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Re-evaluating benzodiazepines for anxiety disorders – déjà-vu all over again?[†]

COMMENTARY

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SUMMARY

Benzodiazepines have attracted controversy from shortly after their introduction. They have been subject to periodic calls for their use to be re-evaluated on the basis that their risks have been overstated and their benefits underappreciated. Claims made in recent editorials from the International Task Force on Benzodiazepines in support of their wider use are critiqued in this issue. I examine here whether there is a case to change the conclusions of previous reconsiderations of the question.

KEYWORDS

Benzodiazepines; anxiety disorders; antidepressants; dependence; guidelines.

Benzodiazepines largely superseded more toxic and problematic anxiolytic and sedative drugs in the 1960s, leading to them becoming the most prescribed psychotropic group by the mid-1970s (Starcevic 2012) in what Peter Tyrer called the 'benzodiazepine bonanza' (Lader 2011). Concerns about their overuse and dependence potential led to their fall from favour, although they have continued to be widely prescribed. Current guidelines overwhelmingly recommend that benzodiazepines should only be used for short-term treatment restricted to a few weeks, something that can be difficult to square with both the longer-term nature of anxiety disorders (and insomnia) and how benzodiazepines are often used in practice. This can cause tension when balancing clinical need against guidelines, leading to reluctance to prescribe benzodiazepines, restrictions in their use and even stigma. The clinical value of benzodiazepines has continued to be debated, with periodic calls for re-evaluation arguing for a more central role in the longer-term management of anxiety disorders. The editorials from the International Task Force on Benzodiazepines, critiqued in this issue (Brandt 2022), can be viewed as part of this periodic cycle, but are perhaps more strident than before about what they feel is scientific bias and unjustified propaganda against benzodiazepines, arguing that 'they have come to be stigmatized by a fear narrative that has precluded evidence-based reasoning' (Silberman 2022).

In a previous iteration of the process a decade ago representatives from the Royal College of Psychiatrists' Psychopharmacology Special Interest Group and the British Association for Psychopharmacology undertook a 'reconsideration' of the risks and benefits of benzodiazepines (Baldwin 2013). Their recommendations for clinical practice were that benzodiazepines could be safely prescribed in the short term and that intermittent or longer-term use was not necessarily a deviation from good clinical practice but needed deciding on an individual basis by balancing benefit against the potential risks of dependence and other side-effects. They concluded that in the absence of risk factors for dependence (e.g. dependence history or lifestyle) a conscious decision to continue benzodiazepines may be more reasonable for some individuals than the alternatives, provided that periodic attempts to reduce dose and, if possible, stop treatment were made. Given that the evidence base has not changed, it is unsurprising that the ground covered in their review is essentially the same in a very recent review co-authored by a member of the International Task Force on Benzodiazepines (Dubovsky 2022), with no major differences in the interpretation of the data, rather a different emphasis on the balance of benefits and risks. In writing this commentary I was struck by a sense of déjà-vu when reading articles by Peter Tyrer (Tyrer 2012) and Malcolm Lader (Lader 2011), both veterans of the 'bonanza' years, in which the arguments for and against benzodiazepine use are elegantly expounded.

A contextual shift

But things rarely come full circle and the context, if not the evidence, can shift. It is still the case that good-quality evidence for the longer-term use of benzodiazepines for anxiety disorders is poor and considerably weaker than that for selective serotonin reuptake inhibitors (SSRIs). However, there is now

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greater acceptance and emphasis on the occurrence of withdrawal symptoms in up to half of those taking long-term SSRIs, and that these can sometimes be severe and prolonged (Horowitz 2022). With this new emphasis, the disadvantages of longer-term benzodiazepines, when used with care, may no longer seem so starkly different from SSRIs, especially given the current boom in antidepressant prescriptions (bearing some comparison with the situation with benzodiazepines in the 1970s).

Nevertheless, unlike benzodiazepines, SSRIs are not addictive in terms of dose escalation and drug-seeking behaviour, so there is a counterweight in the increased concern and sensitisation to the problem of addiction with prescription medication. This has been fuelled by the 'opioid crisis' that has developed over the past 25 years, notably in the USA, where there has also been a large increase in benzodiazepine prescriptions, some even comparing it to the early days of opioid prescribing, and drug poisoning deaths involving benzodiazepines have increased sharply (although interpretation is complicated by their common co-prescription with opioids) (Hamzelou 2020). Drug poisoning deaths involving benzodiazepines (in combination with other drugs) have also doubled in the past 10 years in the UK (Office for National Statistics 2022), but in contrast to the USA, benzodiazepine prescriptions are relatively stable or falling slightly (Hamzelou 2020). This raises caution in drawing any simple cause and effect relationship between volume of prescription and harms, but the US experience suggests that an increased availability of prescription benzodiazepines is more likely than not to exacerbate the situation.

Reconsidering the risk/benefit balance

Have guidelines got the wrong balance between benefits and risks, resulting in them being overly restrictive about the longer-term use of benzodiazepines for anxiety disorders? For me there are two additional aspects that warrant caution in addition to the ones addressed by Brandt (2022). First, anxiety is an extremely common symptom, and anxiety disorders are a heterogeneous and comorbid classificatory 'jungle' treated almost exclusively in primary care, so that even if indications for first-line and long-term use were specific (e.g. for panic disorder) it is highly likely that in reality benzodiazepine use would be poorly targeted and widespread, with careful individual assessment and monitoring for potential dependence extremely hard to carry out. It seems inevitable that liberalisation of use would greatly increase overall prescriptions with limited safeguards and lead to greater harm. Second, the evidence that benzodiazepines are effective in treating depression is weak, and many would say absent. Symptoms of anxiety and depression are more likely than not to coexist and, although imperfect, SSRIs do have 'broad spectrum' efficacy in both anxiety and depressive disorders, whereas benzodiazepines do not, so that there is a danger that first-line treatment with the latter could lead to undertreating depression. None of this takes away from the limitations of current treatments for anxiety disorders and the fact that some individuals may benefit from carefully considered longer-term (or intermittent) benzodiazepine treatment if other options have been insufficiently helpful. To my mind, rather than changing current guidance to help these individuals, the recommendations made by Baldwin and colleagues (Baldwin 2013) still provide a balanced approach to prescribing benzodiazepines to maximise benefit and minimise risk.

Declaration of interest

None.

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