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Diabetes & its Complications

Experience in Prescribing Gliflozines and GLP 1 Receptor Agonists: Study in a Population of Diabetics followed up at the Institut de Prévoyance Médico-social de l'Université Cheikh Anta DIOP de Dakar

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ABSTRACT

Introduction: *In our low-income countries, very few data are reported on the prescription of gliflozins and GLP-1 receptor agonists. The aim of our study was to describe the characteristics of patients treated with these new molecules and to assess their impact on metabolic parameters.*

Methodology: *We conducted a longitudinal study over a six-month period. Diabetic patients on AR GLP1 or i SGTL2 were included. Socio-demographic data, diabetes-related data, data relating to the molecules evaluated and evolutionary data at 3 and 6 months were collected.*

Results: *Our cohort comprised 56 patients with a mean age of 64.6 ± 12.1 years. The socioeconomic status of our patients was considered average (85.7%) and high (14.3%). The mean duration of diabetes was 109.7 months ± 50. Our study population consisted of e T2DM patients at very high cardiovascular risk; with associated cardiovascular risk factors (dyslipidemia, hypertension or overweight-obesity) and cardiovascular or renal complications. This justified iSGTL2 or ARGLP1 treatment in accordance with international recommendations. Therapeutically, 46 patients were on iSGLT2 (82.1%) and 10 on AR GLP-1 (17.9%), i.e. a hospital prescription prevalence of 8%. Treatment was adhered to in 91.1% of cases. Progression was marked by a significant improvement in all parameters assessed in both subgroups. Weight reduction and HbA1c reduction were much greater in the AR GLP-1 subgroup. The improvement in GFR and CAR was more significant in the iSGLT2 subgroup.*

Conclusion: *We find that iSGLT2 and AR GLP-1 are highly effective therapeutic agents in terms of glycemic control, weight reduction, control of cardiovascular risk factors and cardiac and renal protection.*

Keywords
Gliflozins, GLP-1 receptor agonists, Diabetes.

Introduction
Gliflozins (iSGTL-2) and GLP-1 receptor agonists (GLP-1 RAs) have attracted particular attention for their ability to improve cardiovascular prognosis in T2DM patients. In Africa, the number of diabetics is estimated at 24 million adults in 2021, and 55 million are expected in 2045. Diabetes is estimated to be responsible for 416,000 deaths in 2021 in Africa [1]. The estimated prevalence of diabetes in Senegal was 3.1% in 2021 [1]. In sub-Saharan Africa, the consensus developed by a group of experts for the management of hyperglycemia in T2DM has been adapted to the inadequacy of financial, organizational, material and human resources, which constitute a serious obstacle to the management of T2DM [2]. In the absence of data updated with the arrival of new molecules in our low-income countries, we deemed it necessary to study the metabolic impact of these new therapies on a population of diabetics undergoing follow-up. The primary objective of our study is to describe the characteristics of patients treated with the new molecules. The secondary objective is to assess the impact on metabolic parameters: weight, blood pressure (BP), HbA1c, albuminuria/creatininuria ratio (ACR), glomerular filtration rate (GFR).

Methodology
This was a longitudinal study lasting 6 months. All patients with diabetes, according to WHO criteria, on GLP1 or iSGTL2 AR were included. The following data were collected:

- **Socio-demographic data:** Age, gender, socio-economic level
- **Diabetes data**
  - Duration of diabetes (in months) ;
  - Cardiovascular risk factors associated with diabetes:
  - Metabolic profile
    - Anthropometric parameters: Weight in kg, BMI in kg/m2
    - PAS and PAD in mmHg
    - Level of diabetes control
    - Renal parameters: GFR according to CKD-EPI (ml/mn/1.73m^2), CAR (mg/mmol)
    - Lipid parameters: Total cholesterol (TC), LDL, HDL, TG (g/l).
  - Complications
  - Cardiovascular risk
  - Treatment
- **Data on molecules evaluated:** molecules, dosage, monthly cost, compliance
- **Progressive data at 3 and 6 months:** weight reduction, reduction in blood pressure, reduction in HbA1c, improvement in renal parameters.

SPSS software version 27.0 was used for data entry and analysis. Data were considered significant for a p value <0.05.

Results
During our study period, out of a total number of seven hundred (700) diabetics monitored, fifty-six (56) patients were recorded. These represented the number of diabetics on AR GLP1 or iSGLT-2, i.e. a hospital prescription prevalence of 8%.

Socio-Demographic Characteristics of the Study Population
The mean age was 64.6 ± 12.1 years, with extremes of 30 and 89 years. The [60-70] age group was the most represented, accounting for 42.9% of our workforce. Females predominated (64.3%), giving a sex ratio of 0.55. The socio-economic level of our patients was judged to be average to high.

Diabetes Data
The mean duration of diabetes was 109.7 months ± 50. Diabetes was associated with dyslipidemia in 91.1% of cases, with hypertension or overweight-obesity in 87.5% of cases. Patients had a mean BMI of 30.2kg/m2±4.9. Mean arterial pressure was 148.3 mmHg±14.5 systolic and 90.3 mmHg±12 diastolic. The table below summarizes the biochemical parameters initially assessed in our patients, expressed as mean or median.

Table 1: Basic biochemical parameters.

Parameters	Unit	Mean ± SD or Median
HbA1c	%	7,7 ± 1,9
RAC	mg/mmol	1,8 (1,1 - 7,8)
DFG	ml/min/1.73	59,5 (45,1 - 80)
LDL	g/l	0,9 (0,7 - 1,1)
HDL	g/l	0,4 (0,3 - 0,5)
CT	g/l	1,5 (1,3 - 1,8)
TG	g/l	0,8 (0,7 - 1,1)

Diabetic complications were dominated by retinopathy (78.5%) and chronic kidney disease (60.7%). To a lesser extent, patients had neuropathy (35.7%), coronary heart disease (32.1%) and heart failure (14.3%). The overall cardiovascular risk was very high for almost all patients. Figure 1 shows the different treatment regimens initially used in our patients.

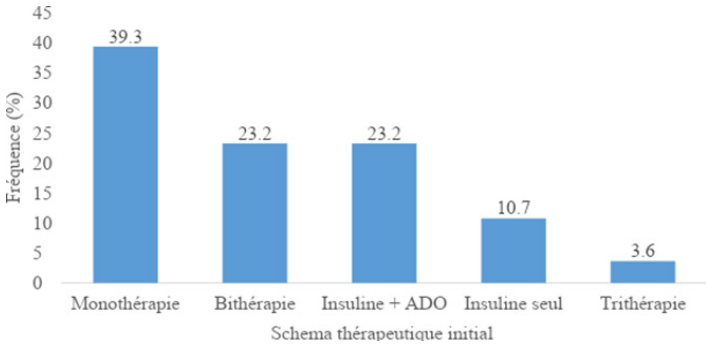

Figure 1: Distribution of patients by initial treatment regimen.

Data on Molecules Evaluated
In the iSGLT2 family, the main molecules prescribed were Dapagliflozin (80.4%) and Empagliflozin (1.8%). For GLP-1 ARs, the molecules prescribed were Semaglutide (14.3%) and Dulaglutide (3.6%). Table 2 gives details of the different molecules evaluated and their forward dosages

Table 2: Distribution of patients by INN and dosage. Patients by INN and dosage.

Therapeutic family	DCI	Dosage	Workforce	Frequency
AR GLP 1	Semaglutide	0.5mg/week	1	1,8%
		1mg/week	5	8,9%
		2mg/week	2	3,6%
	Dulaglutide	1.5mg/week	2	3,6%
iSGTL2	Dapagliflozin	10mg/d	45	80,4%
	Empagliflozin	10mg/d	1	1,8%
Total			56	100%

The average monthly cost of medication was 54,000 F CFA. Treatment was more expensive for the ARGLP1 subgroup, at 192,000 F CFA. Treatment was observed in 91.1% of patients.

Evolutionary Data at 3 and 6 Months

Weight Reduction

Figure 2 shows weight trends in the two subgroups over the follow-up period.

In the long term, weight reduction was significant, with a much greater drop in the AR GLP-1 subgroup (p<0.001).

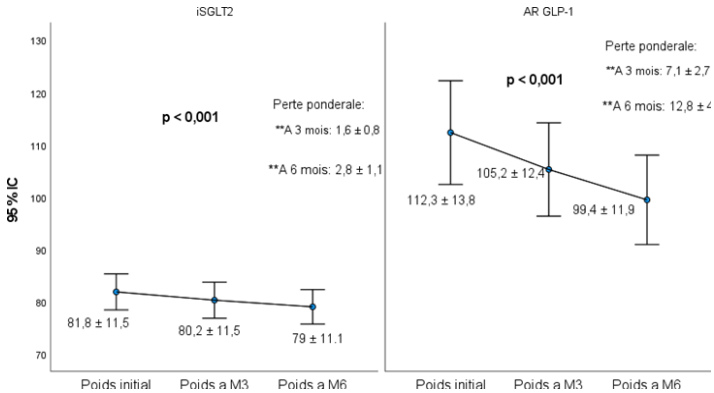

Figure 2: Weight trends in the two subgroups.

Lower blood pressure

At 3 and 6 months, there was a significant reduction in blood pressure in both subgroups (Figure 3).

Decrease in HbA1c

The fall in HbA1c was significant at 3 and 6 months in both subgroups (Figure 4). In the iSGLT2 subgroup, there was a fall of 0.5 ± 0.4% at 3 months and 0.8 ± 0.5% at 6 months (p < 0.001). The AR GLP-1 subgroup showed an HbA1c reduction of 1.5 ± 1.4% at 3 months and 2.1 ± 1.7% at 6 months (p < 0.001).

Evolution of GFR and CAR

At 3 and 6 months, the improvement in GFR and CAR was significant in both groups, and even greater in the subgroup of patients on iSGLT2 (Figure 5).

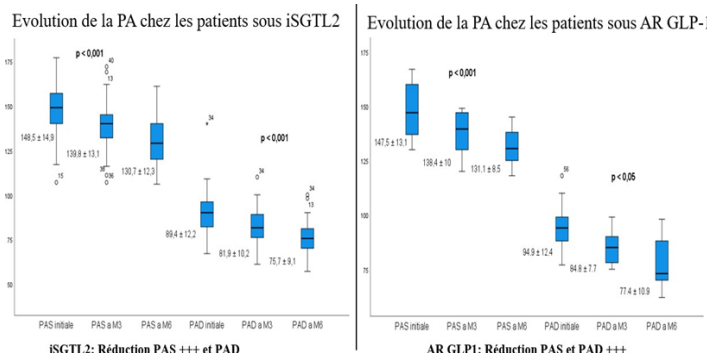

Figure 3: Changes in blood pressure in the two subgroups.

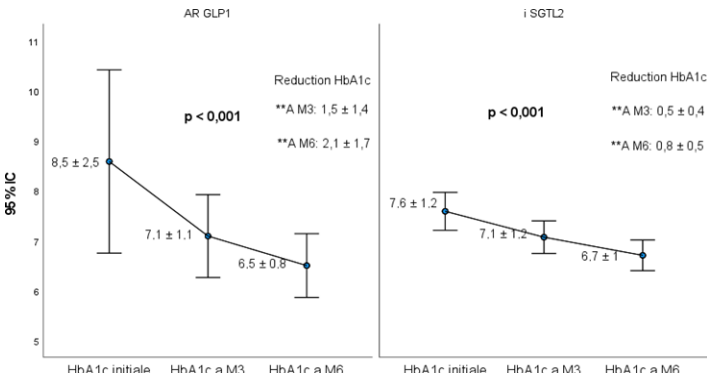

Figure 4: HbA1c trends in the two subgroups.

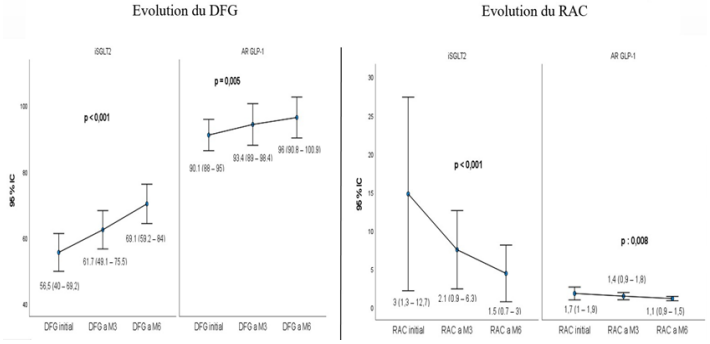

Figure 5: GFR and CAR trends in the two subgroups.

Discussion

This is a landmark study in sub-Saharan Africa. Limitations include hospital population and sample size. In our study, the mean age was 64.6 ± 12.1 years. This was consistent with the age of onset of T2DM. Demographic characteristics were generally similar to those reported in the literature. In fact, in studies describing the characteristics of users of the new therapies, mean ages ranged from 54 to 71.4 years [3-5]. The high average socio-economic level of our patients made it easy to prescribe these expensive new molecules. In our cohort, the mean duration of progression of diabetes was 109.7 months ± 50, which is longer than that found in the DISCOVER study, which was 68.4 months ± 63.6 [6]. This difference could be explained by the high mean age of our study

population, which was 64.6 ± 12.1 years versus 57.5 ± 12.0 years in the DISCOVER study. Our study population consisted of T2DM patients at high or very high cardiovascular risk, with cardiovascular or renal complications. This warranted iSGTL2 or ARGLP1 treatment in line with international recommendations. Of the patients monitored, 46 were on iSGLT2 (82.1%) and 10 on AR GLP-1 (17.9%), representing a hospital prevalence of prescription of 8%. This low prevalence raises the question of the availability of these new molecules in our regions. Weight reduction was significant in both groups, with an ultimate reduction of 12.8 kg (ARGLP1) and 2.8 kg (i SGTL2). These results are in line with those reported in the literature. In direct pairwise meta-analyses, compared with placebo, weight loss ranging from -1.47 kg to -11.47 kg was observed in overweight/obese patients on AR GLP-1 or i SGLT-2. Both agents conferred similar reductions in body weight. Semaglutide 2.4 mg (DM: -11.51 kg, 95% CI) showed the greatest reduction in body weight, followed by Semaglutide 1.0 mg (DM: -5.67 kg, 95% CI), Liraglutide 3.0 mg (DM: -4.65 kg, 95% CI) [7]. In the subgroup of patients on GLP 1 AR in our study, Semaglutide was the most prescribed, with a dosage of 1mg to 2mg per week. This could explain the greater weight loss compared with the iSGTL2 subgroup. At 3 and 6 months, there was a significant reduction in blood pressure in both subgroups. The reduction in PAS was much more marked in the iSGLT2 subgroup. The same observations were made by Diallo et al., who reported a mean reduction in SBP of 2.2 mmHg [8]. HbA1c reduction was significant in both groups, with a 2.1% (ARGLP1) and 0.8% (i SGTL2) reduction over time. In fact, the results of the network meta-analysis showed that both molecules were more effective in lowering HbA1c than placebo. The reduction was more marked with semaglutide [7]. Renal parameters improved more significantly in patients treated with i SGLT2. These results are similar to those reported in the meta-analysis by Wai Lui et al. This analysis revealed that i SGLT2 was superior to AR GLP1 in terms of composite renal outcomes, thanks to the reduction in incident end-stage renal disease [9]. In our study we did not note the initial decrease in GFR under i SGTL2, known as "dip". This could be a particularity of the black African subject. To corroborate this finding, a larger longitudinal study with a larger cohort and long-term follow-up is needed.

Conclusion

We note that iSGLT2 and AR GLP-1 are highly effective therapeutic agents in terms of glycemic control, weight reduction, control of cardiovascular risk factors and cardio-renal protection. A larger longitudinal study with a larger cohort and long-term follow-up will enable us to confirm this trend. A number of recommendations can be drawn from this study, addressed to decision-makers and pharmaceutical companies Facilitate the availability and accessibility of new anti-diabetic therapies in sub-Saharan Africa.

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