Background

- The long term safety of antipsychotics remains questionable and the Institute of Medicine has listed the comparison of atypical antipsychotic therapy among users of pharmacologic treatment as one of its hundred initial priority topics in comparative effectiveness research.
- Several observational studies indicate that atypical antipsychotic use in the elderly population is associated with a higher number of falls and hip fractures.1,2
- In a meta-analysis of 12 cohort or case–control studies examining the association between use of antipsychotics and the risk of fracture the relative risk was 1.59 (95% CI 1.27–1.98).
- Evidence about the differential risk conveyed by conventional and atypical antipsychotics remains inconclusive.

Objectives

To study the association between type of antipsychotic drug use and the occurrence of hip fracture in an elderly Medicare population.

Methods

- This retrospective cohort study used data from 2006-2007 of 5% national sample of Medicare claims data.
- Medicare beneficiaries with continuous Part A, B, and D enrollment in 2006-2007 and who initiated atypical or typical antipsychotic drug therapy during July 1st 2006-June 30th 2007 were identified from Part D claims.
- New users of antipsychotic drugs was identified by linking the Part D drug claims to the M stimulated drug database via the national drug codes of medications.
- Only those patients without a prescription of any antipsychotic drug before July 1st 2006 were included.
- To ensure a minimum follow-up period of six months for the observation outcomes, the study cohort included only those patients who remained on their first prescription for an antipsychotic before July 1st, 2007.
- Patients were classified into two groups: conventional (typical) and atypical users.

Results

- Users of combinations of atypical and typical antipsychotics and users who switched from one type of antipsychotic to another were excluded.
- The two groups of patients were matched using propensity score matching to control observation bias thereby ensuring that the two treatment cohorts are more comparable at baseline.
- For each patient, a propensity score was determined using the predicted probability from logistic regression models predicting type of antipsychotic use.
- Patients were matched on this score using the previously validated Greedy 5–1 matching algorithm to perform a 1:1 match.
- The variables used in the logistic regression model to estimate propensity scores included:
  - Measures of patient demographic characteristics such as age, sex, race.
  - Dichotomous variables for the prior history of individual medical conditions like acute myocardial infarction, congestive heart failure, peripheral vascular disease, cerebrovascular disease, chronic pulmonary disease, connective tissue disease, ulcer disease, mild liver disease, diabetes, hemiplegia or paraplegia, moderate or severe liver disease, and metastatic cancer.
  - Dichotomous variables for the prior history of use of antidepressant, anti-seizure, anti-parkinson’s, anti-diabetic, immunosuppressant, anti-reflective, cardiovascular, gastrointestinal, benzodiazepine and other sedative and hypnotic medications.
- Previous studies employing propensity score matching techniques to compare typical and atypical antipsychotic users have shown that such a non-parametric model discriminates well between the types of drug used.
- So, 67 covariates were used to estimate a propensity score for each individual.
- A conditional logistic regression model stratified on propensity score matched pair was used to compare the risk of hip fracture for new users in new users of atypical vs. typical antipsychotic drugs within a 180 day follow-up period starting from the date of first prescription.

Conclusion

- In the matched cohort, 40 (1.72%) typical antipsychotic users and 38 (1.63%) atypical antipsychotic users had a hospitalization for hip fracture during follow-up.
- Typical antipsychotics users did not differ significantly from atypical users on the odds of being hospitalized for hip fracture in the follow – up period (odds ratio: 1.06, 95% CI: 0.669–1.665).
- Sensitivity analysis using propensity score as a continuous variable in a multivariable logistic regression model yielded similar results (odds ratio: 1.06, 95% CI: 0.775–1.56).