



Benzodiazepine dependence



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BACKGROUND

Benzodiazepine dependency can occur as a result of treatment for anxiety disorders or sleep disturbance. While benzodiazepine withdrawal can be challenging, cessation of use can be even more difficult if there are other comorbidities such as oestrogen deficiency with vasomotor symptoms and anxiety disorders.

OBJECTIVE

This article provides practical information for general practitioners in the management of patients with benzodiazepine dependence.

DISCUSSION

Some patients may have common medical presentations and coexisting drug dependence. It is often difficult to separate these two issues. In the case of benzodiazepine dependence, gradual withdrawal over time and nonpharmacological treatment of the symptoms of withdrawal such as anxiety or insomnia is effective. Better outcomes are achieved where the GP discusses and plans strategies well in advance with the patient. Treatment often involves multiple interventions from various health professionals. General practitioners are ideally placed to coordinate such treatment.

This is the eighth article in a series of case files from general practice that explore treatment issues around substance use and commonly encountered general practice presentations.

Case history – Shelley

Shelley, 46 years of age, has recently moved into the neighbourhood. She presents with difficulty sleeping, hot flushes, mood swings, irritability and tiredness. Her sister suggested that her symptoms are typical of menopause. Shelley works as a secretary and lives in a de-facto relationship with John, a 40 year old plumber. Neither has ever wanted children. Shelley drinks three glasses of wine spread throughout the week, smokes about 20 cigarettes per day and takes no other recreational drugs or prescribed medication. She has no family history of breast cancer and a recent screening mammogram was normal, as was her Pap test. Medical notes from her previous general practitioner indicate she attended the clinic on average about once per fortnight for various minor complaints.

Shelley says she is reluctant to take hormone therapy (HT) because she read a newspaper article suggesting an increased risk of breast cancer associated with HT. However, nothing she has tried seems to help and her symptoms are affecting her work performance. In particular, sleepless nights cause her to be tired and short tempered the next day and she is making silly mistakes at work.

Shelley says that she has always been an anxious person, but feels more anxious than ever before. She is stressed about her relationship with John and concerned about whether John, who is 6 years younger, will view her differently now that she is going through the 'change of life'.

Initial assessment

Your initial assessment is that Shelley does have vasomotor symptoms suggestive of menopause, but many of her symptoms may also relate to anxiety or depression and there are a number of psychosocial issues causing her distress.

You examine Shelley and reassure her that all is normal. Although Shelley asks for 'something to help her sleep', you decide not to prescribe any medication at this stage. Instead, you encourage her to maintain her active lifestyle, consider smoking cessation, and you give her information about menopause and hormone therapy (HT). You order appropriate blood tests and ask her to return in 1 week to discuss a management plan.

Shelley's blood tests are all normal: in particular she is not anaemic, has normal thyroid function and a normal lipid profile. However, she doesn't attend for review the following week.

Shelley returns 2 months later for an influenza vaccination. You remember wanting to explore her anxiety problems at the last visit. She tells you she visited another doctor on recommendation from her sister. She indicates that the drugs this GP has prescribed have helped immensely with her tiredness and sleep problems and she feels like a 'new woman'. Unfortunately, when you enquire as to the medication, Shelley says she can't remember the name, but it is not HT. She says she was too worried about the risk of breast cancer to try HT. You are intrigued to know what she is taking and ask Shelley to bring the prescription or medication with her to her next appointment. You take this opportunity to ask her more about her anxiety symptoms and conclude that she has significant anxiety personality traits.

A problem emerges

About 3 months later, Shelley presents in distress. She says that she is back where she started – sleepless nights, hot flushes and mood swings. The medication she was taking is no longer working even when she doubled the dose. You make a mental note that Shelley is experiencing tolerance to whatever the drug is. She shows you a bottle of oxazepam. Although she was told to use it only as needed, she ended up taking them every day. When the oxazepam didn't seem to help any longer, she increased the dose. This increase helped initially, but she didn't want to take more as she experienced drowsy after effects. Shelley has since wanted to stop using oxazepam, but feels worse when she doesn't use them. Currently she is taking 3 x 30 mg oxazepam per day.

Anxiety symptoms and benzodiazepines

As in Shelley's case, physical and psychological causes of anxiety are often difficult to separate. Both are temporarily helped by benzodiazepines (BZD). Benzodiazepines are central nervous system depressants acting through GABA-A receptors. The use of BZD can result in physical and psychological dependence.^{1,2} This can occur with the usual prescribed doses and with short term use.³ The features of dependence include: feeling unable to cope without the drug, unsuccessful attempts to cut back or stop drug use, and feeling uncomfortable when not taking the drug.⁴

Benzodiazepine dependence

Table 1. Benzodiazepine withdrawal symptoms¹¹

Anxiety	Somatic symptoms of anxiety
Depressed mood	Depersonalisation, de-realisation
Sleep disturbance	Hypersensitivity to touch, pain
Tremor, shakiness	Muscular aches, pains, twitches
Headache	

You suspect that Shelley has developed dependence on oxazepam. This is complicated by the fact that she has premorbid anxiety traits and symptoms related to menopause that can be similar to symptoms of BZD withdrawal (Table 1).

You explain to Shelley that her symptoms have likely originated from a combination of factors. These are physical changes in her body (oestrogen deficiency), stresses in her life (relationship, family issues) – and how she copes with these stresses – as well as the effect of now being dependent on oxazepam. You explain that oxazepam is one of a class of drugs called 'BZD'. You describe how BZD relax and sedate, but also describe how the body responds to continued use by becoming tolerant to the effects of the drug. This means that a higher dose of drug is required to achieve the same effect. This ever increasing and frequent use eventually creates a physical dependency on the drug so that when the drug is not taken the body feels unwell – a state only relieved by more use.

Management plan

You tell Shelley there are many ways of helping her feel better such as treating oestrogen deficiency, working on family/home issues, more appropriate treatments for anxiety and depression such as behavioural treatments (eg. relaxation techniques and exercise), and if necessary, nonaddictive drug treatments (eg. selective serotonin reuptake inhibitors) and gradually withdrawing from BZD.

You ask Shelley to identify the symptoms that most bother her and to keep a diary for 1 week noting the time and severity of each symptom, factors which have contributed to these and her responses, as well as time and

amount of oxazepam taken. You tell her these will be used to identify simple and practical cognitive behavioural strategies to help reduce her symptoms.⁵

Shelley returns with her diary. With her assistance you are able to identify that insomnia and embarrassment about hot sweats during the day are the two symptoms that most concern her. Shelley worries a great deal about what others think, and has a tendency to catastrophise about small things that escalate quickly into anxiety about both her current situation and the future. For instance if she gets hot flushes at work, she starts to think that everyone is watching her, she gets nervous, makes mistakes, then worries about her superiors noticing and losing her job, gets more nervous and makes more mistakes. Oxazepam still helps her feel calmer during the day, but is not helping with her sleep.

You explain to Shelley that you would like to help her establish better sleep habits and teach her relaxation techniques (*Table 2*), as well as helping her reduce oxazepam use. You explain that these simple techniques are more likely to help her in the long term than any medication. You also recommend counselling to help her develop strategies to reduce unhelpful negative thoughts.

Withdrawing from benzodiazepines

To withdraw Shelley from oxazepam you first convert the drugs into an equivalent dose of diazepam (*Table 3*); this works out to 30 mg diazepam per day. You plan to first stabilise her on 10 mg of diazepam three times per day before working further on the reduction regimen. Shelley agrees to give this a try and is given information on the possible withdrawal symptoms.

Dealing with anxiety

Shelley is responsive to the suggestion of learning practical ways to manage stress on her own. This is ideal, as you want her to take responsibility for handling her own problems, learn new techniques to improve the way she handles stress, and then practise these techniques on a regular basis.

The primary use of relaxation techniques are in anxiety disorders, physical conditions with a strong psychological component, and in conditions that can be modulated by levels of arousal (eg. pain). They are also commonly used in programs for stress management.⁶

A good night's sleep

People with insomnia often complain of poor concentration, changes in mood, feeling irritable or anxious, and problems in their ability to function at work or home. Patients (and some doctors) may be unaware that the onset of insomnia can signal a serious medical condition or psychiatric illness. In some people, a medical aetiology such as the vasomotor symptoms of oestrogen deficiency is the cause of insomnia.

The management strategy used to treat insomnia is dependent upon the duration, severity and underlying cause. Appropriate advice about good sleep habits is essential,

eg. avoiding stimulants or high activity before attempting sleep. Nonpharmacological interventions have been shown to be effective in managing persistent insomnia.⁷

Medications can be used to induce sleep. However, although they may provide some relief, they do not treat the underlying cause. The efficacy of BZD for the long term treatment of insomnia is controversial. Evidence of continued efficacy beyond 4 months is not well documented.^{3,8} If BZD are used, a brief, interrupted course of 2–4 weeks duration using a short acting BZD with a tapered withdrawal is recommended. It is important to regularly assess the efficacy of treatment and the need for continued medication (*Table 4*).

There are also newer classes of drugs that can be used in treating insomnia, but the National Health Service's National Institute for Clinical Excellence (NICE) appraisal committee recently found no compelling

Table 2. Relaxation techniques: progressive muscle relaxation

- Lie on your back in a comfortable position. Allow your arms to rest at your sides, palms down on the surface next to you
- Inhale and exhale slowly and deeply
- Clench your hands into fists and hold them tightly for 15 seconds. As you do this, relax the rest of your body. Visualise your fists contracting, becoming tighter and tighter, then let your hands relax slowly
- Now, tense and relax the following parts of your body in this order: face, shoulders, back, stomach, pelvis, legs, feet, toes. Hold each part tensed for 15 seconds and then relax your body for 30 seconds before going on to the next body part
- Finish the exercise by shaking your hands and imagining the remaining tension flowing out of your fingertips
- When you have finished releasing tension throughout the body, continue deep breathing and relaxing for another minute or two. At the end of this exercise, you should feel lighter and more energised

Table 3. Benzodiazepines in equivalent doses of diazepam²

	Diazepam 10 mg is approximately equivalent to:
Alprazolam (Xanax)	1 mg
Chlordiazepoxide (Librium)	20 mg
Flunitrazepam (Rohypnol)	2 mg
Lorazepam (Ativan)	1 mg
Nitrazepam (Mogadon)	10 mg
Oxazepam (Serepax)	30 mg
Temazepam (Normison, Euhypnos)	20 mg

Table 4. Guide for benzodiazepine cessation

Goal	<ul style="list-style-type: none"> Define a realistic goal with the patient
Withdrawal symptoms	<ul style="list-style-type: none"> Explaining the likely course of withdrawal. Likely length and intensity of withdrawal symptoms may result in patients experiencing reduced withdrawal severity¹²⁻¹⁴ The severity and duration of withdrawal syndrome is influenced by factors such as duration of drug use, doses used, drug half life, individual personality style and the expectations of both patient and doctor⁸
Regimen and rate	<ul style="list-style-type: none"> Define the rate of reduction together with the patient. Giving the patient a sense of control helps to increase commitment and success Convert short acting to long acting benzodiazepines (Table 3). Short acting drugs result in repeated withdrawal as the drug wears off, and repeated use (which relieves withdrawal symptoms) reinforces drug use. The use of long acting drugs reduces and gives better control of withdrawal symptoms
Review	<ul style="list-style-type: none"> Maintain close contact with patient during the withdrawal phase Titrate dose reduction according to withdrawal symptoms Monitor for increased alcohol or nicotine consumption during withdrawal Be aware of any mood shifts or relationship difficulties Give patient information about withdrawal
Support	<ul style="list-style-type: none"> Keep an 'open door' policy If unsuccessful, encourage patient and try again when they are ready

evidence of a clinically useful difference between the 'z' drugs (zolpidem and zopiclone) and short acting BZD in terms of effectiveness, adverse effects, or potential for misuse or dependence.^{9,10}

The outcome

Shelley decided to try HT after a detailed discussion about the advantages for symptom relief and a realistic appraisal of the risks for short term use in a woman of her age and risk profile. Her sleeping gradually improved by following good sleep habit guidelines. In addition to the relaxation techniques you gave her, she enrolled in relaxation classes provided at her workplace, increased her regular exercise and gave up smoking. She saw a counsellor for a number of sessions of cognitive therapy.

John attended with Shelley for a consulta-

tion where the issues of HT, anxiety and BZD withdrawal were openly discussed. To Shelley's evident joy, John was most interested and willing to be of assistance. Shelley managed to successfully withdraw from BZD in about 4 months.

Conclusion

General practitioners may see patients having both medical presentations and drug dependence. It is often difficult to separate the two, and treatment often involves multiple interventions. In the case of BZD dependence, gradual withdrawal over time and the nonpharmacological treatment of anxiety and insomnia can be effective.

Conflict of interest: none declared.

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