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Regular Review

Clinical management of benzodiazepine dependence

ANNA C HIGGITT, M H LADER, P FONAGY

The development of dependence after the long term use of benzodiazepines is now supported both by clinical evidence and by the results of double blind studies.[1-3] Withdrawal symptoms have been reported after treatment for as little as four to six weeks.[4,5] The withdrawal symptoms observed are wide ranging, and, while they include some related to anxiety, they are clearly distinguishable from a simple re-emergence of pre-existing anxiety.[6-8] Particularly frequently reported are instances of increased sensory perception such as hyperacusis, photophobia, paraesthesiae, hyperosmia, and hypersensitivity to touch and pain, but gastrointestinal disturbances, headaches, muscle spasms, vertigo, and sleep disturbances are also frequent.[3,9,10] The proportion of long term users of benzodiazepines in whom withdrawal symptoms may be expected to emerge has been variably estimated to be between 15% and 44%.[3,8] The symptoms typically emerge in the first week after stopping the drug but may develop after a reduction in dosage.[7,10] Until recently the withdrawal syndrome was reported as lasting for up to three months,[7] but we are now seeing more patients whose symptoms have persisted for more than six months—in some cases for a year or more.

Yet no one doubts that most patients currently taking benzodiazepines should stop them. One and a quarter million of the British population take benzodiazepines for more than a year,[11] although data supporting their continued effectiveness over such a period are sparse—to say the least.[12] A recent review concluded that benzodiazepines are no more effective than brief counselling by the general practitioner for the common minor affective disorders and that their prescription should be cut.[13] There is, in addition, evidence suggesting possible psychological impairment and neuroradiological changes associated with long term administration.[14,15] Recent extensive publicity about tranquillisers has led to an increased consumer demand for medical guidance about withdrawal.[16] Information on optimal withdrawal procedures is lacking—for little systematic research has been done on the treatment of benzodiazepine dependence,[6] and the studies that have been published have had methodological limitations.[17] The guidelines set out below are based in part on a review of published work and also experience in our unit in withdrawing more than 60 patients over the past seven years.

Setting

In general withdrawal is best tackled in the outpatient setting.[2,9] Patients having high doses or with a history of seizures or psychotic episodes during previous attempts at withdrawal are more safely treated as inpatients.

Rate of withdrawal

Stopping the drug abruptly is more likely to lead to severe withdrawal symptoms such as fits or confusional states[18,19]—and to loss of patients from the withdrawal programme.[3] No consensus exists, however, on the precise duration of the withdrawal process or the size of each reduction in dosage. Four weeks is probably the minimum period,[1,2,9] and programmes as long as 16 weeks have been recommended.[20] Over the withdrawal period dosage should gradually be tapered off in steps ranging from 0·5 to 2·5 mg diazepam or its equivalent.[3,4,7,12,21] The table sets out equivalent doses for benzodiazepines on the limited list.

Some patients referred for withdrawal of benzodiazepines may already be complaining of withdrawal symptoms.[10] Published reports tend, however, to emphasise patients who had severe problems in withdrawing and so need appraisal by specialists. Some and possibly most patients will suffer less severe withdrawal symptoms and will cope well with a fairly rapid reduction in dosage over a few weeks.[22]

In our view—and certainly for patients who have previously had problems withdrawing—the rate of reduction of dosage should not be fixed at the outset but should be "titrated" against the patient's withdrawal symptoms.

Generally withdrawal symptoms emerge in four or five days after a reduction in dosage but they may not become evident until several steps in the withdrawal programme have been completed. Thus reduction can be in weekly steps until the first withdrawal symptoms emerge, at which stage the rate of reduction should be reduced. A further reduction should be made when the withdrawal symptoms have waned sufficiently for the patient to be willing to contemplate the likely consequent accentuation of symptoms. This procedure should be followed until the last few milligrams. At this stage psychological aspects of dependence are likely to intensify[6] and if necessary may be dealt with by judicious use of placebo.[9] Another useful technique for handling this stage of withdrawal is to advise the patient to reduce the frequency of taking the final dose from daily to alternate days (or even less frequently) before finally withdrawing the drug. Some patients may not experience such a reduction in intensity of withdrawal symptoms and may achieve that only when totally drug free. In such cases the process should not be prolonged excessively.

A special problem in determining rate of withdrawal arises with patients having a highly variable daily intake. With this group it is probably best to set a ceiling to the total daily intake, which is then gradually reduced using the procedure outlined above.

Alternative medication

As long acting benzodiazepines are associated with less pronounced withdrawal symptoms,[3] several workers recommend substituting long acting for short acting drugs before withdrawal is begun.[7 9 10 21] Long acting benzodiazepines will produce a more gradual reduction in drug concentrations and will delay the emergence of withdrawal symptoms by two to four days.

On the basis of research on withdrawal of opiates and alcohol,[23 24] clonidine (an α_2 adrenoceptor stimulator) has been recommended as an adjunct to benzodiazepine withdrawal programmes,[21] and it is moderately, though not dramatically helpful.[10] Similarly, the β blocker propranolol attenuates some feature of withdrawal symptoms,[19] but it decreases neither their frequency nor their subjective aspects.[10] Withdrawal is commonly associated with frank depressive episodes, and treatment with antidepressants may be needed[25]—and, furthermore, sedative antidepressants have anxiolytic properties that may help suppress symptoms of withdrawal. Antidepressants should be prescribed in adequate dosage to treat the depressive episode, and the duration of treatment should be determined by the depression irrespective of the withdrawal programme. The use of major tranquillisers to suppress withdrawal symptoms is contraindicated by the risk of severe complications such as fits and tardive dyskinesia; similarly, barbiturates—with their own risks of dependence and toxicity—are generally avoided, though some workers have found phenobarbitone of benefit.[26]

Intermittent flexible dosage

Patients having long term benzodiazepines tend to use medication in preference to other ways of coping with life's difficulties. Almost invariably, therefore, at the time of withdrawal they will be short of the skills for dealing not only with difficulties in their lives but also with the additional strains which their withdrawal symptoms may impose on them. In the early stages after withdrawal such patients may be told to use tranquillisers on an occasional basis[3] but the circumstances meriting such self medication need to be clearly defined and made increasingly rigorous as withdrawal progresses. Patients will need help at this time in developing alternative coping strategies if other maladaptive ways of dealing with stress (for example, alcohol, cigarettes, or street drugs) are not to emerge.

Doses of benzodiazepines on limited list of medicinal products roughly equivalent to 2·5 mg diazepam. (Widely varying half lives make precise equivalents impossible to establish)

	Diazepam	Chlordiazepoxide	Lorazepam	Nitrazepam	Oxazepam	Temazepam	Triazolam
Dose	2·5 mg	5 mg	0·5 mg	5 mg	7·5 mg	5 mg	0·125 mg

Psychological adjuncts

The treating physician should maintain close contact with the patient during withdrawal, and in the initial stages patients should be seen at least weekly.[7 9] With inpatients even daily contact has been found to be useful.[10] At these meetings the physician should show that he or she understands the problems of withdrawal and be ready to offer guidance on non-medical as well as medical issues. Patients frequently arrive with numerous misconceptions and negative expectations about tranquillisers and withdrawal; these need to be elicited, identified, and corrected within a broadly educational framework. For example, patients may regard tranquillisers in the same way that they think about antibiotics—a "course" of treatment needing to be taken around the clock; or they may believe that they must not take any other tablets during withdrawal, even for a coincidental physical illness.

Special care should be taken to identify complications of withdrawal such as increased alcohol consumption and smoking, depression, and difficulties with personal relations. During the process of withdrawal the sources of anxiety which precipitated the anxiolytic treatment originally may become clear and require treatment in their own right.

Patients need most advice concerning the management of the withdrawal syndrome itself. Most symptoms can be dealt with by reassurance and simple practical advice. With more persistent difficulties, requesting patients to keep diaries so that they may monitor particular symptoms may provide important clues to the source of the difficulty. During the withdrawal period patients are likely to attribute almost all physical and psychological changes they experience to the withdrawal. This simplistic view must be corrected, for patients may otherwise come to have unrealistic expectations about the likely outcome.

Formal psychological help has not yet been shown to be particularly effective. Relaxation treatment and training in anxiety management skills in the framework of group therapy can boast of only moderate effectiveness.[27] Possibly more rigorous administration of such techniques in close coordination with withdrawal procedures and with more

regard to the specific problems of individual patients might help in group based withdrawal programmes. This possibility is being investigated in our unit. In the long run recent developments in psychological intervention, especially in cognitive treatments, may provide the ideal solution to these problems.[28] A counselling approach to outpatient benzodiazepine detoxification has been found to be of benefit by American workers.[29]

An important determinant of success in withdrawal may be the social support received by patients. The process of withdrawal needs to be explained to spouses, and in some cases children, and their support elicited whenever possible. In the absence of (or in addition to) family support some patients find local self help groups a useful adjunct. Unfortunately, but probably inevitably, those members of the community most active in founding support groups for tranquilliser dependence are likely to be those with the worst experiences of withdrawal, who may thus inadvertently set up unnecessarily gloomy expectations in patients.

Success rates

There have been no large scale studies with an adequately long follow up to permit an accurate estimate of the likelihood of recovery. Though drop out rates from withdrawal programmes are high when withdrawal is relatively abrupt,[19] on gradual withdrawal regimens almost all (88-100%) volunteers are successful in stopping their benzodiazepine intake.[2 3 10 12] Roughly one third of these patients are free of problems after withdrawal.[9 12] Of the remaining patients, about half tend to respond to antidepressants,[9 12] but many may return to using benzodiazepines. Complete recovery is slow, and patients are likely to have symptoms for a year or more.[10] Thus, though on the whole gradual withdrawal programmes are successful, most participants are left with psychiatric problems and the long term effectiveness of withdrawal is unknown. Certain groups of patients may fail to benefit from benzodiazepine withdrawal. Patients prone to psychotic disorders or with a history of alcoholism may relapse as a consequence of withdrawal and if admitted to a programme should be monitored closely.[3 30]

Prevention

A strategy that is preferable to withdrawal once a patient is dependent is the prevention of dependence. The best way of avoiding dependence is by thoughtful prescribing. The duration of prescription of benzodiazepines should be decided in advance and set at a short period at the lowest possible dose.[7] Intermittent flexible dosage should be encouraged, as it tends to result in lower total intake and a reduced dependence risk,[6] and possible non-pharmacological interventions should be seriously considered.[17] These considerations are particularly important in patients requiring hypnotics. Benzodiazepines should not be prescribed for normal people at times of acute stress such as bereavement or divorce,[17] and a recent study found brief counselling by general practitioners to be as effective as benzodiazepines in cases of minor affective disorder.[31] Repeat prescription should also be avoided for patients with major personality problems—whose difficulties are in any case unlikely ever to resolve.

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