Loop diuretics and angiotensin converting enzyme inhibitors increased risk of hospital admission for lithium toxicity


Clinical impact ratings GP/FP/Primary care ★★★★★★ IM/Ambulatory care ★★★★★★ Emergency Medicine ★★★★★★ Neurology ★★★★★★ Geriatrics ★★★★★

Q In older persons, is use of diuretics, angiotensin converting enzyme (ACE) inhibitors, or non-steroidal anti-inflammatory drugs (NSAIDs) associated with hospital admission for lithium toxicity?

METHODS

**Design:** population based, nested, case control study with analysis of multiple linked healthcare databases over 10 years.

**Setting:** Ontario, Canada.

**Patients:** 10 615 patients >66 years of age (mean age 72 y, 62% women) who were receiving uninterrupted lithium treatment and resided in Ontario, Canada.

**Assessment of risk factors:** use of diuretic (alone or in combination with another agent), ACE inhibitor, or prescription NSAID (including cycloxygenase 2 inhibitors). Thiazide type and loop diuretics were examined separately.

**Outcome:** hospital admission with diagnosis of lithium toxicity within 28 days of exposure.

MAIN RESULTS

413 patients (3.9%) had ≥1 hospital admission for lithium toxicity. After adjustment for potential confounders, patients treated with a loop diuretic or ACE inhibitor in the preceding 28 days had modest increased risk of hospital admission for lithium toxicity (table); these increased risks were particularly high among patients newly treated with loop diuretics or ACE inhibitors in the preceding 28 days (table). Patients treated with thiazide diuretics, NSAIDs, or topical corticosteroids did not have an increased risk of hospital admission for lithium toxicity, even during the first month of treatment.

CONCLUSION

In older persons, the use of loop diuretics or angiotensin converting enzyme inhibitors increased the risk of hospital admission for lithium toxicity, especially during the initial month of treatment.

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<table>
<thead>
<tr>
<th>Medication exposure</th>
<th>Adjusted relative risk (95% CI)</th>
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<tbody>
<tr>
<td>Any use of loop diuretics</td>
<td>1.7 (1.1 to 2.7)</td>
</tr>
<tr>
<td>Any use of angiotensin converting enzyme (ACE) inhibitors</td>
<td>1.6 (1.1 to 2.3)</td>
</tr>
<tr>
<td>New use of loop diuretics (&lt;28 d)</td>
<td>5.5 (1.9 to 16.1)</td>
</tr>
<tr>
<td>New use of ACE inhibitors (&lt;28 d)</td>
<td>7.6 (2.6 to 22.0)</td>
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*Relative risks adjusted for other potential interacting medications, previous admission for lithium toxicity, renal disease, and number of different prescription drugs in the preceding year.