Risk of Serious Cardiac Events in Older Adults Using Antipsychotic Agents

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ABSTRACT

Background: Antipsychotic agents can lead to severe cardiovascular adverse events due to multiple mechanisms involving electrophysiologic and metabolic effects. Few epidemiologic studies have evaluated the risk of serious cardiovascular-related events in typical and atypical antipsychotic users.

Objective: The purpose of this study was to compare the risk of serious cardiac events in older adults taking typical antipsychotics with those taking atypical antipsychotics.

Methods: Prescription and medical information were derived from the IMS LifeLink Health Plan Claims database. The study involved a retrospective cohort of older adults (≥50 years) taking atypical or typical antipsychotics from July 1, 2000, to December 31, 2007. The primary outcome measure was hospitalization or emergency room visit due to serious cardiac events, including thromboembolism, myocardial infarction, cardiac arrest, and ventricular arrhythmias within 1 year after the index date. The 2 groups were matched on a propensity score to minimize the baseline differences between the groups. Survival analysis was conducted on the matched cohort to assess the risk of serious cardiovascular events in typical versus atypical users.

Results: A total of 5580 patients were selected in each antipsychotic users group after propensity score matching. Serious cardiac events were found in 666 (11.9 %) atypical antipsychotic users and 698 (12.4%) typical antipsychotic users. Survival analysis revealed that typical antipsychotic users were at increased risk of serious cardiovascular events compared with atypical antipsychotic users (hazard ratio = 1.21; 95% CI, 1.04–1.40) after controlling for other factors.

Conclusions: Moderate increases in risk of serious cardiac events are associated with older adults using typical antipsychotic agents compared with atypical users. Health care professionals should carefully evaluate the benefit/risk ratio of antipsychotic agents before prescribing these agents to a vulnerable population. (*Am J Geriatr Pharmacother*. 2011;9:120–132)

Key words: antipsychotics, atypical, cardiac, cohort, elderly, typical.

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INTRODUCTION

Cardiovascular disease is a leading cause of mortality. A number of studies have suggested that the incidence of cardiovascular events has increased in patients with psychiatric disorders.[1–5] One of the factors that increases the risk of cardiovascular events in psychiatric patients is the possible adverse effects of antipsychotic medications.[6–9] Antipsychotic agents pose a substantial burden of cardiovascular events through multiple mechanisms. The use of antipsychotic agents can lead to electrophysiologic changes, such as prolongation of the QT interval and Torsade de pointes.[10,11] Recently, the US Food and Drug Administration (FDA) issued a warning to inform health care professionals about increased risk of death in elderly patients taking typical or atypical antipsychotic agents.[12] In the FDA analysis, cardiovascular events were the most common reason for death.[12] Typical antipsychotic agents (eg, thioridazine, mesoridazine, droperidol, and pimozide) and atypical agents (eg, ziprasidone) received black box warnings from the FDA for increased risk of cardiovascular events, such as sudden cardiac death and myocardial infarction (MI).[6]

Typical antipsychotics were associated with orthostasis related to α_1 adrenergic blockade and tachycardia from muscarinic cholinergic antagonism.[6] The newer so-called atypical antipsychotics, through their central histamine and 5-hydroxytryptamine antagonism, have a high predisposition for metabolic syndromes, such as obesity, diabetes, and hyperlipidemia, which are traditional risk factors for cardiovascular events.[13] The use of newer antipsychotic agents is increasing among older adults, mainly due to their use in wide range of psychiatric disorders.[14] However, data from comparative clinical trials suggested that typical agents were equally effective compared with atypical agents for the treatment of schizophrenia.[15,16] In light of recent comparative effectiveness data, it is important to establish a cardiac safety profile in older adults who are the most common recipients of antipsychotics and are associated with a substantial burden of cardiovascular morbidities.[17]

Few case–control,[18–23] cohort,[24–27] and other epidemiologic studies[1–10,28] that examined risk of adverse cardiac events associated with antipsychotics found increased cardiac risk with either typical or atypical antipsychotic use. Recently, 2 observational studies revealed greater risk of certain cardiovascular-related events with typical antipsychotics compared with atypical antipsychotics in the elderly.[29,30] Setoguchi et al[30] showed increased risk of cardiovascular specific death associated with typical antipsychotics among elderly British Columbia residents. Wang et al,[29] found a modest increase in risk of ventricular arrhythmias in Medicare enrollees within 30 days after initiation of typical antipsychotic use. However, the findings were insignificant for acute MI and congestive heart failure. Consequently, there is a need to provide further evidence related to the comparative cardiovascular safety profile of typical versus atypical antipsychotics in the community dwelling older adults in the United States. Therefore, a propensity-matched retrospective cohort study was conducted to compare the effect of typical antipsychotic agents versus atypical antipsychotic agents on the risk of hospitalization or emergency visits due to serious cardiac events in the older adults.

METHODS

Data Source: The IMS LifeLink Health Plan Claims Database

The present study analyzed data from the IMS LifeLink Health Plan Claims Database (formerly PharMetrics). Medical claims records were obtained from 94 managed care organizations, which encompassed >60 million unique patients from January 2000 to June 2008. The database included patients' enrollment, pharmacy, medical, and institutional claims. Pharmacy data included claims for each drug prescriptions' date of dispensing, the quantity dispensed, and the length of the supply. Provider and facility claims included date of service, diagnoses codes (*International Classification of Diseases, Ninth Revision, Clinical Modification* [ICD-9-CM] codes) and procedures based on the *American Medical Associations Current Procedure Terminology* (CPT-4 codes) and CMS' *Health Care Common Procedure Coding System* (HCPCS codes).

All claims in the database included a unique encrypted identifier for each patient. This identifier can be used to construct a longitudinal history of medical care utilization for each patient. Records in IMS LifeLink Health Plan Claims Database are representative of the national, commercially insured population and include various demographic characteristics such as age, gender, and plan type.[31] The standard extract from the Health Plan Claims Database consists of 2 files: a claims detail file and an eligibility file. The claims detail file contains claim-specific elements, has a number of the output variables, and is the larger of the 2 files. The eligibility file contains the enrollment information for the specific individuals included in the claims data file who meet the requestor's criteria. Only health plans submitting data for all members are included in the database, which ensures complete data capture and representative samples. As data comes from a number of different sources, they undergo a series of quality checks to ensure a standardized format. The data are also longitudinal, with a mean member enrollment time of 2 years. The IMS