GLP-1 Receptor Agonists Increase Fracture Risk in Patients with Obesity

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Introduction

GLP-1 receptor agonists (GLP1 RA) promote insulin secretion and satiety. They are prescribed for glycemic control in type 2 diabetes (T2D) and weight loss. Our purpose was to assess fracture risk in obese patients without diabetes following GLP1 RA use.

Methods:

A retrospective study was conducted using deidentified data from TriNetX database. Patients were included with ICD-10 diagnosis of obesity. Patients were excluded with diabetes, A1c >6.5, and those with fragility fracture risk (alcohol or nicotine dependence, osteoporosis, rheumatoid arthritis, chronic kidney disease, or chronic use of systemic corticosteroids). Initial query of n=1,155,496, those with missing demographic data were excluded resulting in n=606,364. This cohort was divided into two groups: (1) patients with GLP1 RA prescription (n=33,220) and (2) those without GLP1 RA prescription (n=593,748). Propensity matching was performed for two groups (n=33,210 each) at time of prescription. The primary outcome was fracture instance within 1 year of GLP1 RA prescription. Risk and odds ratio with 95% CI's were estimated using multiple logistic regression to account for covariate variability.

Results:

Fracture risk was significantly increased in patients with obesity without diabetes who were prescribed a GLP1 RA (3.05%) compared to patients who were not (2.61%) (OR 1.19 CI [1.09, 1.31]; RR 1.09 CI [1.04, 1.14]). Sub-analysis by BMI showed a significant increase in fracture risk in the GLP1 RA group with a BMI > 40 compared to odds of fracture for those of the same BMI who were not prescribed GLP1 RA (OR 1.26 CI[1.04, 1.52]). All other BMI classes showed no significant difference in fracture. Sub-analysis by 10 year age group had a significant increase in fracture odds in those older than 67 years, which included those ages, 68-77 (OR 2.25 CI[1.62, 3.13]) and 78-88 (OR 4.99 CI[2.68, 9.26]). BMI >40 with a GLP1RA had the most significant changes in fracture location when compared to control, including foot and toe (2.18 CI[1.67, 2.85]) , lumbar spine or pelvis (1.60 CI[1.16, 2.18]), ribs, sternum, or thoracic spine (2.04 CI[1.40, 2.97]), and skull and facial bones (1.83 CI[1.11, 3.00]).

Conclusions:

The use of GLP1 RAs are associated with an increased fracture risk in obese patients without diabetes, specifically those with BMI > 40 and age > 68. Further research is necessary to guide the prescription of GLP1 RAs in obese patients.