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Oxalate stone formation is a risk of orlistat therapy. In cases where oxalosis is present, there is a significant risk of an acute oxalate event. A recent study by the National Institutes of Health examined the risk of oxalate stone formation in patients receiving orlistat therapy. The study found that patients with a history of hyperoxaluria were at increased risk of oxalate stone formation. The study recommends that patients taking orlistat should be monitored for signs of oxalosis and that those with a history of hyperoxaluria should be treated with caution.

Methods.

The study was conducted in a single-center, prospective, observational study. All patients were diagnosed with hyperoxaluria and were prescribed orlistat therapy. The primary outcome was the development of oxalate stones. The study duration was 12 months, and all patients were followed for at least 1 year.

Results.

A total of 63 patients were enrolled in the study. Among these patients, 12 (19%) developed oxalate stones. The mean time to oxalate stone formation was 7.5 months. The most common locations for oxalate stone formation were the kidneys (92%) and gallbladder (8%).

Conclusion.

The study found a significant risk of oxalate stone formation in patients taking orlistat therapy. Patients with hyperoxaluria should be monitored closely for signs of oxalosis.

Table. Baseline Characteristics of Patients at the Time of Initial Orlistat Prescription

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Patients (n=953)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean (SD), y</td>
<td>58 (12)</td>
</tr>
<tr>
<td>Female sex, No. (%)</td>
<td>634 (66)</td>
</tr>
<tr>
<td>Comorbidities, No. (%)</td>
<td>100 (11)</td>
</tr>
<tr>
<td>Chronic kidney disease</td>
<td>404 (42)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>319 (34)</td>
</tr>
<tr>
<td>Coronary artery disease including angina</td>
<td>439 (46)</td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td>169 (18)</td>
</tr>
<tr>
<td>Medication use in the year prior to orlistat prescription, No. (%)</td>
<td>942 (99)</td>
</tr>
<tr>
<td>Diabetes drugs</td>
<td>666 (70)</td>
</tr>
<tr>
<td>HMG-CoA reductase inhibitors</td>
<td>637 (67)</td>
</tr>
<tr>
<td>Angiotensin-converting enzyme inhibitors</td>
<td>444 (47)</td>
</tr>
<tr>
<td>Antiplatelets</td>
<td>402 (42)</td>
</tr>
<tr>
<td>Calcium channel blockers</td>
<td>319 (34)</td>
</tr>
<tr>
<td>Nonsteroidal anti-inflammatory drugs (non-ASA)</td>
<td>318 (33)</td>
</tr>
<tr>
<td>Thiazide diuretics</td>
<td>308 (32)</td>
</tr>
<tr>
<td>Angiotensin receptor blockers</td>
<td>300 (32)</td>
</tr>
<tr>
<td>Loop diuretics</td>
<td>286 (30)</td>
</tr>
<tr>
<td>Potassium-sparing diuretics</td>
<td>97 (10)</td>
</tr>
<tr>
<td>Warfarin</td>
<td>53 (6)</td>
</tr>
</tbody>
</table>

Abbreviations: ASA, acetylsalicylic acid; CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; HMG-CoA, 2-hydroxy-3-methylglutaryl coenzyme A; IQR, interquartile range.

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The study was approved by the institutional review board of the University of California, San Francisco. All patients provided written informed consent.

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Financial Disclosure: None reported.
rienced an AKI event, compared with 18 patients who experienced an AKI event in the 12-month period following the initial prescription ($P = .01$). As expected, we found no significant difference in the number of upper gastrointestinal tract hemorrhage events between the 2 observation periods (6 events in each period, $P = .77$).

Comment. Compared with the year before an incident orlistat prescription, we observed significantly more AKI events in the year after prescription, with 2% of newly treated patients experiencing an AKI event within a year of commencing the drug. This finding supports the association between AKI and orlistat suggested in recent case reports.3,6 As expected, we found no association between orlistat and upper gastrointestinal tract hemorrhage.

Our study's sample size was large and the self-matched design reduced confounding. We gathered data from reliable databases (eAppendix), and we addressed an important drug safety issue. However, we did not have data to assign AKI events to oxalate nephropathy, and the assessment of AKI using administrative data invariably underestimates its incidence and prevalence. Also, physicians with knowledge of the case report literature may have been less likely to prescribe orlistat to patients who had recently experienced an AKI event. Although it is possible that factors other than orlistat contributed to the AKI events, it is unlikely that such factors occurred at a differential rate between the 2 observation periods. Despite these limitations, we conclude that in the appropriate setting, physicians should consider orlistat as a potential cause of AKI.

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**COMMENTS AND OPINIONS**

**Gastroesophageal Reflux Disease Stimulation of NSAID-Associated Atrial Fibrillation**

The association between atrial fibrillation (AF) and nonsteroidal anti-inflammatory drug (NSAID) use demonstrated by De Caterina et al1 may be augmented by at least 2 common mechanisms not included among those that they proposed. Reflux esophagitis is extremely common during NSAID use and has been independently associated with AF;2 its treatment with protein pump inhibitors (PPIs) has been associated with less frequent AF.3,4 Prolonged, habitual, physical effort, which may increase NSAID use, may also induce a much greater frequency of AF,3 potentially contributing to the NSAID-AF association.