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Title: A STUDY OF 50 PACIENTS WITH POLYCYTHEMIA INDUCED BY SODIUM-GLUCOSE COTRANSPORTER-2 INHIBITORS

Abstract Type: Publication Only

Topic: Myeloproliferative neoplasms - Clinical

Background:

SGLT2 inhibitors, or sodium-glucose co-transporter 2 inhibitors, are widely used for the treatment of diabetes mellitus, chronic heart failure and chronic kidney disease. One of the most characteristic side effects is the increase in hematocrit, likely explained by the involvement of different mechanisms such as hemoconcentration due to its diuretic effect, increased erythropoiesis associated with iron availability and EPO production. In some cases, the rise in hematocrit is notable, and this has been associated with a significant increase in hematological consultations for the study of polycythemia.

Aims:

The characteristics and the management of polycythemia associated with SGLT2 inhibitors are currently under-researched. We decided to carry out a study to help diagnose, characterize and improve the therapeutic attitude with these patients.

Methods:

A retrospective study was conducted on a cohort of 50 patients undergoing treatment with SGLT2 inhibitors and referred to the hematology clinics at CHUS from January 2018 to January 2024 for the study of polycythemia.

74% of the included patients were males with an average age of 68 years. The most common SGLT2 inhibitor was empagliflozin (52%). The primary indication was Diabetes Mellitus. The average duration of treatment from prescription to the study date in hematology was 41.26 months. A standard study was conducted in all patients to rule out severe polycythemia, including at least a complete blood count, serum biochemistry with LDH, serum ferritin, serum erythropoietin, and JAK2V617F mutation analysis. Other studies (polysomnography, arterial blood gas analysis, imaging studies, etc.) were individually conducted based on clinical decision-making.

Results:

The final diagnosis was: polycythemia secondary to SGLT2 inhibitors in all patients except 3 who had it previously but with an increase in levels after the start of SGLT2 treatment. Associated clinical factors studied included tobacco use (26%), obstructive sleep apnea syndrome (16%), dyslipidemia (70%), obesity (26%), and hypertension (70%), with many cases presenting two or more associated factors. Only one patient had the JAK2 mutation and had a previous diagnosis of essential thrombocythemia (TE).

The average values of hemoglobin and hematocrit before the initiation of treatment were 16.13 and 47.74 in men, and 15.44 and 46.82 in women, respectively. There was observed variability in individual responses, with average increases from baseline values of 2.33 points in hemoglobin and 7.75 points in hematocrit. It took an average time of 26 months to reach these peak values compared to baseline levels. Ferritin levels decreased in the majority of patients an average of 104.04 ng/mL.

The decision was made to discontinue treatment with SGLT2 inhibitors in 11 patients (22%). The discontinuation of treatment resulted in an average decrease of 1.83 in hemoglobin and a 7.46% decrease in mean hematocrit in these patients. There was a subsequent slight increase in ferritin levels in these patients after discontinuation.

Only 6% of the patients experienced mild symptoms suggestive of an association with polycythemia during treatment (itching, palmoplantar tingling, uvular hypertrophy, blurry vision). Two patients experienced a thrombotic event during the treatment, with cases of strokes of unexplained causes.

Summary/Conclusion:

In conclusion, treatment with SGLT2 inhibitors is one of the most common causes of polycythemia in patients referred to our clinics. Therefore, it is important to be aware of this and avoid unnecessary studies or treatments. Although it is exceptional for it to be associated with a myeloproliferative neoplasm, we always recommend excluding it. We have not clearly observed vascular complications, but a larger series of patients would be desirable. The decision to discontinue the SGLT2 inhibitor should be evaluated on an individual basis.

Keywords: Generic drugs, Side effects, Erythrocytosis