Efficacy of Anti-obesity Medications Among Breast Cancer Survivors Taking Aromatase Inhibitors

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Background: Aromatase inhibitors (AIs) block estrogen synthesis and are used as adjuvant treatment for breast cancer. AIs are associated with weight gain that can lead to increased cardiometabolic risk, thereby affecting health and survivorship quality in these patients. The role of anti-obesity medications (AOMs) in patients using AIs has not been studied. We sought to investigate weight loss outcomes to AOMs in patients taking AIs for breast cancer treatment.

Methods: This is a matched case-control retrospective cohort study of breast cancer survivors on AI using FDA-approved AOMs (AI/AOM group). We compared their weight loss outcomes with a group of female patients with obesity, without a history of breast cancer or AI use, on AOMs (AOM group). We matched patients by age and body mass index (BMI). Exclusion criteria: AOM initiation prior to AI therapy, ≤3 months of AOM use, history of bariatric surgery, active malignancy, or pregnancy. Primary endpoint: total body weight loss % (TBWL%) at 12 months. Secondary endpoints: TBWL% at 3 and 6 months and % of patients achieving categorical TBWL ≥5%, ≥10% and ≥15% at 12 months. We used Pearson $\chi 2$ and unpaired t-test to compare baseline characteristics and outcomes between groups, and univariate analyses to estimate the contribution of variables to TBWL% in the AI/AOM group. We present results as mean ± standard deviation.

Results: We included 99 patients: 63 in the AI/AOM group (63.5±10 years, BMI 34.4±7.0 kg/m2) and 36 in the AOM group (60.4±8.7 years, BMI 36.3±6.9 kg/m2). Liraglutide, semaglutide and phentermine were the only AOMs used. There was no difference in the frequency of use of these three AOMs among both groups (p= 0.1). AI/AOM group had a lower TBWL% compared to the AOM group during follow-up: 3.7± 4.3% vs. 5.6± 4.1% (p= 0.03) at 3 months, 3.9± 4.3% vs. 9.5± 4.7% (p< 0.0001) at 6 months, and 5.2± 5.3% vs. 10.5± 6.8% (p< 0.0001) at 12 months. Although the AI/AOM group was more likely to use lower doses of AOMs (p= 0.0004), TBWL% differences persisted among groups at 12 months after adjusting for AOM dosing (p< 0.0001). There was no difference in nutritional and behavioral modification sessions among groups (p=0.06 and p=0.9, respectively). At 12 months, the percentage of patients achieving ≥5%, ≥10%, and ≥15% TBWL was greater in the AOM group compared to the AI/AOM group: ≥5% TBWL, 85.7% vs. 50.0% (p< 0.0001); ≥10%, 57.1 vs. 20.0% (p< 0.0001); and ≥15%, 28.6 vs. 5.0% (p< 0.0001); respectively. We found no predictors of TBWL% at 12 months in the AI/AOM group.

Conclusion: Weight loss outcomes in breast cancer survivors on AIs taking AOMs are poorer compared to patients without breast cancer history and not taking AIs. Studies are needed to assess the mechanisms behind the different weight loss response to AOMs in women taking AIs, which we hypothesize may relate to AIs' anti-estrogenic effect on lean and fat mass.

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