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More on prescribing controlled substances

I was disheartened with the June 2023 issue of Current Psychiatry. This issue included "Optimizing benzodiazepine treatment of anxiety disorders" (p. 22-33,39, doi:10.12788/cp.0365). While these medications may be helpful for short-term treatment, I find their irresponsible use to be a much greater problem than their underutilization.[1]

The benzodiazepine pharmacology discussed in this article is interesting, but it would be helpful if it had been integrated within a much more extensive discussion of careful prescribing practices. In 2020, the FDA updated the boxed warning to alert prescribers to the serious risks of abuse, addiction, physical dependence, and withdrawal reactions associated with benzodiazepines.[2] I would hope that an article on benzodiazepines would provide more discussion and guidance surrounding these important issues.

The June 2023 issue also included "High-dose stimulants for adult ADHD" (p. 34-39, doi:10.12788/cp.0366). This article provided esoteric advice on managing stimulant therapy in the setting of Roux-en-Y gastric bypass surgery, yet I would regard stimulant misuse as a far more common and pressing issue.[3,4] The recent Drug Enforcement Administration investigation of telehealth stimulant prescribing is a notable example of this problem.[5]

The patient discussed in this article was receiving large doses of stimulants for a purported case of refractory attention-deficit/hyperactivity disorder (ADHD). The article provided a sparse differential diagnosis for the patient's intractable symptoms. While rapid metabolism may be an explanation, I would also like to know how the authors ruled out physiological dependence and/or addiction to a controlled substance. How was misuse excluded? Was urine drug testing (UDS) performed? UDS is highly irregular among prescribers,[6] which suggests that practices for detecting covert substance abuse and stimulant misuse are inadequate. Wouldn't such investigations be fundamental to ethical stimulant prescribing?

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Drs. Stimpfl and Strawn respond

We thank Dr. Sanders for highlighting the need for clinical equipoise in considering the risks and benefits of medications—something that is true for benzodiazepines, antipsychotics, antidepressants, and in fact all medications. He reminds us that the risks of misuse, dependence, and withdrawal associated with benzodiazepines led to a boxed warning in September 2020 and highlights recent trends of fatal and nonfatal benzodiazepine overdose, especially when combined with opiates.

Our article, which aimed to educate clinicians on benzodiazepine pharmacology and patient-specific factors influencing benzodiazepine selection and dosing, did not focus significantly on the risks associated with benzodiazepines. We do encourage careful and individualized benzodiazepine prescribing. However, we wish to remind our colleagues that benzodiazepines, while associated with risks, continue to have utility in acute and periprocedural settings, and remain an important treatment option for patients with panic disorder, generalized anxiety disorder (especially while wait-

ing for other medications to take effect), catatonia, seizure disorders, and alcohol withdrawal.

We agree that patient-specific risk assessment is essential, as some patients benefit from benzodiazepines despite the risks. However, we also acknowledge that some individuals are at higher risk for adverse outcomes, including those with concurrent opiate use or who are prescribed other sedative-hypnotics; older adults and those with neurocognitive disorders; and patients susceptible to respiratory depression due to other medical reasons (eg, myasthenia gravis, sleep apnea, and chronic obstructive pulmonary disease). Further, we agree that benzodiazepine use during pregnancy is generally not advised due to the risks of neonatal hypotonia and neonatal withdrawal syndrome[1] as well as a possible risk of cleft palate that has been reported in some studies.[2] Finally, paradoxical reactions may be more common at the extremes of age and in patients with intellectual disability or personality disorders.[3,4]

Patient characteristics that have been associated with a higher risk of benzodiazepine use disorder include lower education/income, unemployment, having another substance use disorder, and severe psychopathology.[5] In some studies, using benzodiazepines for prolonged periods at high doses as well as using those with a rapid onset of action was associated with an increased risk of benzodiazepine use disorder.[5-7]

Ultimately, we concur with Dr. Sanders on the perils of the "irresponsible use" of medication and emphasize the need for discernment when choosing treatments to avoid rashly discarding an effective remedy while attempting to mitigate all conceivable risks.

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Drs. Sarma and Grady respond

Dr. Sanders' letter highlights the potential caveats associated with prescribing controlled substances. We agree that our short case summary includes numerous interesting elements, each of which would be worthy of further exploration and discussion. Our choice was to highlight the patient history of bariatric surgery and use this as a springboard into a review of stimulants, including the newest formulations for ADHD. For more than 1 year, many generic stimulants have been in short supply, and patients and clinicians have been seeking other therapeutic options. Given this background and with newer, branded stimulant use becoming more commonplace, we believe our article was useful and timely.

Our original intent had been to include an example of a controlled substance agreement. Regrettably, there was simply not enough space for this document or the additional discussion that its inclusion would deem necessary. Nevertheless, had the May 2023 FDA requirement for manufacturers to update the labeling of prescription stimulants[1] to clarify misuse and abuse been published before our article's final revision, we would have mentioned it and provided the appropriate link.

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