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EDITORIALS

Tackling benzodiazepine misuse

The time to take decisive action has come

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Discovered in the 1950s by Leo Sternbach,[1] benzodiazepines were enthusiastically adopted as a safer alternative to barbiturates for management of insomnia and anxiety. Evidence quickly accrued, however, of substantial risk of dependence. Despite recommendation that they be prescribed for no more than four weeks, long term use remains common, with 300 000 long term users in the UK.[2]

Benzodiazepines, and the related z drugs (zopidem, zopiclone, and zalepon), potentiate the rapid neuroinhibitory effect of the neurotransmitter γ aminobutyric acid (GABA) in the brain and spinal cord. This results in reduction of anxiety, induction of sleep, and muscle relaxation. Consequently, benzodiazepines are commonly prescribed for anxiety and sleep disorders, but are also highly effective as muscle relaxants; for treating epilepsy, alcohol withdrawal syndrome, and acute behavioural disturbance; and as a premedicant in anaesthesia.

Patients may develop dependence after only a few weeks of regular use and many long term users experience problems on dose reduction, including rebound anxiety, nausea, perceptual changes, and, rarely, epileptic seizures and psychosis.[3] The muscle relaxant and sedative effects of benzodiazepines increase the risk of falls, particularly in older people, while there is also association with certain infections, and with increased all cause mortality.[4] In addition to short term amnesic effects, evidence exists of medium and longer term impact on cognition, with an increasingly strong association with dementia.[5]

Prescribing and misuse

Benzodiazepines and z drugs are commonly misused to help with sleep, relieve stress, and to ameliorate effects of other drugs. In the UK, 7.7% of respondents admit misuse, comparable with the US,[6] and misuse by children and young people may be increasing.[7] Although safer than barbiturates, benzodiazepine overdose can result in coma and death through respiratory depression. Furthermore, the risk of overdose increases substantially when taken with other drugs, especially opiates.[8]

Misused benzodiazepines are usually obtained through diversion from legitimate sources including pharmacies, pharmaceutical suppliers, and prescription.[9] Higher prescribing rates are associated with increased misuse,[10] and both benzodiazepines and z drugs continue to be widely prescribed in UK primary and secondary care. A small decline in the proportion of patients prescribed benzodiazepines in primary care (from 3.5% in 2000 to 2.6% in 2016),[11] was mirrored by a rise in z drugs, and very long term prescribing is increasing.[11] Prescribing of benzodiazepines and z drugs rises with age[12] and duration of treatment increases with social deprivation[11]; diversion of prescribed drugs may involve exploitation of vulnerable older people and those in financial difficulty.[13]

Growing availability online from unregulated pharmacies and the dark web is concerning, and often involves the significantly more toxic benzodiazepine alprazolam.[7 14] Proliferation of private online primary care services may facilitate diversion of prescribed benzodiazepines: visiting multiple doctors is a recognised strategy for obtaining multiple prescriptions for illicit use,[9] and the Care Quality Commission recently raised concerns about lack of information sharing by online providers in relation to drugs with potential for misuse.[15]

De-prescribing and withdrawal

Professional guidelines recommend treatment withdrawal for most patients on long term benzodiazepines.[16 17] This usually takes 3 to12 months or longer, often supported by switching to diazepam, a benzodiazepine whose long half life and availability in various strengths allows gradual dose reduction. However, there is a paucity of evidence for effective interventions to support withdrawal, and a recent review failed to identify evidence of sufficient quality to support any pharmacological interventions.[18] Psychosocial interventions may be more promising: cognitive behavioural therapy plus tapering is effective in the short term, and relaxation techniques and individualised GP letters to patients can facilitate withdrawal.[3] However, better evidence is urgently required for both drug and non-drug options.

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Practice and policy

Benzodiazepines remain important treatments for certain short term indications, but risk of dependence and growing evidence of other harms demand careful consideration as part of shared decisions with patients.

Patients must be fully informed of all risks, and prescribers should follow guidelines on short treatment duration.[16 17] Mechanisms for early review are essential, and clear documentation of intended treatment duration is particularly important at interfaces of care, such as between secondary and primary care. Primary care professionals should conduct active case finding for patients taking benzodiazepines, and follow guidelines on de-prescribing.[16 17] Prescribers and pharmacists should also have strict protocols regarding management of lost prescriptions and requests for repeat prescriptions, to avoid fuelling misuse; they should also be alert to the possibility of exploitation of vulnerable patients in diversion of prescribed benzodiazepines. Given the current workload pressures on primary care,[19] however, it is essential that this is supported by sufficient resources, with time and funding for de-prescribing interventions, and access to specialist support.

In January 2018 the Department of Health commissioned an evidence review of dependence on prescribed drugs.[20] Expected to report early in 2019, it is hoped this will provide further clarity on prescribed benzodiazepine use and misuse in the UK. However, availability of benzodiazepines through unregulated online sources indicate a need for urgent government intervention to tackle misuse of these drugs obtained without a prescription. This should be accompanied by well resourced campaigns to educate the public about the risks of inappropriate benzodiazepine use.

Competing interests We have read and understood BMJ policy on declaration of interests and declare the following interests: none

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