



Case Series

Prevalence of Antidiabetic Drugs Prescription in Type 2 Diabetes and Chronic Kidney Disease Patients from Tâmega e Sousa

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Abstract

Background: Diabetes mellitus is the most prevalent cause of Chronic Kidney Disease (CKD). Recently, guidelines have supported the use of SGLT-2 inhibitors as first-line therapy in type 2 diabetes mellitus. There is a lack of epidemiologic studies on the patterns and trends of antidiabetic drugs prescription most commonly used in clinical practice in CKD patients. **Methods:** A descriptive and observational single-center study was performed in 2020, by analyzing patients followed up in the Nephrology Department of the Centro Hospitalar Tâmega e Sousa, Portugal. **Results:** A total of 566 patients were observed over one year and 47.0% had diabetes mellitus (n=266). Mean age of diabetic patients was of 74±10.8 years, with a male gender predominance of 57.1% (n=152). Diabetic nephropathy was present in 89.5% (n=238). Remaining causes of chronic kidney disease (CKD) were hypertensive nephrosclerosis (n=12), chronic pyelonephritis (n=6), IgA nephropathy (n=2), focal segmental glomerulosclerosis (n=2), acute tubular necrosis (n=2), mesangio proliferative glomerulonephritis (n=1), immunotactoid glomerulonephritis (n=1), minimal change disease (n=1) and uncertainly (n=1). Mean HbA1c was 7.2±1.4. Mean value of plasmatic creatinine was 1.8±0.7 mg/dL (ClCr: 47±29.6 mL/min) and proteinuria was 1339±2794 mg/24h. One-third of patients were in CKD stage 3b (33.4%), 30.4% in stage 4 and 2.6% in stage 5. Oral antidiabetic drugs were prescribed an average of 1.5±0.7. DPP-4 inhibitors were the most commonly prescribed class of antidiabetic drugs (56.4%), followed by biguanides (32.7%) and SGLT-2 inhibitors (22.6%; n=60). **Conclusions:** A new pattern in antidiabetic drugs prescription could be seen but there is an even broader edge for treatment optimization in type 2 Diabetes Mellitus.

Keywords: Diabetes mellitus; Chronic kidney disease; SGLT-2 inhibitors; Antidiabetic drugs

Introduction

Diabetes mellitus is the most prevalent cause of Chronic Kidney Disease (CKD), due to the growth of obesity, changes in lifestyle and nutrition in the last few decades, with serious clinical and economic implications [1-3]. Recently, guidelines and recommendations for treatment of type 2 diabetes mellitus have praised the use of SGLT-2 inhibitors as first-line therapy not only for glycemic control but also for their long-term benefits on kidney and cardiovascular events [4-6]. Although the underlying mechanisms are not completely understood, the benefits of SGLT-

2 inhibitors appear to be independent of their blood glucose-lowering effects and may be mediated by natriuresis and glucose-induced osmotic diuresis, leading to a reduction in intra glomerular pressure [7,8]. This reason could explain the results seen in the DAPA-CKD trial, in which patients who received dapagliflozin had a significantly lower risk of composite kidney outcomes compared to placebo, independent of the presence or absence of type 2 diabetes [8]. There is a lack of epidemiologic information about current patterns and trends of the most commonly prescribed antidiabetic drugs in clinical practice in CKD patients [9,10]. Despite several advantages of SGLT-2 inhibitors, few studies point out that providers under prescribe these new agents for eligible patients and further efforts are needed to prevent CKD progression [11,12].

Methods

A descriptive, observational and cross-sectional single-center study was performed in 2020, by analyzing patients followed up by one physician in the Nephrology Department of the Centro Hospitalar Tâmega e Sousa, Portugal. The following variables were sought: age, gender, cause of CKD, HbA1c, creatinine, creatinine clearance, proteinuria and antidiabetic drugs prescription, according to the clinical records in the last evaluation in 2020. Both creatinine clearance and proteinuria were determined by 24-hour urine collection. Statistical analysis was performed using SPSS (version 28.0). Continuous variables with a normal distribution were expressed by mean and state deviation and compared by t-test. Non-parametric continuous variables were presented by median and interquartile range and compared by the Mann-Whitney U Test. Proportions were used for categorical data and compared by χ^2 test. P values < 0.05 were considered statistically significant.

Results

A total of 566 patients were observed in the Nephrology Department in 2020 and 47.0% had type 2 diabetes mellitus (n=266). Mean age of diabetic patients was of 74±10.8 years, with a male gender predominance of 57.1% (n=152). Diabetic nephropathy was present in 89.5% (n=238). Remaining causes of chronic kidney disease were hypertensive nephrosclerosis (n=12), chronic pyelonephritis (n=6), IgA nephropathy (n=2), focal segmental glomerulosclerosis (n=2), acute tubular necrosis (n=2), mesangio proliferative glomerulonephritis (n=1), immunotactoid glomerulonephritis (n=1), minimal change disease (n=1) and uncertainly (n=1) (Table 1). Mean HbA1c was 7.2±1.4. Mean value of plasmatic creatinine was 1.8±0.7 mg/dL (ClCr: 47±29.6 mL/min) and proteinuria was 1339±2794 mg/24h. One-third of patients were in CKD stage 3b (33.4%), 30.4% in stage 4 and 2.6% in stage 5 (Figure 1). Oral antidiabetic drugs were prescribed an average of 1.5±0.7 per patient and nearly one-third were taking insulin (34.6%; n=92). DPP-4 inhibitors were the most commonly prescribed class of antidiabetic drugs (56.4%), followed by biguanides (32.7%), SGLT-2 inhibitors (22.6%; n=60), sulfonylureas (11.6%), GLP-1 agonists (3.4%), α -glucosidase inhibitors (1.5%) and thiazolidinediones (0.7%). In 7.5% of patients, diabetes was controlled only with diet and without medication (Figure 2, series 1). Comparing with data from an Internal Medicine and Diabetology consultation almost ten years before in 2011 (n=301), biguanides were the most commonly prescribed class of antidiabetic drugs (59.3%), followed by DPP-4 inhibitors (49.4%), sulfonylureas (35.7%), thiazolidinediones (28%), GLP-1 agonists (0.5%) and anyone with SGLT-2 inhibitors (Figure 2, series 2).

Variables	
Mean age	74±10,8 years
Male gender	57,1% (n=152)
HbA1c (%)	7,2±1,4
Cr (mg/dL)	1,8±0,7
ClCr (mL/min)	47,0±29,6
Proteinuria (mg/dia)	1339±2794
CKD causes	
Diabetic nephropathy	89,5% (n=238)
Hypertensive nephrosclerosis	4,5% (n=12)
Chronic pyelonephritis	2,3% (n=6)
FSGS	0,7% (n=2)
Acute tubular necrosis	0,7% (n=2)
IgA Nephropathy	0,7% (n=2)
Mesangio-proliferative GN	0,4% (n=1)
Immuntactoid GN	0,4% (n=1)
Minimal Change Disease	0,4% (n=1)
Uncertain	0,4% (n=1)

Table 1: Descriptive baseline characteristics.

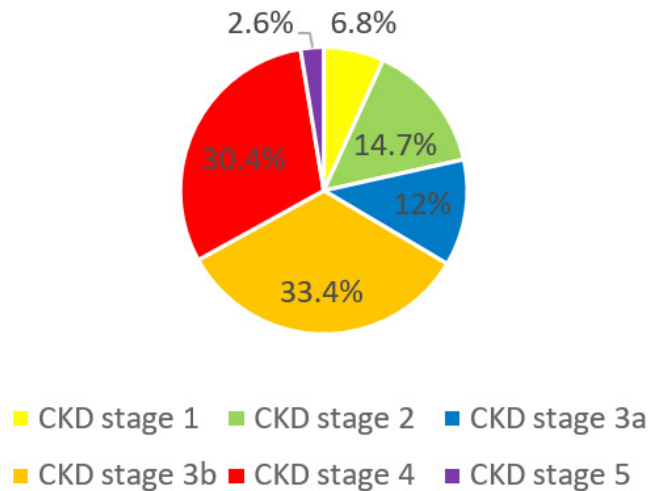


Figure 1: Prevalence of CKD by stages 1 – 5.

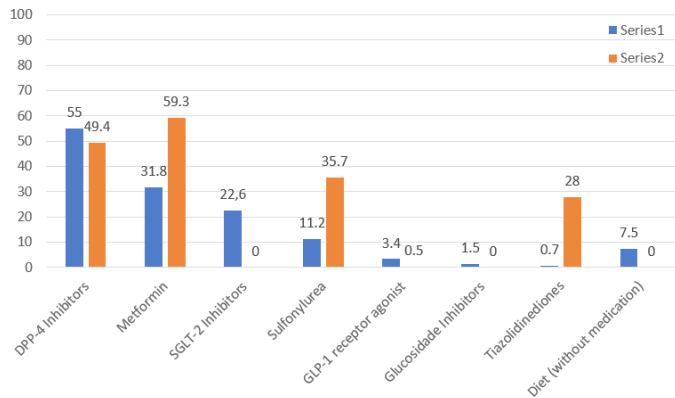


Figure 2: Proportion of antidiabetic drugs prescription in Nephrology Department in 2020.

Discussion

During a period of ten years (2011-2020), we can see that the two most widely prescribed antidiabetic drugs in Portuguese clinical practice were DPP-4 inhibitors and biguanides, probably because of a large amount of experience, safety profile and efficacy. An Australian study had similar conclusions in 3505 patients between January 2015 and June 2017, documenting a higher use of biguanides, sulfonylureas and DPP-4 inhibitors [13]. Our descriptive study shows that SGLT-2 inhibitors increased in drug prescriptions to 22.6% in 2020, being the third agent most widely used in the Nephrology outpatient clinic. This fact could be explained by recent published trials which enhance the importance of the SGLT-2 inhibitors in long-term benefit on kidney and cardiovascular outcomes [2,8]. In comparison with other studies, we could be witnessing a general trend of growth and enthusiasm for these new antidiabetic drugs [9,10]. For example, McCoy et al showed a lower prescription proportion of this drug class, of only 5% in a cross-sectional study in 3779 adults with type 2 diabetes and proteinuric chronic kidney disease from the United States, in 2017 [14]. The Harris et al study showed a prevalence prescription of 8% in SGLT-2 inhibitors in 2019 [15]. Engler et al reported a similar proportion, compared to our study, of 23.4% taking these new antidiabetic agent in the Tyrol region (Austria) in 2018 [10]. However, in line with KDIGO guidelines, which recommend the use of SGLT-2 inhibitors in case of a glomerular filtrate rate superior to 30 mL/min, there are too many patients who still fail to receive this nephroprotection. In our study, 71.4% of diabetic patients followed in the Nephrology Department in 2020 had a $\text{ClCr} \geq 30$ mL/min, so 48.8% of eligible patients were not treated with SGLT-2 inhibitors. A possible reason for this fact is the presence of an elderly sample with mean age of 74 ± 10.8 years, more susceptible to adverse effects such as hypovolemia, urinary tract infections and bone fractures. In this study the patients treated with SGLT-2 inhibitors were younger than the rest (68 vs 76 years, $p < 0,001$). A

few studies support the same association between younger age and initiation of SGLT-2 inhibitors [15-17]. Another reason explored by some studies could be related to some clinical inertia, reduced time for re-evaluation and performing drug changes to improve diabetes control [18]. In this study, mean HbA1c was $7.2 \pm 1,4$, which is a good metabolic target for this diseased population. Finally, the lack of multidisciplinary discussion as well as cost assessment could also represent barriers to initiate the use of these new antidiabetic drugs [18-20]. The greatest strength of this study is of being the first one to report the proportion of new antidiabetic drugs prescribed among CKD patients in Portugal. Limitations are the small sample and the fact that data have been extracted from only one Nephrology Department of a northern region of Portugal, and probably fails to reflect the reality of the whole country.

Conclusion

This study showed that SGLT-2 inhibitors were the third most widely used agent in clinical practice in a Nephrology Department during 2020, accounting for 22.6%. The author believes that the proportion of chronic kidney patients with and without diabetes treated with SGLT-2 inhibitors will increase further in the future with better knowledge of the benefits and greater experience in the handling of these drugs by clinicians.

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