

The information in this column is not intended as a definitive treatment strategy but as a suggested approach for clinicians treating patients with similar histories. Individual cases may vary and should be evaluated carefully before treatment is provided. The patient described in this column gave informed consent for the publication of the column.

Mindfulness-based intervention for benzodiazepine deprescription in hemodialysis patients with anxiety and depressive symptoms

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A 35-year-old female hemodialysis (HD) patient with end-stage renal disease was able to successfully withdraw from benzodiazepines, which had been prescribed for managing psychiatric and pain symptoms, following a mindfulness-based stress reduction (MBSR) intervention. The patient, who had been undergoing HD since the age of 6 years, enrolled in an MBSR program for HD patients consisting of 20- to 40-minute sessions over 8 weeks centred on breath work and directing attention to physical sensations (body scan) and thoughts. The sessions were delivered via Zoom during HD by an MBSR-certified psychologist.

The patient had a long-standing history of mild depressive, anxiety, insomnia, restless leg syndrome (RLS) and chronic pain symptoms. In addition to polypharmacy for HD, she had been regularly taking a benzodiazepine since the age of 20 years, clonazepam 0.75 mg twice daily for her anxiety and RLS, as well as citalopram 40 mg/d for her depressive symptoms, quetiapine 75 mg nightly for her insomnia, pregabalin 150 mg nightly for her pain symptomatology and pramipexole 0.5 mg/d for her RLS. The patient had previously tried to discontinue her benzodiazepine use by her own initiative and with the help of a psychiatrist, but was unsuccessful. This discontinuation was attempted with a gradual taper of approximately 10% of her dose every 2–3 weeks. Unfortunately, the discontinuation was

unsuccessful because of resulting rebound anxiety and insomnia.

After the 8-week MBSR program, the patient reported experiencing a substantial decrease in her anxiety, pain and depressive symptoms. Most notably, after her previously unsuccessful attempts at discontinuing benzodiazepines, she was finally able to do so. She slowly decreased her dose by 0.125 mg weekly and successfully withdrew from clonazepam over 12 weeks following the MBSR program by using the breathing techniques she learned for managing the withdrawal symptoms. Furthermore, she reported successful self-management of insomnia, chronic pain and RLS without benzodiazepines for more than 18 months following the program. She reported practising daily mindfulness meditation for 5–10 minutes per day at least 4 days per week. Through this practice, she developed the capability to face new health challenges and difficult emotions by calming down with the breath and detaching herself from worries and negative self-talk.

Patients undergoing HD commonly experience symptoms of stress (29%), anxiety (12%–52%), depression (25%) and chronic pain (60%).^{1–3} Restless leg syndrome is also common in these patients and is associated with the accumulation of uremic solutes and toxins that are not completely removed during renal replacement therapy, generating substantial levels of discomfort and suffering.⁴ Benzodiazepines are one of the most prescribed drugs worldwide,⁵ and are given to 8%–26% of HD patients⁶ without any precise data on adverse events and their efficacy in this population. They are prescribed for their anxiolytic properties, insomnia and mild cases of RLS.^{7,8} Benzodiazepines act as positive allosteric modulators of the activity of the main inhibitory neurotransmitter of the central nervous system,

γ-aminobutyric acid (GABA), producing sedative and anxiolytic effects, muscle relaxation and the interruption of seizures.⁹ International guidelines recommend ideally only short courses of benzodiazepines,^{10,12} as long-term use is associated with physical and psychological dependence,⁸ cognition decline and increased risk of falls, car accidents and possibly dementia.^{8,11,12}

Benzodiazepine withdrawal is associated with distressing symptoms, including tachycardia, headache, flu-like symptoms, nausea, vomiting and diarrhea, paresthesia, muscle rigidity, sensory hypersensitivity, anxiety, agitation, panic attacks, depression, irritability and insomnia.^{8,13} Physiologic dependence occurs after 3–6 weeks of regular use.^{8,13} Predictive factors of severe withdrawal include short half-life, longer duration of use, high chronic doses, use of multiple benzodiazepines and rapid discontinuation.^{8,13} Currently, there are few strategies to promote benzodiazepine discontinuation in the general population, but none for HD patients. The most useful nonpharmacological interventions targeting withdrawal symptoms have been relaxation techniques and cognitive behavioural therapy in addition to gradual tapering of the medication.¹⁴ Although mindfulness interventions have not been studied in benzodiazepine deprescribing, they have shown promising results in opioid dose reduction in individuals with chronic pain, opioid withdrawal and cravings, by increasing self-control.^{15–17} Furthermore, a recent meta-analysis of mindfulness-based interventions in patients with cancer reported positive results on alleviating sleep disturbance and decreasing benzodiazepine use.¹⁸

Mindfulness meditation has been shown to alleviate stress and anxiety through neurobiological mechanisms, including the modification of large-scale

functional networks and neurotransmission patterns.¹⁹ Furthermore, meditation has been found to improve emotion regulation through increased activation of the prefrontal cortex, decreased amygdala activation and increased GABA neurotransmission in GABAergic interneurons, which modulate cortical excitability.¹⁹⁻²¹ Therefore, mindfulness-based interventions may have a therapeutic impact for benzodiazepine deprescription. A systematic review of mindfulness treatments for substance misuse disorders (e.g., mindfulness-based relapse prevention, mindfulness-oriented recovery enhancement, Vipassana meditation)²² found that, although each mindfulness-based therapy differed, the main components of mindfulness were used in each: paying attention to one's present experience with a non-judgmental and accepting attitude, and cultivating bodily awareness, attention and emotion regulation.²² However, it cannot be concluded that a specific kind of mindfulness therapy is best for substance overuse, and thus a personalized approach may be most beneficial.

Given the prevalence of benzodiazepine use with knowledge gaps on their safety and efficacy for anxiety, insomnia and RLS as well as polypharmacy in this vulnerable HD population, our patient's case illustrates mindfulness-based interventions as a potential adjunctive behavioural intervention for symptom management and benzodiazepine deprescribing in HD patients, which could be further investigated in future clinical trials.

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References

- Rhee CM, Edwards D, Ahdoot RS, et al. Living well with kidney disease and effective symptom management: consensus conference proceedings. *Kidney Int Rep* 2022;7:1951-63.
- Davison SN, Rathwell S, Ghosh S, et al. The prevalence and severity of chronic pain in patients with chronic kidney disease: a systematic review and meta-analysis. *Can J Kidney Health Dis* 2021;8:2054358121993995.
- Palmer S, Vecchio M, Craig JC, et al. Prevalence of depression in chronic kidney disease: systematic review and meta-analysis of observational studies. *Kidney Int* 2013;84:179-91.
- Salib M, Memon AN, Gowda AS, et al. Dialysis patients with restless leg syndrome: Can we relieve their suffering? *Cureus* 2020;12:e10053.
- Milani SA, Raji MA, Chen L, et al. Trends in the use of benzodiazepines, z-hypnotics, and serotonergic drugs among US women and men before and during the COVID-19 pandemic. *JAMA Netw Open* 2021;4:e2131012.
- Wyne A, Rai R, Cuerden M, et al. Opioid and benzodiazepine use in end-stage renal disease: a systematic review. *Clin J Am Soc Nephrol* 2011;6:326-33.
- Carlos K, Prado GF, Teixeira CD, et al. Benzodiazepines for restless legs syndrome. *Cochrane Database Syst Rev* 2017;3:CD006939.
- Soyka M. Treatment of benzodiazepine dependence. *N Engl J Med* 2017;376:1147-57.
- Brett J, Murnion B. Management of benzodiazepine misuse and dependence. *Aust Prescr* 2015;38:152-5.
- Kurko TA, Saastamoinen LK, Tahkapaa S, et al. Long-term use of benzodiazepines: definitions, prevalence and usage patterns — a systematic review of register-based studies. *Eur Psychiatry* 2015;30:1037-47.
- Tapiainen V, Taipale H, Tanskanen A, et al. The risk of Alzheimer's disease associated with benzodiazepines and related drugs: a nested case-control study. *Acta Psychiatr Scand* 2018;138:91-100.
- Lynch T, Ryan C, Hughes CM, et al. Brief interventions targeting long-term benzodiazepine and Z-drug use in primary care: a systematic review and meta-analysis. *Addiction* 2020;115:1618-39.
- Puening SE, Wilson MP, Nordstrom K. Psychiatric emergencies for clinicians: emergency department management of benzodiazepine withdrawal. *J Emerg Med* 2017;52:66-9.
- Darker CD, Sweeney BP, Barry JM, et al. Psychosocial interventions for benzodiazepine harmful use, abuse or dependence. *Cochrane Database Syst Rev* 2015;5:CD009652.
- Garland EL, Froeliger B, Howard MO. Effects of mindfulness-oriented recovery enhancement on reward responsiveness and opioid cue-reactivity. *Psychopharmacology (Berl)* 2014;231:3229-38.
- Garland EL, Hanley AW, Nakamura Y, et al. Mindfulness-oriented recovery enhancement vs supportive group therapy for co-occurring opioid misuse and chronic pain in primary care: a randomized clinical trial. *JAMA Intern Med* 2022;182:407-17.
- Kundal D, Raj R, Garg R, et al. Therapeutic efficacy of rhemercise: a novel mindfulness technique in patients with opioid use disorder. *Prim Care Companion CNS Disord* 2022;24:39599.
- Yang B, Nie Q, Yang Y. The effects of mindfulness-based intervention on sleep disturbance and benzodiazepine hypnotics use in patients hospitalized with cancer: a systematic review and meta-analysis. *J Psychosom Res* 2021;146:110483.
- Tang YY, Hölzel BK, Posner MI. The neuroscience of mindfulness meditation. *Nat Rev Neurosci* 2015;16:213-25.
- Guglietti CL, Daskalakis ZJ, Radhu N, et al. Meditation-related increases in GABAB modulated cortical inhibition. *Brain Stimul* 2013;6:397-402.
- Elias AN, Guich S, Wilson AF. Ketosis with enhanced GABAergic tone promotes physiological changes in transcendental meditation. *Med Hypotheses* 2000;54:660-2.
- Li W, Howard MO, Garland EL, et al. Mindfulness treatment for substance misuse: A systematic review and meta-analysis. *J Subst Abuse Treat* 2017;75:62-96.