Sleep and the elderly – Part II

By Helen Brown

This article is a follow-on from last month. The previous article focussed on the physiology of sleep, insomnia and non-pharmacological therapies to treat insomnia. This article will outline the role of hypnotics, their adverse effects and how to effectively cease long-term benzodiazepine use.

Mrs EF is a 78-year-old woman living alone at her home. Her current medication list is below and her main concern is long-term use of oxazepam which she feels may no longer be effective for her:

- Paracetamol SR 665 mg
  - 2 when necessary
- Aspirin 100 mg
  - 1 in the morning
- Fish Oils 1,000 mg
  - 1 daily
- Indapamide SR 1.5 mg
  - 1 in the morning
- Venlafaxine SR 150 mg
  - 1 in the morning
- Risedronate/Ca 35/500 mg
  - 1 daily
- Vitamin D3 1,000 IU
  - 2 in the morning
- Oxazepam 30 mg
  - 1 at night

Hypnotics

As discussed previously, the use of cognitive and behavioural therapies (CBT) is the recommended initial treatment for insomnia. However, these strategies can take several weeks to become effective: a short-acting benzodiazepine (BDZ), zolpidem or zopiclone can be used where immediate short-term relief of insomnia is required, e.g. situational stress or family grief where an immediate effect is desired or where CBT has been ineffective in chronic insomnia.

BDZs potentiate the inhibitory effects of gamma-aminobutyric acid (GABA) throughout the central nervous system. This results in several effects: anxiolytic, sedative, hypnotic, muscle relaxant and antiepileptic effects. Oxazepam and temazepam are the BDZs that are most commonly used for their hypnotic effects, although only temazepam is recommended in the Australian Therapeutic Guidelines for this indication.

BDZs have proven efficacy for improving sleep when used 2–5 days per week for less than two weeks – effectiveness beyond two weeks has not been demonstrated. This level of use enables the agent to maintain efficacy whilst minimising tolerance or dependence. Both oxazepam and temazepam are considered short-acting agents: oxazepam has been reported to have a half-life of 4–15 hours and temazepam 5–20 hours – half-lives may be longer in woman than men. Side effects of benzodiazepines are dose related but can be unpredictable due to the wide variation in half-life. Effects such as sedation, cognitive impairment and psychomotor impairment are more common in the first few days of therapy and may reduce with continued use. BDZs cause an increase in stage 2 (light sleep) and reduce the duration of stage 3 and 4 sleep (restorative sleep phases): this leads to daytime fatigue and somnolence.

Zolpidem and zopiclone (sometimes called the ‘z-drugs’) have similar sedative properties to the benzodiazepines, but minimal anxiolytic, muscle relaxant and antiepileptic properties. There is no evidence to suggest that these are more or less effective hypnotics than the BDZs and they also are associated with an increased risk of falls in the elderly (although less so than the BDZs).

The z-drugs cause similar adverse effects to BDZs and may produce tolerance, dependence and withdrawal symptoms that are typical of benzodiazepines. In addition, they commonly cause diarrhoea and there have been reports of visual hallucinations, psychosis and bizarre behaviours with amnesia (e.g. sleep-driving). Zopiclone has been associated with a metallic taste, dry mouth and dizziness. One advantage of these agents is that they appear to preserve stage 3 and 4 sleep – the restorative stages of sleep. These drugs have been purported to have less potential for abuse, cause less dependence and have fewer withdrawal effects. Nonetheless, there have been reports of such problems with the z-drugs.

Older people are more prone than younger ones to the adverse effects of any hypnotic and the likelihood of such effects does not appear to diminish with time. The increased sensitivity of older people to the effects of BDZs is due to age-related alterations in the receptors of the central nervous system. BDZ receptors in the brain become more sensitive with age and the result is increased sedation, unsteadiness.
and memory loss. Meta-analyses suggest that 13 people over the age of 60 need to be treated for one month with a benzodiazepine in order for one person to have improved sleep, i.e. NNT* of 13. However, one in every six people treated will have an adverse effect, i.e. NNH* is 6.

Older people taking BDZs are at 4.8 times the risk for memory loss, confusion and disorientation compared to a similar aged person who is not taking a hypnotic. Dizziness and loss of balance occurs in people taking hypnotics at twice the rate of the remainder of the population and urinary incontinence is 40% more common in those taking BDZs.

The risk of falls in the elderly increases by 60% with the use of hypnotics and hip fracture risk increases by 50%. In fact, by using epidemiological measures of population-attributable risk, this would translate to about 1,500 hip fractures in Australia each year that may be attributed to the use of benzodiazepines.

Withdrawal of long-term hypnotics

Tolerance to the sedative effects of hypnotic agents occurs quickly – generally within 2–4 weeks of regular use, but the adverse effects continue to be problematic. BDZ use reduces the time spent in deep restorative sleep – stage 4 – and this stage is important for memory consolidation. Reduction in stage 4 sleep may explain adverse effects of BDZs such as cognitive decline and memory loss.

Stopping regular, long-term BDZ use in an older person can reduce the risk for falls and improve memory, alertness and concentration. (Elderly nursing home residents who were tapered off BDZs showed improvements in memory and cognitive function. Sudden cessation of a benzodiazepine can result in anxiety, insomnia, irritability, increased heart rate and increased blood pressure.

A tailored approach is essential to achieve successful withdrawal; a dose reduction of 10–20% of the weekly dose should be carried out over 8–12 weeks – or even longer for some patients who have been taking BDZs for many years.

If a person is taking multiple BDZs, or high doses, it may be more effective to stabilise them on an equivalent dose of diazepam and then commence a gradual reduction in dose. (Table 1) Diazepam is preferred due to its long half-life which diminishes withdrawal effects when gradually tapered: MIMS states a half-life of 20–48 hours, but this can increase to 90 hours, or more, in 80 year olds. Specialist involvement is recommended with patients on very high doses of benzodiazepines.

Recommendations

1. Mrs EF requires advice on good sleep practice (Table 2) but, in chronic insomnia, this is not effective unless used with at least one other therapy. After discussion with her, it appears that her main problem is falling asleep and so stimulus control therapy may be of the most benefit to her.
   a) Stimulus Control Therapy (SCT) can be taught to a patient by the GP or pharmacist and involves going to bed only when sleepy. If the person does not fall asleep within a perceived 20 minutes, they should get out of bed.
   b) For some patients, referral to a psychologist is of value. (Mrs EF has osteoarthritis and depression – both known causes of insomnia. From discussion with her, it does not appear that these factors are affecting her sleep. However, it is imperative that these conditions are well controlled before commencing SCT and are continually monitored.)

2. Behavioural therapies need to be utilised in conjunction with a gradual reduction in BDZ dose, as outlined in Table 3.

Although the evidence is clear that BDZs are only effective in the short-term, it is common to see long-term use of such agents, especially in the elderly. The community has a lack of awareness of the risks of continued use and clinicians may have the misconception that discontinuation attempts in the elderly will fail. Qualitative studies of clinicians have uncovered a belief that withdrawal is not possible, yet various other studies have shown cessation success rates of up to 80% with relapse rates of less than 50% over 1–5 years.

Interestingly, it has been postulated that the slower clearance of benzodiazepines

Table 1. Dose equivalent for common benzodiazepines

<table>
<thead>
<tr>
<th>Drug</th>
<th>Approximate dose equivalent to 5 mg diazepam</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nitracepam</td>
<td>2.5 mg</td>
</tr>
<tr>
<td>Oxazepam</td>
<td>15 mg</td>
</tr>
<tr>
<td>Temazepam</td>
<td>10 mg</td>
</tr>
</tbody>
</table>

* There is good evidence for sunlight exposure to help insomnia. In a study of older people, daily exposure to bright light reduced the time spent awake during sleep time by an hour. It also improved efficiency of sleep from 78% to 90%

Table 2. Sleep hygiene measures

<table>
<thead>
<tr>
<th>Activities that improve sleep</th>
<th>Activities that impair sleep</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Choose a regular time to go to sleep</td>
<td>• Daytime nap (unless it is &lt;15 minutes)</td>
</tr>
<tr>
<td>• Choose a regular time to get up each day</td>
<td>• Excessive alcohol intake</td>
</tr>
<tr>
<td>• Regular daytime exercise – preferably in the sun. * (Not within 3–4 hours of sleep)</td>
<td>• Smoking</td>
</tr>
<tr>
<td>• Take a hot bath before bedtime</td>
<td>• A heavy meal within 3 hours of bedtime</td>
</tr>
<tr>
<td>• Relax and unwind before getting into bed</td>
<td>• Caffeine-containing drinks within 4–6 hours of bedtime</td>
</tr>
<tr>
<td>• Drink warm milk and have a small carbohydrate snack before bed</td>
<td>• Highly illuminated digital clocks in the bedroom</td>
</tr>
<tr>
<td>• Ensure sleep is at a comfortable temperature and in a quiet environment</td>
<td>• Pets sleeping in the bedroom</td>
</tr>
<tr>
<td>• In bed awake for longer than 20 minutes</td>
<td>• Lying in bed awake</td>
</tr>
</tbody>
</table>

* * There is good evidence for sunlight exposure to help insomnia. In a study of older people, daily exposure to bright light reduced the time spent awake during sleep time by an hour. It also improved efficiency of sleep from 78% to 90%.
Table 3. Reduction plan for Mrs EF

<table>
<thead>
<tr>
<th>The table indicates the number of oxazepam 30 mg tablets to be taken each night.</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Mon</strong></td>
</tr>
<tr>
<td>-------------------</td>
</tr>
<tr>
<td>Week 1</td>
</tr>
<tr>
<td>Week 2</td>
</tr>
<tr>
<td>Week 3</td>
</tr>
<tr>
<td>Week 4</td>
</tr>
<tr>
<td>Week 5</td>
</tr>
<tr>
<td>Week 6</td>
</tr>
<tr>
<td>Week 7</td>
</tr>
<tr>
<td>Week 8</td>
</tr>
</tbody>
</table>

Ask the GP to prescribe 15 mg tablets from week 6.

Week 9 1 1 1 ½ 1 1 1
Week 10 1 ½ 1 ½ ½ 1 ½

Continue with a 10–20% reduction in total weekly dose every 1–2 weeks.

in the elderly leads to less severe withdrawal symptoms during a gradual taper. There is also a diminished neuronal capacity in the elderly and this results in less rebound overactivity and withdrawal symptoms. An HMR is an ideal time to educate a person about the potential problems associated with benzodiazepines and to support them to attempt a gradual withdrawal – in consultation with their GP.

For consumer and health professional information and handouts about sleep, visit: www.nps.org.au/sleep

Questions

1. Which of the following statements is correct?
   a) There is good evidence to suggest that zolpidem and zopiclone are more effective hypnotics with fewer adverse effects when compared to benzodiazepines.
   b) Zolpidem and zopiclone cause similar adverse effects to benzodiazepines and may produce tolerance, dependence and withdrawal symptoms that are typical of benzodiazepines.
   c) Benzodiazepines are preferable to zolpidem and zopiclone in older adults since they appear to preserve stage 3 and 4 sleep.

2. Based on the results of meta-analyses, how many people over the age of 60 years need to be treated for one month with a benzodiazepine so that sleep will improve for one person?

   a) 6.
   b) 9.
   c) 13.
   d) 17.

3. An elderly lady has been taking one 30 mg Murelax tablet each night plus one Mogadon 5 mg tablet each night for several years. Which of the following options would be most appropriate?
   a) These agents should be stopped immediately, since they are having little hypnotic benefit due to tolerance.
   b) Change to 20 mg diazepam at night and stabilise her for a few days. Then reduce dose by 10–20% of the weekly dose – every 1–2 weeks.
   c) Reduce the dose of each agent by 15–25% of the weekly dose (every 1–2 weeks).

4. Which of the following activities are all useful for improving sleep?
   a) Room at a comfortable temperature, daily exercise – preferably in the sun.
   b) Keep bedroom temperature cold, glass of alcohol before bed, daytime nap.
   c) Exercise late at night, bright light therapy.
   d) Small meal just before bed, cup of tea, go to sleep at the same time each night.

References