjects: Type II diabetic patients of El Rio Health Center that were 18 years and older on SGLT2 inhibitors from July 2019-July 2020 were included in the study. Patients meeting these criteria prior to or after this time period were excluded from the study. Additionally, patients not meeting the criteria specified were excluded from our evaluation.

Treatment: The independent variable for this study will be if the patient is taking an SGLT2 inhibitor to help manage their diabetes.

Measures: A list of type II diabetic patients on SGLT2 inhibitors with renal function labs in order to assess if they were being used appropriately given the patient's renal function. Specifically, eGFR in these patients was analyzed since dosing guidance and appropriate use of SGLT2 inhibitors is based on eGFR. Renal function labs often include measurement of serum creatinine and eGFR.

Data Collection: Data was collected by the informatic specialist at El Rio Health Center who generated a de-identified list of patients meeting our eligibility criteria. Evaluation of this information was used to assess if SGLT2 inhibitors were used appropriately prescribed based on their renal function.

Data analysis: The original intent in the proposal was to assess how SGLT2 inhibitors impacted renal function in type II diabetics at El Rio Health Center but based on IRB guidance the intent became to evaluate the appropriateness of SGLT2 inhibitors given eGFR in order to bypass the requirement of IRB approval for human research. Thus, originally the intent was to calculate the mean and standard deviation

using a t-test to compare renal function of those on SGLT2 inhibitors and those not on SGLT2 inhibitors. Instead with the new recommendations made by the IRB, only a Chi-Square Test was used to evaluate the categorical data.

RESULTS

Of the 234 patients evaluated, the average age of the subjects was 69 years of age with 54% being of Caucasian descent. Of the patients evaluated, 47.8% were female and 52.2% were male (Table 1). An average eGFR of 85 mL/min./1.73m^2 in patients with included comorbidities of 94% hyperlipidemia, 87% hypertension, and 15% cardiovascular disease (Table 1). In the observed population, 94.8% of patients were appropriately prescribed SGLT2 inhibitors based on their current eGFR and current dosing guidelines (Chart 1). Only 3 patients of 234 analyzed were inappropriately prescribed SGLT2 inhibitors. Trends across these patients included being males and 70 years and older. Additionally, they all had hyperlipidemia. After performing a chi square test of the SGLT2 inhibitors evaluated, all except Steglatro (p=0.057) were found to have a significant p-value indicating association between appropriateness and medication (Table 2).

DISCUSSION

The major findings of the study are 95% of patients were appropriately prescribed SGLT2 inhibitors based on their eGFR; thus, suggesting that El Rio effectively executes guideline directed therapy for their patient population.

A chi square test was performed to analyze the relationship between appropriate versus inappropriate use of SGLT2 inhibitors. Per the American Diabetes Association (ADA), each SGLT2 inhibitor has a unique eGFR cutoff for inappropriate use. Based on the therapeutic dosing guidelines for each medication, we evaluated appropriate versus inappropriate use with eGFR for the SGLT2 inhibitors. After performing the chi square test, the results revealed all except Steglatro (p=0.057) were found to

have a significant p-value suggesting that prior to initiation to an SGLT2 inhibitor that El Rio takes into consideration patients' eGFR when prescribing this class of medications.

Based on the studies reviewed prior to initiation of the project, the primary intent in our study was to evaluate SGLT2 inhibitor use in those with renal impairment compared to those without; however, under the advice given from IRB we evaluated whether SGLT2 inhibitors were used appropriately or inappropriately for patients based on eGFR.

The study had multiple limitations in regard to its findings. A major limitation is that since only patients from El Rio Health Center were analyzed, our study results lack generalizability. We did not analyze the eGFR throughout the patient's entire duration of medication therapy. When the data was obtained there were many unknown or missing data points which may have influenced the findings. Specifically in regard to cardiovascular disease, given that SGLT2 inhibitors have cardiovascular benefit, it was unclear if this disease state was a parameter considered when initiating therapy with this class of medications. Based on our results, for future studies the evaluation of change in eGFR from initiation of therapy to present day via a pre and post analysis would be clinically significant. Our initial proposal illustrated current studies evaluating similar outcomes.

Due to unforeseen circumstances with the global pandemic, we were provided with limited data than our initial recommendations. An opportunity for future studies should include evaluation of eGFR prior to initiation of therapy of an SGLT2 inhibitor as well as if the eGFR fell below the recommended cutoff for each medication in this class that an appropriate clinical intervention was made.

CONCLUSIONS

In type II diabetic patients at El Rio Health Center, majority of patients were appropriately prescribed SGLT2 inhibitors based on current dosing guideline recommendations. From this data, it can be inferred that El Rio appropriately follows evidence-based guideline recommendations for renal function when prescribing SGLT2 inhibitors.

REFERENCES

1. National Institute of Diabetes and Digestive and Kidney Diseases. Diabetic Kidney Disease. Accessed 2020 March 27.

2. Centers for Disease Control and Prevention. Chronic Kidney Disease Initiative. Accessed 2020 March 27.

3. Standards of Care (PDF). *Diabetes Care*. Published online February 28, 2021. Accessed March 3, 2021.

4. Statistics About Diabetes | ADA. Accessed March 27, 2020.

5. Learn about Diabetes | CDC. Accessed March 27, 2020.

6. Practice Guidelines Resources | American Diabetes Association. Accessed March 27, 2020.

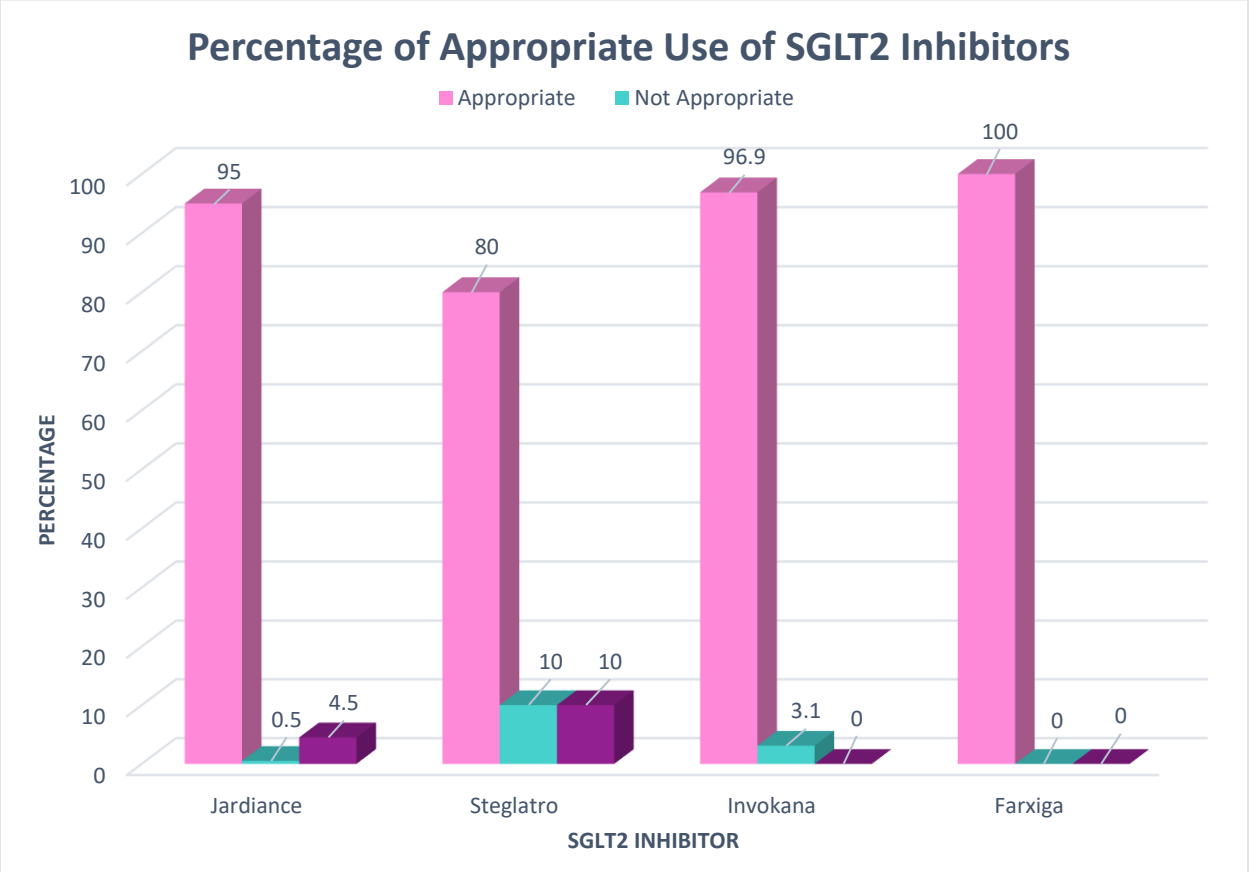
Table 1.

Baseline Characteristics	
Age (Mean)	59
Gender (%)	
	47.8 Female
	52.2 Male
Race (%)	
	15.8% Native American
	53.4% White
	3.8% Black
	2.1% Asian
	4.7% Other
	19.7% Unknown
BMI (Mean)	
	32.8
Disease States (%)	
HTN Diagnosis	87%
Hyperlipidemia Diagnosis	94%
Cardiovascular Disease	15%

Table 2.

Medication	eGFR	N	P value
Jardiance	Appropriate	177	<0.05
	Inappropriate	8	
Steglatro	Appropriate	8	0.057
	Inappropriate	2	
Farxiga	Appropriate	6	0.01
	Inappropriate	0	
Invokana	Appropriate	32	<0.05
	Inappropriate	1	

Chart 1.


Percentage of Appropriate Use of SGLT2 Inhibitors
Appropriate
Not Appropriate
PERCENTAGE
100
90
80
70
60
50
40
30
20
10
0
95
0.5
4.5
80
10
10
96.9
3.1
0
100
0
0
Jardiance
Steglatro
Invokana
Farxiga
SGLT2 INHIBITOR

APPENDICES

Column	Item No.	Variable Name	Code
A	1	Age	Years
B	2	Gender	1=Male, 2=Female
C	3	Race/Ethnicity	Caucasian=1, African American=2, Hispanic= 3, American Indian= 4, Asain= 5
D	4	Dx of HTN	Yes= 1, No=2
E	5	Dx of Dyslipidemia	Yes=1, No= 2
F	6	Dx of Cardiovascular Disease	Yes=1, No= 2
G	7	SGLT-2	Canagaflozin, Dapagliflozin, Empagliflozin, Ertugliflozin
H	8	eGFR	ml/min/1.73m^2: >/= 60= 1, < 60->/=45= 2, <45->/= 30=3, < 30= 4