ACUTE KIDNEY INJURY ASSOCIATED WITH ATYPICAL ANTIPSYCHOTICS IN OLDER ADULTS

Atypical antipsychotics, specifically quetiapine, risperidone, and olanzapine, are frequently prescribed in elderly patients to manage valid psychotic illnesses. These agents are also commonly given in this population to minimize behavioral symptoms of dementia; however, this is an off-label use of antipsychotic medications and inappropriate due to increased risk of mortality. This issue of CLIPS briefly summarizes an article that addresses the increased risk of adverse events linked to development of acute kidney injury in older adults who are prescribed an atypical antipsychotic medication. If you need further information, please contact the Samford University Drug Information Service at (205) 726-2659.


Background
- Several case reports link atypical antipsychotic use in elderly patients with abrupt loss of kidney function, or acute kidney injury (AKI).
- Known causes of AKI include hypotension, acute urinary retention, neuroleptic malignant syndrome or rhabdomyolysis, pneumonia, acute myocardial infarction, and ventricular arrhythmia, all of which have also been associated with atypical antipsychotics.
- If not treated quickly and appropriately, AKI can cause irreversible damage and even death.
- The U.S. Food and Drug Administration has placed black-box warnings on atypical antipsychotics due to increased risk of death, as compared to placebo, when used in older adults.

Methods
- Study design: population-based, retrospective cohort study.
- Participants: older adults with a new outpatient prescription for oral quetiapine, risperidone, or olanzapine.
- Exclusion criteria: previous prescription for any antipsychotic in the 180 days before the index date, patients discharged from a hospital in the two days before the index date, evidence of end-stage renal disease, receiving a prescription for more than one type of antipsychotic, no outpatient prescription in the 90 days before the index date.
- Patient characteristics, prescription drug use, diagnostic and procedural information on all hospitalizations, covariate information, and outcome data were obtained from five different databases in Ontario, Canada.
- A total of 97,777 drug-recipients were matched with 97,777 patients of similar health status who were not receiving these medications.

Outcome Measures
- Primary outcome was hospitalization from AKI in patients newly prescribed atypical antipsychotics.
- Secondary outcomes were known causes of AKI and all-cause mortality.

Results
- Patient demographics:
  - The mean age was 80.7 years and nearly 54% of participants had a diagnosis of dementia.
  - Roughly 24% of patients lived in a long-term care facility.
  - The two groups showed no statistically significant differences in baseline characteristics.

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Hospitalization with AKI occurred in 1,002 patients (1.02%) receiving quetiapine, risperidone, or olanzapine, and in 602 participants (0.62%) who were not receiving one of these drugs (RR, 1.73, [95% CI, 1.55 to 1.92]).

**Table 1. Significant Secondary Endpoints**

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Drug Recipients N = 97,777 n (%)</th>
<th>Non-recipients N = 97,777 n (%)</th>
<th>Relative Risk (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All-Cause Mortality</td>
<td>6666 (6.82)</td>
<td>2985 (3.05)</td>
<td>2.39 (2.28 – 2.50)</td>
</tr>
<tr>
<td>Acute Urinary Retention</td>
<td>329 (0.34)</td>
<td>170 (0.17)</td>
<td>1.98 (1.63 – 2.40)</td>
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<tr>
<td>Hypotension</td>
<td>384 (0.39)</td>
<td>215 (0.22)</td>
<td>1.91 (1.60 – 2.28)</td>
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<tr>
<td>Pneumonia</td>
<td>1692 (1.73)</td>
<td>1137 (1.16)</td>
<td>1.50 (1.39 – 1.62)</td>
</tr>
<tr>
<td>Ventricular Arrhythmia</td>
<td>214 (0.22)</td>
<td>151 (0.15)</td>
<td>1.47 (1.18 – 1.82)</td>
</tr>
<tr>
<td>Acute Myocardial Infarction</td>
<td>652 (0.67)</td>
<td>492 (0.50)</td>
<td>1.36 (1.20 – 1.53)</td>
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</table>

- A large majority of prescribers were family physicians (82.2%). Only 6.8% of prescribers were psychiatrists and 4.7% were geriatricians.
- AKI was significantly more associated with patients living in the community [RR=1.90 (95%CI, 1.67-2.16)] than those living in long-term care facilities [RR=1.46 (95%CI, 1.14-1.71)]. This was likely due to patients in the community receiving less regular monitoring and follow-up than patients in long-term care facilities.

**Conclusion**

- Due to increased risk of hospitalization with AKI, **atypical antipsychotics should be prescribed in the elderly for treatment of indicated mental illnesses only**.
- **Patients currently receiving atypical antipsychotics should be reevaluated to assess need for continuation.**
- Clinicians should educate both patients and caregivers of the risks of treatment and should proactively monitor for potential adverse effects.

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