Iran J Psychiatry 2026; 21: 2: 154-155

Letter to the Editor *https://doi.org/10.18502/ijps.v21i2.21217*

Repurposing Vinpocetine: A Potential Management Strategy for Selective Serotonin Reuptake Inhibitors (SSRI)-Induced Sexual Dysfunction

Zahra Nazari Taloki[1,2*]

1.Cellular and Molecular Biology Research Center, Health Research Institute, Babol University of Medical Sciences, Babol, Iran.
2.Department of Clinical Pharmacy, School of Pharmacy, Babol University of Medical Sciences, Babol, Iran.

***Corresponding Author:**
Address: Department of Clinical Pharmacy, School of Pharmacy, Babol University of Medical Sciences, Babol, Iran, Postal Code: 4717647745
Tel: 98-011 32207571, Email: z.nazari@mubabol.ac.ir

Article Information:
Received Date: 2025/12/08, Revised Date: 2026/01/28, Accepted Date: 2026/02/07

Dear Editor,

Selective serotonin reuptake inhibitors (SSRIs) are first-line pharmacotherapy for major depressive and anxiety disorders; however, treatment-emergent sexual dysfunction is a highly prevalent and distressing adverse effect, contributing substantially to non-adherence and reduced quality of life (1). This dysfunction—encompassing impaired libido, arousal (including erectile dysfunction), and orgasm—arises from complex central and peripheral serotonergic effects, notably the inhibition of dopaminergic pathways and disruption of the nitric oxide (NO)/cyclic guanosine monophosphate (cGMP) signaling cascade, that is crucial for genital vasodilation (1,2). Importantly, symptoms may persist post-discontinuation in some patients and may be accompanied by non-sexual manifestations such as cognitive impairment, underscoring the clinical significance of this condition (3).

Current management strategies, including dose adjustment, drug holidays, switching antidepressants, or the use of phosphodiesterase type 5 (PDE5) inhibitors, provide incomplete or suboptimal relief for many patients (1). This highlights the need for novel, mechanistically targeted interventions.

We propose repurposing vinpocetine, a selective phosphodiesterase type 1 (PDE1) inhibitor, as a promising candidate for managing SSRI-induced sexual dysfunction (SSRI-ISD). PDE1 hydrolyzes both cyclic adenosine monophosphate (cAMP) and cGMP, and its inhibition by vinpocetine increases intracellular levels of these second messengers, thereby promoting vasodilation in vascular smooth muscle, including urogenital tissues (4). By directly enhancing peripheral cGMP signaling, vinpocetine may counteract the SSRI-induced impairment of cavernosal relaxation, offering a potential alternative or adjunct to PDE5 inhibitors for arousal and erectile components.

Notably, vinpocetine readily crosses the blood-brain barrier and exhibits multifaceted neuropsychiatric properties relevant to SSRI therapy, including neuroprotective, anti-inflammatory, antioxidant, and cognitive-enhancing effects (5). These actions are thought to involve PDE1 inhibition processes–mediated elevation of neuronal cAMP/cGMP, subsequent activation of neuroplasticity pathways such as cAMP response element-binding protein/Brain-derived neurotrophic factors (CREB/BDNF), and modulation of neuroinflammation via inhibition of NF-κB signaling, along with reduction of pro-inflammatory cytokines and oxidative stress linked to neurotoxicity in mood disorders—implicated in depression and antidepressant response (5,6). Preclinical studies support vinpocetine's antidepressant-like activity and potential synergy with SSRIs (7,8). Accordingly, its central effects may also alleviate SSRI-associated blunting of reward and dopaminergic pathways, as well as residual depressive or cognitive symptoms, and thereby indirectly improve libido and other centrally mediated aspects of sexual function.

Although vinpocetine has demonstrated efficacy in other urogenital conditions, such as urge incontinence (9), its application in SSRI-ISD remains unexplored. Dosing regimens reported across cognitive and cerebrovascular studies range from 10 to 60 mg/day (commonly 15-30 mg/day in divided doses) and provide a pragmatic starting point for clinical investigation. Vinpocetine generally exhibits a favorable safety profile, with commonly reported mild adverse effects such as headache or flushing. Caution is warranted regarding its vasodilatory potential, particularly in patients with hypotension or those receiving concomitant vasoactive medications. While no established contraindications with SSRI have been reported, potential interactions (e.g., with anticoagulants) warrant monitoring (10,11).

In conclusion, vinpocetine offers a distinctive pharmacological profile that combines peripheral PDE1 inhibition—targeting genital blood flow—with central neuropsychiatric modulation. This dual mechanism addresses both the physiological and neuropsychiatric dimensions of SSRI-ISD. Given its established safety profile and repurposing potential, we advocate for systematic preclinical studies followed by randomized controlled trials to evaluate vinpocetine's efficacy and safety in this clinically significant and underserved indication.

References

1. Montejo AL, Prieto N, de Alarcón R, Casado-Espada N, de la Iglesia J, Montejo L. Management Strategies for Antidepressant-Related Sexual Dysfunction: A Clinical Approach. J Clin Med. 2019;8(10):1610.
2. Joca SRL, Sartim AG, Roncalho AL, Diniz CFA, Wegener G. Nitric oxide signalling and antidepressant action revisited. Cell Tissue Res. 2019;377(1):45–58.
3. de Aquino ACQ, Sarmento ACA, Teixeira RLA, Batista TN, de Freitas CL, Mármol JMP, et al. Pharmacological treatment of antidepressant-induced sexual dysfunction in women: A systematic review and meta-analysis of randomized clinical trials. Clinics (Sao Paulo). 2025;80:100602.
4. Dong ZC, Shi Y, Liu LJ, Feng TT, Zhou Y, Pan BW. Synthesis and pharmacological activity of vinpocetine derivatives. RSC Adv. 2024;14(12):7981–91.
5. Zhang YS, Li JD, Yan C. An update on vinpocetine: New discoveries and clinical implications. Eur J Pharmacol. 2018;819:30–4.
6. Duman RS, Aghajanian GK. Synaptic dysfunction in depression: potential therapeutic targets. Science. 2012;338(6103):68–72.
7. Agarwal B, Pal P, Parihar L, Singh L. Evaluation Of Protective Effect Of Vinpocetine In Reserpine-Induced Depression In Wistar Rats. Journal of Positive School Psychology. 2022;6(10).
8. Kaur S, Kumar P, Deshmukh R. Neuroprotective potential of vinpocetine in epilepsy induced co-morbid depression & cognitive dysfunction in PTZ kindled rats.
9. Uckert S, Oelke M. Phosphodiesterase (PDE) inhibitors in the treatment of lower urinary tract dysfunction. Br J Clin Pharmacol. 2011;72(2):197–204.
10. Petric Z, Paixão P, Filipe A, Guimarães Morais J. Clinical Pharmacology of Vinpocetine: Properties Revisited and Introduction of a Population Pharmacokinetic Model for Its Metabolite, Apovincaminic Acid (AVA). Pharmaceutics. 2023;15(10):2502.
11. Khalil NY, Bakheit AH, Alkahtani HM, Al-Muhanna T. Vinpocetine (A comprehensive profile). Profiles Drug Subst Excip Relat Methodol. 2022;47:1–54.