Sodium glucose cotransporter 2 inhibitors treatment in acromegalic patients with diabetes - a case series and literature review

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ABSTRACT

- ✓ Purpose: DM represents one of the most frequent comorbidities in patients with acromegaly. Sodium glucose cotransporter 2 inhibitors (SGLT2i) represent an important class for diabetes management. However, limited data is reported regarding the use of this class in patients with acromegaly and diabetes.
- ✓ Methods: Reporting data regarding patients with acromegaly and DM under treatment with SGLT2i
- ✓ Results: 29 acromegalic patients with DM were identified. Treatment with SGLT-2i was documented in nine patients, with a mean age of 61 ± 12 yr. The mean duration of treatment with SGLT2i was 27.5 ± 7.3 months. Mean HbA1c before and after SGLT-2i initiation was 8.1 ± 1.1 and 7.0 ± 0.9% respectively. Mean IGF-1 level before SGLT-2i initiation was 177 ± 68 ng/mL and the mean GH level was 0.7 ± 0.5 µg/L. All nine patients are still under treatment with SGLT2i and none of them had reported any adverse reaction related to SGLT2i.
- ✓ Conclusion: The present article provides us for the first time with new data regarding the use of SGLT2i among acromegalic patients with diabetes.

INTRODUCTION

- ✓ Acromegaly is caused by a GH secreting pituitary adenoma. GH excess causes insulin resistance and impair β cell function, predisposing a large number of patients with acromegaly to develop DM.
- ✓ Treatment of DM has been revolutionized since the introduction of SGLT2i. This important class with a unique mode of action is widely used in type 2 diabetes mellitus and recently was approved for patients with heart failure and for patients with chronic kidney disease without diabetes
- ✓ Despite the known favorable aspects of SGLT2i, is less recommended for acromegalic patients with diabetes due to increased risk of diabetic ketoacidosis
- ✓ SGLT2i increases plasma ketone levels through enhanced fat oxidation and augments synthesis as a result of increased glucagon to insulin ratio. Moreover, the decreased in plasma glucose levels that result in decreased insulin secretion, which is followed by decreased paracrine insulin inhibition of glucagon secretion also contributing to increasing ketonemia. The later effect is further augmented by decreased alpha cell glucose uptake as a result of SGLT2 inhibition. Furthermore, a decrease in ketones elimination occurs during SGLT2i.
- ✓ The excess GH in patients with active acromegaly increases lipolysis and ketone bodies production, predisposing this group of patients to develop DKA. For patients with unrecognized, active acromegaly with diabetes, treatment with SGLT-2i may increase the tendency for DKA and euglycemic DKA development particularly in patients with insulin deficiency
- ✓ Limited data is reported in the literature regarding the use of SGLT2i among patients with already diagnosed acromegaly and diabetes

METHODS and RESULTS

- ✓ Data was collected using electronic computerized registry at Clalit Medical Health Services from Western Galilee and Haifa district between the years 2000–2020 and during patients visits for routine follow-up in our department.
- ✓ Charts of patients with acromegaly and diabetes were reviewed thoroughly for current and previous anti-diabetic and acromegaly medications. Notably, that electronic computerized files enable health care practitioners to follow the monthly treatment dispensing and reported drug side effects.
- ✓ Laboratory results for fasting plasm glucose, hemoglobin A1c, IGF-1, and GH were reported before SGLT2i administration. In addition, actual hemoglobin A1c, body mass index (BMI), duration of diabetes, tumor size was reported for patients with and without SGLT2i treatment.

Table. 1 Summarizing mean results of patients identified with acromegaly and diabetes

	SGLT2i treated group	Other anti-diabetic agents treated group
Patients with acromegaly and Diabetes, n	9	20
Mean age ± SD Range (years)	61 ± 12 41-80	70 ±11 45-87
Male/Female	4:5	10:10
Type of pituitary adenoma Macroadenoma Microadenoma Not reported	 5 2 2	 9 10 1
Duration of diabetes, mean ± SD Rang (years)	9.3 ± 5.8 3-17	11.6 ± 9.7 2.5 - 40
Duration of SGLT-2i treatment (mean) ± SD Range (months)	27.5 ± 7.3 13-36	-
Other anti-diabetic treatment classes	Biguanides, Basal Ins. SUs, TZDs GLP- 1RA	Biguanides, Basal Ins. SUs, DPP-4i, GLP-1RA Glinides
FPG (mg/dl), mean ± SD	142 ± 22	121 ± 33
HbA1c, mean ± SD*	8.1 ± 1.1	-
Current HbA1c (%) mean ± SD	7.0 ± 0.9	6.6 ± 1.2
BMI kg/m², mean ± SD	32 ± 3.3	32 ± 10.3
GH (µg/L) ± SD	0.7 ± 0.5	1.65 ± 2
IGF-1 (ng/mL) ± SD	177 ± 68	145 ± 55

* The reported mean HbA1c before SGLT2i initiation.

DISCUSSION

- ✓ The results of this case series provide us for the first time with a new data regarding DM management in acromegaly, focusing on the use of SGLT-2i class.
- ✓ Treatment with SGLT-2i could be considered for diabetes management in the following categories of patients with acromegaly
- ✓ In patients with previously diagnosed T2DM and controlled acromegaly after surgery, patients with diabetes and controlled acromegaly under treatment with Somtostatin or Pegvisomant either as monotherapy or in combination, Pasireotide controlled acromegalic patients with worsening hyperglycemia or new-onset diabetes.
- ✓ SGLT-2i in the above categories can be used with metformin, as monotherapy or in combination with Dipeptidyl Peptidase 4 inhibitors or GLP-1 receptor agonists
- ✓ Insulin dose reduction is needed if the patient develops hypoglycemia.
- ✓ Essentially, all patients with acromegaly and T2DM can be treated with SGLT2i, even those with uncontrolled GH/IGF-1 levels. However, caution is needed in patients with uncontrolled acromegaly to be in lookout for DKA or EDKA