Benzodiazepines: risks, benefits or dependence

A re-evaluation

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A College statement

Since the College statement on the subject of benzodiazepine dependence was published in March 1988 there have been further developments in our knowledge of dependence on benzodiazepines and these have been examined by the Royal College of Psychiatrists Psychopharmacology Committee. This statement is the result.

Whenever benzodiazepines are prescribed, the possibility of dependence and other harmful effects must be considered. However, the risks of dependence have to be balanced against the benefits that in many cases follow from the use of benzodiazepines. The risk:benefit ratio may be hard to measure and is ultimately a matter of clinical judgement.

Benefits

Anxiety-reducing effects

Benzodiazepine anxiolytics should be prescribed primarily for the short-term relief of anxiety and related symptoms, when it is disabling and severe resulting in significant distress or problems in social functioning. Other forms of anxiety are best treated by psychological means or pharmacological treatments suitable for long-term use. To reduce the risk of dependence on benzodiazepines they should not be prescribed regularly for longer than one month, and ideally be given on an as-required basis and intermittently every few days. Benzodiazepines are rapidly effective, with their maximum benefit shown in the first few weeks of treatment. Thus they may offer a period of respite while other more effective treatments such as cognitive–behavioural therapy or antidepressants have time to act.

There are circumstances in which longer-term prescription of benzodiazepines may be considered desirable because the alternatives to benzodiazepines are considered worse than the use of benzodiazepines. This may be in conditions such as chronic treatment-resistant anxiety or in patients who have established dependency and are unable to withdraw successfully. In rare instances long-term prescriptions of benzodiazepines may be seen as maintenance treatment or harm-limitation in patients who would otherwise consume illicit benzodiazepines. There are other situations where anxiety is complicated by other illnesses and where the risk of dependence may be considered acceptable because of the severity of the other disorder such as, for example, schizophrenia. In other instances, for example obsessive–compulsive disorder, there is much less evidence to support the use of benzodiazepines. In general, anxiolytic benzodiazepine use has dropped to about one-quarter of its use 15 years ago.

Sleep

Benzodiazepines are effective hypnotics for the short-term treatment of insomnia. Again, their use should be limited to between 2 and 4 weeks and at the lowest dose and intermittently. Care should be taken to exclude any other primary condition such as depression or substance misuse as a cause for insomnia. Some conditions such as sleep apnoea will also be aggravated by the use of benzodiazepines. They should be used in the short-term while more appropriate longer-term treatments are instituted, if the problem is long-term. The majority of hypnotic sleeping tablets are consumed by the elderly whose insomnia is chronic. They often have co-existing physical disease and a pragmatic approach to their treatment needs to be adopted. In general the consumption of benzodiazepine sleeping pills has remained steady over the years without the reduction which has been seen with anxiolytics. Newer

alternatives such as zopiclone and zolpidem are now available. They may have relative advantages in terms of dependence and withdrawal over traditional benzodiazepines and should be considered instead.

Depression

Depression is not a primary indication for benzodiazepines. However, if the depression is accompanied by anxiety or severe distress then, in severe cases, benzodiazepines may be prescribed for short-term relief when the patient is subject to extreme distress. They may offer symptomatic relief for a few days while antidepressants have time to act, or cover the initial increase in anxiety that may occur when some antidepressants are prescribed.

The prescribing of benzodiazepines in cases of depression may have serious consequences and there is the possibility that they may precipitate suicide attempts in impulsive individuals. Withdrawal from benzodiazepines in many cases may unmask and sometimes precipitate depression as this is one of the symptoms frequently found in benzodiazepine withdrawal syndromes.

Anticonvulsant and muscle relaxant actions

Benzodiazepines have anticonvulsant and muscle relaxant effects independent of their anti-anxiety ones. These are often invaluable, particularly in the emergency treatment of epilepsy and the management of spasticity or muscle spasms.

Excitement, agitation and severe psychotic disturbance

Patients with excitement, agitation and severe psychotic disturbance may be prescribed short-term benzodiazepines as part of 'rapid tranquillisation' or as an adjunct to their antipsychotic drugs. The dose and duration of such treatment needs to be monitored closely.

Risks

Dependence

Dependence on benzodiazepines is mainly manifest by withdrawal symptoms on cessation which may sometimes be prolonged and result in symptoms which may be hard to distinguish from other anxiety-related disorders such as panic disorder. In general, withdrawal reactions are short-lived, lasting for up to a month, but there is controversy about whether symptoms persisting for weeks and months and up to a year are really withdrawal reactions or the manifestations of a chronic underlying neurosis or an exacerbation of the underlying condition triggered by tranquilliser withdrawal.

Long-term dependence should be treated by gradual withdrawal and psychological support with the addition of cognitive–behavioural therapy to attenuate any symptom which may occur. Unfortunately, pharmacological and psychological aids have only a minor benefit and many patients are unable to stop their drugs, or show persistent symptoms after withdrawal. In patients with persistent symptoms, a decision needs to be taken about whether they are generally better off with or without the medication. This decision needs to be taken in conjunction with the patient. Again, the long-term risks of using benzodiazepines need to be balanced against the benefits.

Depression

Benzodiazepines may worsen or mask the symptoms of depression. This can have serious consequences, denying the patient the opportunity of effective antidepressant medication or resulting in disinhibition which may lead to suicide attempts. Withdrawal from benzodiazepines may in some cases unmask or even precipitate a depression as one of the symptoms of benzodiazepine withdrawal. A substantial proportion of patients become depressed on tranquilliser withdrawal and then need antidepressants. The question then is whether long-term antidepressants are better than long-term benzodiazepines.

Misuse

A small but important sector of the population abuse benzodiazepines, especially temazepam, flunitrazepam and diazepam, as part of a wider drug and alcohol problem. Intravenous injection of temazepam has had disastrous effects resulting in emboli and subsequent gangrene and amputation. Attempts have been made to address this by altering formulations of the drug to make them less easy to inject and by restricting the most widely abused, temazepam, by altering its legal categorisation to limit its use. Benzodiazepines for misuse are often obtained on the black market or as a result of deception of a prescriber. Doctors should be aware that medication they prescribe may fall into the wrong hands. Maintenance benzodiazepines given to addicts are often used to supplement illicit sources. Doctors

should be wary of such prescribing and should consider screening the urine to establish that the benzodiazepines are being taken.

Cognitive impairment

Cognitive impairment, mainly involving memory disturbance, may be a side-effect of the use of benzodiazepines and not just a coincidental symptom of emotional disorder. Benzodiazepines may also cause subtle learning impairment. In an acute crisis the cognitive impairment may not allow patients to make an optimum response to the situation which they are facing. In cases of loss or bereavement the psychological adjustment to this trauma may also be inhibited by benzodiazepines. On the other hand, short-term symptomatic relief may aid the natural healing process.

Disinhibition

Studies of the disinhibiting effects of benzodiazepines prescribed for patients with personality disorders have shown that they may increase the incidence of suicidal behaviour, that is thoughts of suicide may become actions. The combination with alcohol is common and dangerous. The use of benzodiazepines by this category of patient may facilitate aggressive behaviour not only towards the self but also towards others. It is very important to recognise that benzodiazepines can exacerbate these problems. Extreme caution should therefore be used in prescribing such compounds in patients with severe personality disorders.

Psychomotor impairment

There is a danger that higher doses of benzodiazepines may cause psychomotor impairment which could affect such activities as driving and working with machinery. The longer-acting compounds may accumulate and cause side-effects such as dysarthria, ataxia and diplopia. These problems are more likely early in treatment before the ideal dosage has been chosen. It is advised that when starting benzodiazepines a low dose is given initially. There is a particular problem with the elderly, who are more sensitive to benzodiazepine effects and who metabolise long-acting benzodiazepines slowly. There is a build-up of drug over time which may result in chronic intoxication, a pseudodementia-like state, and falls resulting in fractures.

Tolerance

Tolerance to benzodiazepine effects does occur. This is most notable for the anticonvulsant and sedative effects. Tolerance to hypnotic actions and the anxiolytic effects may also occur but to a lesser degree. Dosage escalation in uncomplicated cases is rare. If this occurs the reason needs to be explored since it might indicate an underlying panic disorder or depressive illness or substance misuse.

Dosage regimes

Benzodiazepines should be prescribed in as low a dose as possible to afford symptomatic relief. Although it is difficult to produce a risk table, in general compounds of higher potency incur a greater risk of dependence.

The arguments against long-term use of these compounds are well recognised and unless there are clear risks of more severe problems if the drug is stopped, patients should be encouraged to withdraw gradually after long-term use. Most patients who can withdraw successfully will now have done so and those who remain on benzodiazepine anxiolytics will usually have trouble stopping. The issues around hypnotics are less clear. Sudden withdrawal may be extremely distressing and possibly dangerous. Dependence is more likely after higher dosage but can also occur in low therapeutic dosage. Pharmaceutical companies should produce formulations of their compounds at lower strengths which could be used to help patients reduce from higher doses.

Even after the short-term use of benzodiazepines for therapeutic reasons, it is recommended that a tapering-off regime (i.e. at least 2 weeks at reduced dosage) should be used to minimise rebound phenomena. After longer use this reduction period could be extended, sometimes to several months in extreme cases.

Recommendations

Benzodiazepines may be prescribed safely in the short-term and are highly effective treatments for anxiety, insomnia and some forms of epilepsy and spasticity. Dependence is now recognised as a significant risk in patients receiving treatment for longer than one month and the practitioner has to be conscious of this when evaluating the relative benefits and risks of continued prescription. It is recommended that every clinician examines the benefit:risk ratio in each individual case early in treatment, so that if dependence occurs, it is anticipated by therapist and patient alike. The decision to allow dependence to develop is sometimes defensible but it must be appreciated that, once dependence has become established, it is often extremely difficult to treat and may become a long-term or even permanent state.

Suggested reading list

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