**Abstract**

**Background**

Dementia and weight loss are independently associated with a higher risk of mortality and morbidity, and when present as comorbid conditions, further increase these risks in patients. Non-pharmacological interventions to combat weight loss should be utilized first-line, but are often insufficient. While there are multiple FDA-approved appetite stimulants, many are considered inappropriate in older patients or are associated with adverse effects. Mirtazapine is an alpha 2-antagonist commonly used for major depressive disorder, panic disorder, and chronic headaches. Currently, there have been no controlled studies assessing the effect of mirtazapine on weight gain in patients with dementia.

**Objectives**

The primary objective of this study was to compare weight change at 6 months for Veterans with a diagnosis of dementia who were initiated on mirtazapine compared to sertraline (active control). Secondary objectives were to assess weight changes at 3 and 12 months, weight changes at all three endpoints based on body mass index and depression diagnosis, and adverse drug events associated with treatment.

**Design and Methodology**

This was a retrospective cohort study of Veterans with a diagnosis of dementia who were initiated on mirtazapine or sertraline between January 1, 2009 and January 1, 2019. Diagnosis of dementia was identified by ICD-9 and ICD-10 coding or prescription of medications used to treat dementia. Patients were matched by BMI categorization. Descriptive statistics, chi square, and student t-test were used to assess endpoints.

**Results**

Mirtazapine was effective in increasing weight in the majority of patients at 3, 6, and 12 months. At 6 months, weight increased in 54.8% of patients using mirtazapine and 43.1% of patients on sertraline (p=0.0347). Additionally, 13.2% and 4.9% of patients on mirtazapine and sertraline, respectively, had a greater than 5% weight increase at 3 months (p=0.0201). Patients with BMI 25-29.99 demonstrated greater rates of weight gain with mirtazapine compared to sertraline (p=0.0186). Overall, 12 (2.9%) patients experienced an adverse drug event (mirtazapine n=6, sertraline n=6) and no patients reported a severe event.

**Conclusions**

Mirtazapine was effective at increasing weight in the majority of patients at each time point, which was largely driven by weight increase at 6 months in overweight patients. There was a similar frequency and severity of the adverse drug events. Overall, mirtazapine should be considered a safe and effective treatment option to increase weight in patients with dementia.