

CASE REPORT

Time course of effects of venlafaxine on migraine and generalized pruritus in a patient with depression

Yu Miyahara | Hideki Funahashi | Ayaka Haruta-Tsukamoto | Hiroto Hidaka | Takako Fujimoto | Akira Horinouchi | Toshikazu Nishimori | Yasushi Ishida 

Department of Psychiatry, Faculty of Medicine, University of Miyazaki, Miyazaki city, Japan

Correspondence

Yasushi Ishida, Department of Psychiatry, Faculty of Medicine, University of Miyazaki, 5200 Kihara, Kiyotake, Miyazaki city, Miyazaki 889-1692, Japan.
Email: ishiday@med.miyazaki-u.ac.jp

Funding information

None

Abstract

Venlafaxine has potential as a therapeutic option for patients with depressive disorder, migraine, and pruritus unresponsive to antihistamines.

KEYWORDS

depression, generalized pruritus, migraine, venlafaxine

1 | INTRODUCTION

A 37-year-old female patient developed with pruritus unresponsive to antihistamines, migraine and depression with insomnia, agitation, and anxiety. The daily administration of 37.5 mg of venlafaxine alleviated pruritus, migraine, and depression. Therefore, venlafaxine has potential as a therapeutic option for patients with depressive disorder, migraine, and pruritus unresponsive to antihistamines.

Pain and pruritus are common presenting somatic symptoms, and depression is a common mental disorder.^{1–3} Generalized pruritus has been defined as chronic pruritus without skin inflammation and is associated with endocrine diseases, hepatic diseases, renal failure, hematological diseases, and malignancies.⁴ Migraine is a disabling paroxysmal neurovascular condition that is characterized by recurrent episodes of moderate to severe headache associated with physiological disruptions to neurological, gastrointestinal, and sensory functions, as well as mood changes.⁵ Most cases of depression occur idiopathically, and the limited understanding of its etiology is reflected as a list of risk factors, such as stressful life

events, endocrine abnormalities, cancer, and the side effects of drugs, among many others.⁶ Pain/pruritus and depression frequently coexist. At least 50% of patients with chronic pain and pruritus are diagnosed with depression and/or anxiety.^{2,7} Some psychotropic drugs exert their own analgesic and antipruritic effects.^{4,8} These psychotic disorders affect the quality of life of patients, with disturbances in mood, sleep, and social relationships.

Recommended treatments for generalized pruritus include emollients, systemic antihistamines, topical corticosteroids, phototherapy, nalfurafine, and selective serotonin reuptake inhibitors.⁴ Sumatriptan, sodium valproate, topiramate, and antidepressant, such as venlafaxine, are recommended for the treatment of migraine,^{9,10} and antidepressants are prescribed to treat depression. Therapeutic agents for generalized pruritus are limited because the pharmacological characteristics of drugs for generalized pruritus are poorly understood and limited information is currently available on the relationship between pain and/or pruritus and depression. A previous study reported the differential onset times of mirtazapine, a noradrenergic and specific serotonergic antidepressant,

This is an open access article under the terms of the Creative Commons Attribution-NonCommercial-NoDerivs License, which permits use and distribution in any medium, provided the original work is properly cited, the use is non-commercial and no modifications or adaptations are made.

© 2021 The Authors. *Clinical Case Reports* published by John Wiley & Sons Ltd.

on pruritus and depression.¹¹ Therefore, we herein investigated differences in the onset time of venlafaxine, an antidepressant belonging to a group of drugs called serotonin and noradrenaline reuptake inhibitors, on generalized pruritus, migraine, and depression.

2 | CASE REPORT

A 37-year-old female patient developed severe and generalized pruritus without apparent primary lesions on her skin. Pruritus appeared on both forearms at the onset approximately two months ago, and gradually spread to her entire body. Although she had been treated with a conventional antipruritic drug, such as bilastine, and itching was uncontrollable. The patient also had a ten-year history of migraine with frequent attacks. Previous treatments with two different migraine preventative medications, sumatriptan and sodium valproate, were not successful and the patient rejected new medications. Migraine had been poorly controlled with over-the-counter medications, including combinations of caffeine and acetaminophen. The patient had developed more severe and longer lasting headaches in the past several weeks. She developed depression more than two months ago, which was characterized by depressed mood, anxiety, intermediated insomnia, and restlessness associated with irritability. She was diagnosed with a major depressive episode as classified in the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5).¹² Physical examinations and the results of laboratory studies revealed no significant abnormalities. Furthermore, no dermatosis with zoonotic contacts or exposures to chemicals or new cosmetic products prior to pruritus were found. Other than migraine, her medical history was unremarkable. She did not drink alcohol or use recreational drugs.

The depressive state was assessed using the 17-item Hamilton Depression Rating Scale (HDRS-17),¹³ in which a total score of “0–7” represents the normal range and “above 23” represents the greatest severity of depression. The HDRS-17 score before the administration of venlafaxine was 20, indicating severe depression with insomnia and anxiety (Figure 1A, Baseline). The HDRS-17 score was measured every 7 days until day 28 of the administration of 37.5 mg of venlafaxine. The HDRS-17 score gradually decreased after the initial dose of venlafaxine and reached a minimum score between days 21 and 28 of its administration (Figure 1A).

Migraine/pruritus was also assessed using a simple visual analog scale (VAS).¹⁴ The response of migraine to the oral administration of venlafaxine was assessed using VAS on day 0, 7, 14, 21, and 28 of the administration of venlafaxine. She was prescribed 37.5 mg of venlafaxine,

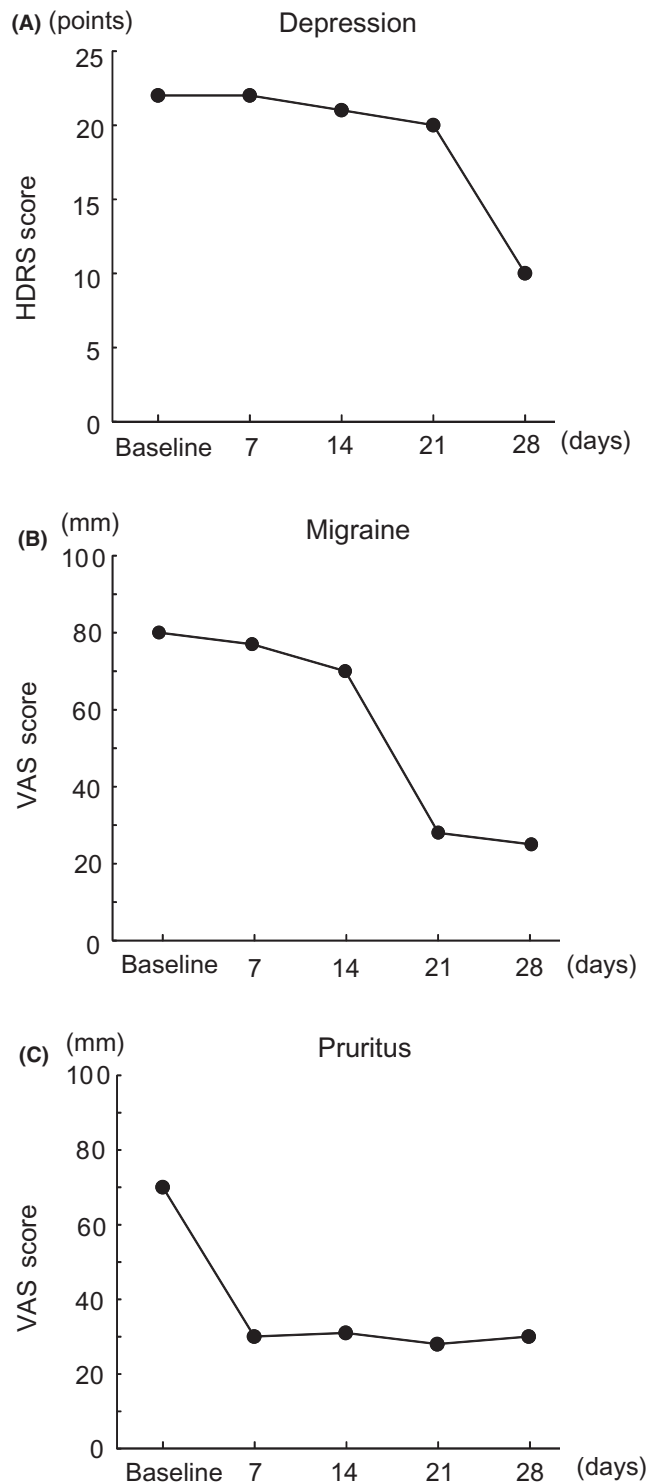


FIGURE 1 Effects of venlafaxine on depression, migraine, and pruritus. (A) Time-dependent changes in depression evaluated by HDRS-17 after the administration of venlafaxine. (B) Time-dependent changes in migraine evaluated by VAS after the administration of venlafaxine. (C) Time-dependent changes in pruritus evaluated by VAS after the administration of venlafaxine

the standard initial dose, once daily to minimize adverse events. The VAS score of migraine before the administration of venlafaxine was 80, indicating severe migraine

(Figure 1B, Baseline). Following the initiation of venlafaxine, the VAS score gradually decreased until day 14, was less than half that before its administration between days 14 and 21, and then remained stable until day 28 (Figure 1B).

A treatment with bilastine, an antihistamine, had no noticeable effects, and the VAS score before the administration of venlafaxine was 70, indicating severe pruritus (Figure 1C, Baseline). The VAS score of pruritus markedly decreased to less than half before the administration of venlafaxine within 7 days, and then remained stable until day 28 (Figure 1C). The administration of venlafaxine for 3 months resulted in the sustained and significant attenuation of pruritus, migraine and depression.

3 | DISCUSSION

Venlafaxine, a serotonin noradrenaline reuptake inhibitor (SNRI), has been prescribed as an antidepressant in patients with major depression disorder. It is generally administered at doses of 75–300 mg for the treatment of major depression with an observation period of 6–10 weeks.¹⁵ Therefore, the dose of 37.5 mg used in the present study was markedly lower than that previously reported, suggesting that 37.5 mg of venlafaxine may be sufficient for the treatment of depression. In this case report, venlafaxine mitigated generalized pruritus and migraine in a patient with depression, which is the first evidence for the efficacy of venlafaxine against pruritus. Venlafaxine at a daily dose of 37.5 mg exerted beneficial effects on and attenuated pruritus within 7 days. Therefore, it has potential as a novel drug for the treatment of pruritus.

Previous studies showed that venlafaxine at a daily dose of 75 mg or higher exerted beneficial effects on migraine.¹⁰ The present case was treated with venlafaxine at a dose of 37.5 mg per day, and migraine was attenuated by day 21. Therefore, 37.5 mg of venlafaxine may be sufficient to exert antinociceptive effects on migraine in patients with depression and pruritus. Since venlafaxine is an SNRI that exerts antipruritic effects, serotonin and noradrenaline receptors appear to be involved in the pruritic process.¹⁶

Venlafaxine exerted antidepressant, antinociceptive, and antipruritic effects in a patient with depression, migraine and chronic pruritus; however, the relationship between the onset times of these effects has not yet been elucidated. In our patient, the treatment with venlafaxine exerted antipruritic effects before the amelioration of migraine and depressive symptoms, indicating that the onset time of antipruritic effects after the treatment with

venlafaxine was faster than those of antinociceptive and antidepressant effects. Furthermore, the treatment with venlafaxine exerted antinociceptive effects before the alleviation of depressive symptoms, indicating that the onset time of antinociceptive effects after the treatment with venlafaxine was faster than that of antidepressant effects. Therefore, the attenuation of pruritus and migraine by antidepressants may ameliorate the depressive state because these symptoms generally cause depression in these patients. Alternatively, pruritus and migraine may induce neuronal plasticity in the brain resulting in severe depression. Although the underlying mechanisms remain unclear, Harmer et al.¹⁷ discussed that the repeated administration of antidepressants restored neuronal plasticity to a normal state. Therefore, based on the present results, the repeated administration of venlafaxine normalized the neuronal changes induced in the brain by chronic pruritus, migraine, and depression at differential onset times and via different mechanisms.

4 | CONCLUSION

The present case is novel in that the administration of venlafaxine attenuated depressive disorder, migraine, and severe pruritus, which was not previously documented in the literature. Generalized pruritus and migraine affect the quality of life of patients due to disturbances in mood, sleep, and social relationships. Therapeutic agents for generalized pruritus and migraine are limited because the underlying pathophysiological mechanisms have not yet been elucidated in detail. Furthermore, it remains unclear how pain and/or pruritus and depression influence each other. We herein described a patient with severe pruritus, migraine, and depression who was successfully treated with venlafaxine, indicating its potential as a new therapeutic option for patients with depressive disorder and severe pruritus unresponsive to conventional antipruritic drugs, including antihistamines. The management of the present case provides insights for similar cases in the future.

ACKNOWLEDGEMENT

None.

CONFLICTS OF INTEREST

All authors declare that they have no conflicts of interest.

AUTHOR CONTRIBUTIONS

YM and TN: Wrote the first draft of the article. YM, HF, AH-T, HH, TF, and AH: Managed the patient. YI: Revised the manuscript. All authors read and approved the final manuscript.

CONSENT

Written informed consent was obtained from the patient to publish this report in accordance with journal's patient consent policy.

DATA AVAILABILITY STATEMENT

The authors declare that data supporting the findings of this study are available within the article.

ORCID

Yasushi Ishida  <https://orcid.org/0000-0002-7601-4906>

REFERENCES

1. Kroenke K, Bair MJ, Damush TM, et al. Optimized antidepressant therapy and pain self-management in primary care patients with depression and musculoskeletal pain: a randomized controlled trial. *JAMA*. 2009;301:2099-2110.
2. Ferm I, Sterner M, Wallengren J. Somatic and psychiatric comorbidity in patients with chronic pruritus. *Acta Derm Venereol*. 2010;90:395-400.
3. Gambassi G. Pain and depression: the egg and the chicken story revisited. *Arch Gerontol Geriatr*. 2009;49(Suppl.1):103-112. <https://doi.org/10.1016/j.archger.2009.09.018>
4. Yosipovitch G, Bernhard JD. Chronic pruritus. *N Engl J Med*. 2013;368:1625-1634.
5. Headache Classification Committee of the International headache Society (IHS). The international classification of headache disorders, 3rd edition. *Cephalalgia*. 2018;38:1-211.
6. Krishnan V, Nestler EJ. The molecular neurobiology of depression. *Nature*. 2008;455(7215):894-902.
7. Torta R, Ieraci V, Zizzi F. A review of the emotional aspects of neuropathic pain: from comorbidity to co-pathogenesis. *Pain Ther*. 2017;6(Suppl.1):11-17.
8. Mika J, Zychowska M, Makuch W, Rojewska E, Przewlocka B. Neuronal and immunological basis of action of antidepressants in chronic pain-clinical and experimental studies. *Pharmacol Rep*. 2013;65:1611-1621.
9. Silberstein SD. Preventive migraine treatment. *Continuum (Minneapolis Minn)*. 2015;21:973-989.
10. Ozyalcin SN, Talu GK, Kiziltan E, Yucel B, Ertas M, Disci R. The efficacy and safety of venlafaxine in the prophylaxis of migraine. *Headache*. 2005;45:144-152.
11. Miyahara Y, Haruta-Tsukamoto A, Funahashi H, et al. Differential onset time of mirtazapine on pruritus and depression in a patient receiving hemodialysis. *SAGE Open Med Case Rep*. 2021;9:1-3.
12. American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders*, 5th Edition. Arlington, VA: American Psychiatric Association; 2013.
13. Hamilton M. A rating scale for depression. *J Neurol Neurosurg Psychiatry*. 1960;23:56-62.
14. Reich A, Heisig M, Phan NQ, et al. Visual analogue scale: evaluation of the instrument for the assessment of pruritus. *Acta Derm Venereol*. 2012;92:497-501.
15. Lyndon GJ, Prieto R, Wajsbrot DB, Allgulander C, Bandelow B. Efficacy of venlafaxine extended release in major depressive disorder patients: effect of baseline anxiety symptom severity. *Int Clin Psychopharmacol*. 2019;34:110-118.
16. Miyahara Y, Funahashi H, Naono-Nakayama R, Haruta-Tsukamoto A, Nishimori T, Ishida Y. Role of serotonin and noradrenaline in the acute itch processing in mice. *Eur J Pharmacol*. 2019;850:118-125.
17. Harmer CJ, Duman RS, Cowen PJ. How do antidepressants work? New perspectives for refining future treatment approaches. *Lancet Psychiatry*. 2017;4:409-418.

How to cite this article: Miyahara Y, Funahashi H, Haruta-Tsukamoto A, et al. Time course of effects of venlafaxine on migraine and generalized pruritus in a patient with depression. *Clin Case Rep*. 2021;9:e05088. <https://doi.org/10.1002/ccr3.5088>