Background  Benzodiazepines (BZDs) are a commonly prescribed for patients receiving palliative care (1). However, BZD therapy should be tapered and discontinued in some circumstances, including situations when extended BZD therapy has not resulted in clinical improvement, when more optimal treatment options exist (such as in the management of nausea and insomnia), the patient is using supra-therapeutic doses, and when a patient’s clinical situation has improved and BZD therapy is no longer recommended (such as when cancer patients enter remission). BZD therapy discontinuation is also favorable in patients with concomitant opioid use (particularly for non-cancer pain indications (2)), substance abuse, cognitive disorders, and advanced age, as well as in patients who request discontinuation. When these situations arise, palliative care providers need to be familiar with how to deprescribe BZDs and how to develop successful tapering schedules.

How Should I Deprescribe BZDs?  A systematic review of interventions to deprescribe BZDs and other hypnotics among older people found mixed interventions yielded discontinuation rates between 27.0 and 80.0% (3). These mixed interventions included: a) temporary pharmacological substitution with trazodone and psychological support; b) patient education with tapering recommendations; and c) tapering with psychological support. Patient education included attendance at a 1-hour lectures on the adverse effects of fall risk increasing drugs (4) and the distribution of an educational booklet (5). Additional BZD deprescribing information pamphlets and patient decision aides are available through the Canadian Deprescribing Network (CaDeN) at http://www.deprescribing.org.

How Should I Counsel a Patient That Needs to Deprescribe BZDs?  Providers should first frame concerns regarding continued use, or simply explain the clinical reason for BZD discontinuation. It is often helpful to educate the patient about additional benefits of discontinuation, which may include improved memory, increased levels of alertness, and reduced risk of falls. Lastly, patients should be informed about possible rebound symptoms, particularly anxiety and insomnia, as well as the risk of BZD withdrawal and the need for careful adherence to the tapering schedule. Emphasis should be placed on the clinician’s continued commitment to symptom management, and keeping the patient safe.

What Evidence is Available to Guide Tapering Schedules?  There are no definitive studies to guide providers to a single, best approach. A Cochrane review did not endorse any specific strategy, apart from noting that tapering over approximately 10 weeks is preferable to more abrupt discontinuation (6). Other studies have concluded tapering schedules lasting > 6 months are associated with worse long-term outcomes (7). Given published strategies (8-12), expert opinion is to gradually taper a patient’s currently administered BZD dose over 8-12 weeks, usually by decreasing it between 10-25% of the baseline dose, every 2-3 weeks or so based on the BZD’s terminal half-life. The Table reviews the pharmacokinetic, pharmacodynamic, and commercially available formulations of commonly utilized BZDs to aid in individualizing tapering schedules.

How Should I Approach Potential BZD Withdrawal?  There is debate as to the prevalence of BZD withdrawal from tapering (13). Even though serious adverse reactions may occur at any dose, and even with short courses of therapy, overall, serious reactions from BZD tapering are thought to be rare (8-12). Withdrawal can include a wide spectrum of symptoms including irritability, insomnia, poor concentration, poor memory, restlessness, increased anxiety, perceptual disturbances, tremors, diaphoresis, nausea, diarrhea, confusion, psychosis, and seizure. The onset of these symptoms varies based on the half-life of the BZD administered (see the Table); ranging from as early as 24-48 hours after dose reduction of BZDs with shorter half-lives to up to three weeks after dose reduction of one with a longer half-life. Mild withdrawal symptoms such as irritability can be treated with reassurance and time. More severe withdrawal may require psychiatry consultation if appropriate with the clinical situation. Such reactions are often treated with the reintroduction of a prior BZD dose that was not associated with withdrawal, or switching to a BZD with a longer half-life than previously. Once the patient has stabilized, the taper can then continue at a slower pace. Additional adjuvant agents that are used to attenuate withdrawal
symptoms include gabapentin (14), pregabalin (15), buspirone (16), and phenobarbital (17), although none of these have high quality clinical evidence to support this use.

Table (8,9): Key: IR: immediate release; T ½: terminal half-life; *: commercially available in the US

<table>
<thead>
<tr>
<th>Generic Name</th>
<th>IR* Formulations (mg)</th>
<th>Pharmacokinetic Properties</th>
<th>Comparative Oral Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alprazolam (Xanax®)</td>
<td>0.25, 0.5, 1, 2</td>
<td>None</td>
<td>Renal</td>
</tr>
<tr>
<td>Clonazepam (Klonopin®)</td>
<td>0.5, 1, 2</td>
<td>None</td>
<td>Renal</td>
</tr>
<tr>
<td>Diazepam (Valium®)</td>
<td>2, 5, 10</td>
<td>Desmethyl-diazepam, Temazepam, Oxazepam</td>
<td>Renal</td>
</tr>
<tr>
<td>Lorazepam (Ativan®)</td>
<td>0.5, 1, 2</td>
<td>None</td>
<td>Renal</td>
</tr>
<tr>
<td>Oxazepam (Serax®)</td>
<td>10, 15, 30</td>
<td>None</td>
<td>Renal, fecal</td>
</tr>
<tr>
<td>Temazepam (Restoril®)</td>
<td>7.5, 15, 22.5, 30</td>
<td>None</td>
<td>Renal</td>
</tr>
</tbody>
</table>

References

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