SRIWIJAYA JOURNAL OF MEDICINE

Non-Hormonal Pharmacological Interventions to Manage Vasomotor Symptoms During Menopause

Gilang Amanda Hambali[1], Adnan Abadi[2*]

[1,2]Department of Obstetrics and Gynecology, Faculty of Medicine, Universitas Sriwijaya, Palembang, Indonesia
*Email: abadi_asnawi@yahoo.com

Abstract

This study reviews a range of non-hormonal pharmacological interventions used to treat vasomotor symptoms in postmenopausal women, including SSRIs, SNRIs, gabapentin, and neurokinin-3 receptor (NK3R) antagonists. Methods used included a literature review of multiple clinical trials and meta-analyses published over the past decade. Results showed that all interventions were effective in reducing the frequency and severity of hot flashes, with efficacy rates ranging from 36 to 72%. In addition, the side effect profile was generally mild to moderate, including nausea, sleep disturbance, and headache. NK3R antagonists, such as fezolinetant, have shown great promise with a rapid onset of action and comparable efficacy to hormone therapy, but longer-term studies are needed to assess safety. This study emphasizes the importance of an individualized approach to therapy selection and the need for monitoring liver function and potential side effects. Conclusions suggest that these non-hormonal interventions are a promising alternative for postmenopausal women for whom hormone therapy is contraindicated.

Keywords: Gabapentin, Vasomotor Symptoms, N3KR, Menopause, SSRI, SNRI, Non-Hormonal Therapy

1. Introduction

Menopause is a natural biological phase that marks the end of menstruation and is caused by a gradual decline in estrogen levels. Vasomotor symptoms, such as hot flashes and night sweats, are the main manifestations that affect the quality of life of menopausal women. The prevalence of these symptoms is quite high, reaching 80% in women during the menopausal transition, and can last for 7 to 10 years.[1-3] Declining hormonal factors, especially estrogen, are believed to trigger instability of the thermoregulatory center in the hypothalamus, causing an exaggerated vasomotor response to small temperature changes.[4]

Hormone therapy (HT) has been the primary treatment option for vasomotor symptoms for many years. However, limited medical contraindications and concerns about long-term risks, such as breast cancer and thromboembolism, have prompted the search for alternative non-hormonal treatments. Several non-hormonal pharmacological agents, including SSRIs, SNRIs, gabapentin, and NK3R antagonists, have been shown to be effective in reducing vasomotor symptoms based on recent clinical studies.[2,5-8] This study aims to comprehensively review the efficacy and safety profiles of these non-hormonal pharmacological interventions, and to provide clinical guidance in the management of menopausal vasomotor symptoms.

In addition, challenges in developing these therapies include individual response variability, potential side effects, and the need for long-term studies to assess ongoing safety and efficacy. With the increasing population of menopausal women and increasing awareness of quality of life, safe, effective, and evidence-based therapeutic approaches are becoming increasingly important.[9-12] Therefore, this review is expected to assist healthcare professionals in clinical decision-making regarding the management of non-hormonal vasomotor symptoms

2. Method

This narrative review is based on a qualitative synthesis of 42 studies retrieved through searches of PubMed, ScienceDirect, and Google Scholar, focusing on publications from 2010 to 2024, including randomized controlled trials, meta-analyses, and clinical reviews. Only studies published in English between 2010 and 2024 were included. Eligible articles comprised randomized controlled trials, observational studies, and systematic reviews that evaluated the efficacy and safety of non-hormonal pharmacological agents for menopausal vasomotor symptoms. Relevant studies were identified using electronic databases including PubMed, ScienceDirect, and Google Scholar with keywords such as “menopause”, “vasomotor symptoms”, “non-hormonal therapy”, “SSRIs”, “SNRIs”, “gabapentin”, and “NK3R antagonists”.

3. Discussion

Menopause and Vasomotor Symptoms

Menopause is a natural biological phase that marks the end of the menstrual cycle and pregnancy, usually occurring at the age of 45-55 years.[1,2] The most dominant hormonal changes during menopause are decreased levels of estrogen and progesterone, which affect various systems in a woman's body.[3,4] The most common symptoms that appear during the menopausal transition are vasomotor symptoms, including hot flashes and night sweats.[5,6] Hot flashes themselves are defined as a sudden sensation of heat that is usually accompanied by flushing and sweating, which can last from a few seconds to several minutes.[7,8]

The prevalence of hot flashes during menopause is very high, reaching around 75-85% of women, and can last for 4 to 10 years. Several studies have shown that genetic factors, lifestyle, and psychosocial status also influence the severity and duration of these vasomotor symptoms. In addition, factors such as stress, obesity, and smoking habits are known to worsen vasomotor symptoms.[9-14]

Vasomotor symptoms can disrupt sleep quality, cause fatigue, and reduce daily productivity. The impact is not only limited to physical aspects, but also affects psychological health, including anxiety and depression. Therefore, managing vasomotor symptoms is an important part of menopausal women's health care.[15-20]

Pathophysiology of Vasomotor Symptoms

The primary pathophysiology of vasomotor symptoms is related to instability of the thermoregulatory center in the hypothalamus. Estrogen plays a major role in regulating this thermoregulatory center. When estrogen levels decrease, there is a decrease in the sensitivity of this center to changes in temperature, causing the body to overreact to small temperature fluctuations. This response causes rapid vasodilation and sweating as a cooling mechanism. In addition, decreased estrogen also affects neurotransmitters such as serotonin and norepinephrine, which play a role in temperature regulation. Changes in these neurotransmitter levels worsen the instability of the thermoregulatory center, increasing the frequency and severity of hot flashes. Other factors that play a role include disruption of the neuroendocrine pathways that regulate body temperature, as well as increased sensitivity to stress. Several studies have also shown that psychological and lifestyle factors can modulate this vasomotor response.[20-24]

Hormone Therapy as the Primary Choice

Hormone therapy (HT) is the main treatment for vasomotor symptoms which is quite effective. HT usually uses single estrogen or a combination of estrogen-progestin, depending on the patient's uterine status. The effectiveness of HT in reducing hot

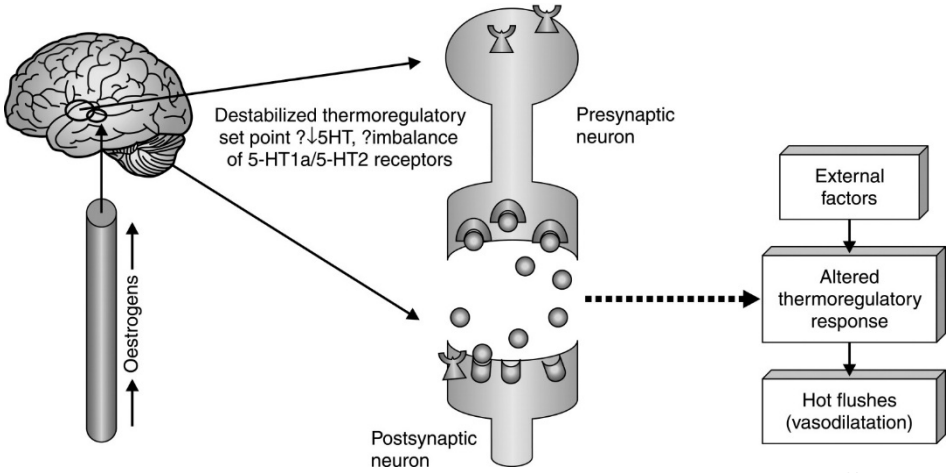

Figure 1. Pathophysiology of vasomotor symptoms during menopause[23]

flashes reach 80-90%, even in some cases, symptoms can disappear completely.[25-27]

However, its use is not free from risks and contraindications. The risk of thromboembolism, breast cancer, and cardiovascular disease are the main concern in the administration of HT. The use of HT must be considered carefully and adjusted to individual medical conditions and risks.[25-27]

In addition, other side effects such as breast tenderness, migraine, and mood disturbances have also been reported. Some women are reluctant to use HT due to concerns about these long-term effects.[25-27] Non-hormonal alternatives are increasingly being sought as an option for the management of vasomotor symptoms.

The Need for Non-Hormonal Alternatives

The limitations and risks inherent in HT have prompted the search for safe and effective alternative therapies. Non-hormonal therapy is expected to provide symptom relief without increasing the risk of long-term side effects. In addition, this therapy is also suitable for women with contraindications to HT, such as a history of breast cancer, thrombosis, or liver disease. [1,4,26-28]

The development of non-hormonal therapies is based on the understanding of vasomotor pathophysiology involving neurotransmitters and neuroendocrine pathways. Pharmacological approaches targeting the thermoregulatory center and neurotransmitter pathways are a major focus of current research. [1,4,26-28]

Non-Hormonal Pharmacological Interventions

A variety of non-hormonal pharmacological agents have been developed and tested to treat vasomotor symptoms. One major group is the selective serotonin reuptake inhibitors (SSRIs), which were originally used as antidepressants. Studies have shown that SSRIs such as paroxetine and citalopram are effective in reducing hot flashes.[1-3,6-8]

In addition to SSRIs, serotonin-norepinephrine reuptake inhibitors (SNRIs) such as venlafaxine have also shown efficacy. SNRIs work by modulating serotonin and norepinephrine pathways in the temperature-regulating center. Gabapentin, an anticonvulsant agent that works on the central nervous system, has also been shown to significantly reduce the frequency of hot flashes.[1-3,6-8]

In addition, neurokinin-3 receptor (NK3R) antagonists such as fezolinetant are recent innovations that target neuropeptide pathways involved in temperature

regulation.[1-3] Early studies suggest that these agents have great potential as effective and safe alternatives.[6-8]

Effectiveness and Mechanism of Action of Non-Hormonal Interventions

SSRIs and SNRIs work by modulating the neurotransmitters serotonin and norepinephrine, which play a role in the thermoregulatory center. This mechanism reduces the sensitivity of the temperature center to small fluctuations, thereby reducing the frequency of hot flashes.[25, 28-30]

Gabapentin works by affecting calcium channels in central nervous system neurons, reducing the activity of neurons that cause the sensation of heat. This mechanism also decreases sensitivity to temperature changes, thereby reducing hot flashes.[25, 28-30]

NK3R antagonists work by blocking the neuropeptide neurokinin B, which plays a role in regulating the temperature center in the hypothalamus. By modulating this pathway, these agents may decrease the frequency and severity of vasomotor attacks. Early studies suggest that this mechanism may provide faster results and a higher success rate.[25, 28-30] While all non-hormonal agents discussed reduce vasomotor symptoms, their efficacy and patient suitability may differ. SSRIs and SNRIs are particularly beneficial for patients with concurrent mood disorders, whereas gabapentin is more suitable for those with nighttime symptoms or intolerance to serotonergic agents.[28-30]

Side Effects of Non-Hormonal Interventions

Although effective, each pharmacological agent has its own side effect profile. SSRIs commonly cause nausea, sleep disturbances, and sexual dysfunction. These side effects are often mild and can be minimized with dose adjustments. SNRIs such as venlafaxine can also cause increased blood pressure, gastrointestinal disturbances, and fatigue. Gabapentin can cause dizziness, drowsiness, and impaired motor coordination.[30-33]

For NK3R antagonists, data on side effects are limited, but early studies have shown a good safety profile with minimal side effects, such as gastrointestinal upset and mild dizziness. These side effects should be closely monitored in long-term studies.[30-33]

Most side effects appear within the first 1–2 weeks of therapy initiation. SSRIs and SNRIs commonly induce early transient side effects such as nausea or insomnia, while gabapentin-related drowsiness usually appears within days. Close monitoring during the initial phase is recommended.[30-33]

Advantages and Disadvantages of Non-Hormonal Interventions

The main advantages of non-hormonal agents are a relatively better safety profile compared to HT, and the ability to be used by women with contraindications to hormones. In addition, the generally mild and tolerable side effects increase patient compliance. Drawbacks to note include individual response variability, certain side effects, and lack of long-term data. Some agents may take several weeks to show maximal effect, which can be challenging in clinical management.[33-35]

Recent Clinical Studies and Meta-Analysis

Several clinical studies have been conducted to assess the effectiveness of these non-hormonal agents. A recent meta-analysis confirmed that SSRIs and SNRIs reduce the frequency of hot flashes by 40-60%. Studies of gabapentin showed a reduction of up to 50%, while NK3R antagonists showed promising potential with an efficacy rate of around 70%.[3,8,21,28]

Long-term studies are needed to assess the sustainability of the benefits and safety of

Table 1. Classification of non-hormonal pharmacological therapies for vasomotor symptoms[28-42]

Drug Class	Agent Example	FDA Approval	Indication
SSRI	Paroxetine	✓	Moderate-to-severe VMS
SNRI	Venlafaxine	✗	Off-label for VMS
Gabapentin	Gabapentin	✗	Off-label for VMS
NK3R antagonist	Fezolinetant	✓	Moderate-to-severe VMS
Others (investigational)	Elinzanetant, Pavinetant	✗ (ongoing trials)	Under clinical investigation

Table 2. Comparison table of drug efficacy, onset, side effects, and FDA Approval[28-42]

Agent	Effectiveness	Onset of Action	Common Side Effects
SSRIs	↓ Hot flashes by 40–60%	1–2 weeks	Nausea, insomnia, sexual dysfunction
SNRIs	↓ Hot flashes by 45–60%	1–2 weeks	GI upset, hypertension, fatigue
Gabapentin	↓ Hot flashes by up to 50%	1 week	Dizziness, sedation, ataxia
NK3R antagonists	↓ Hot flashes by 70%	Days to 1 week	GI upset, dizziness (mild)

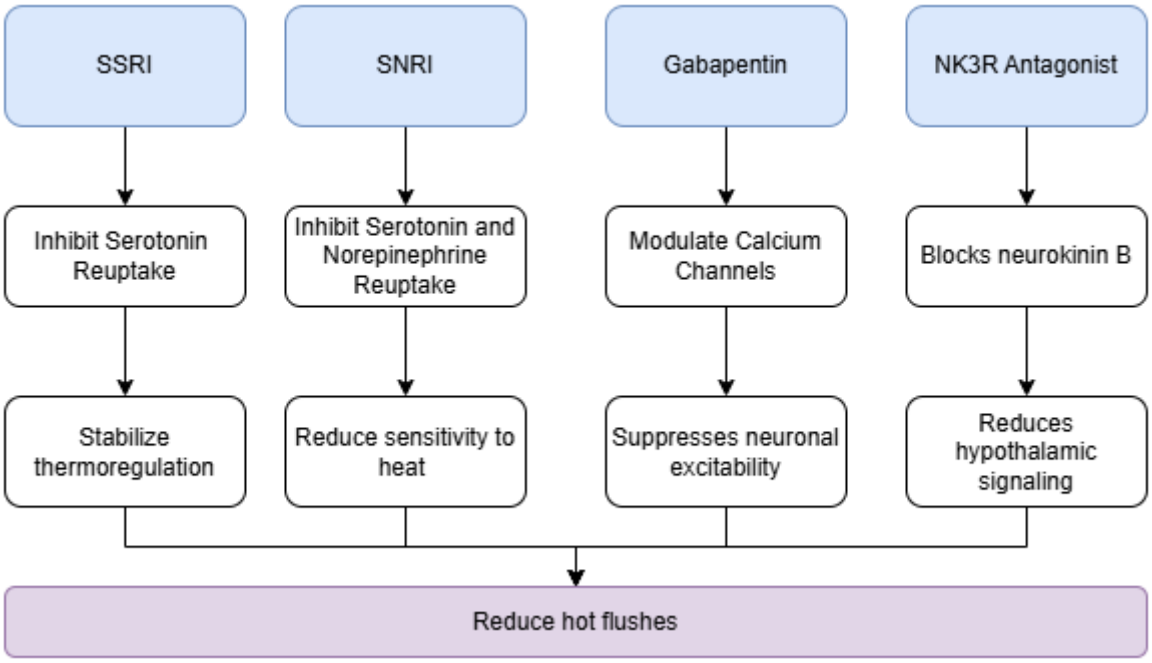

Figure 2. Mechanisms of action of SSRIs, SNRIs, gabapentin, and NK3R antagonists in the thermoregulatory pathway[29]

these agents. In addition, further studies are needed to compare the effectiveness and side effects between agents. Among the reviewed agents, SSRIs, SNRIs, and gabapentin have received regulatory approval for other indications and are often used off-label for menopausal symptoms. NK3R antagonists such as fezolinetant are still under investigation in some regions but have gained approval for vasomotor symptom management in countries such as the United States and Japan. This disparity in global approval underscores the need for harmonized regulatory evaluation and access expansion for effective non-hormonal alternatives. Meta-analyses report that SSRIs and SNRIs reduce hot flash frequency by 40–60%, gabapentin achieves around 50% reduction, while NK3R antagonists show the highest efficacy (~70%). However,

comparative head-to-head trials are still limited, and efficacy may vary depending on individual patient characteristics and comorbidities.[3,8,21,28]

The Role of Psychosocial and Lifestyle in Management

Although this review focuses on pharmacological interventions, lifestyle factors and psychosocial support are often integrated into clinical practice to maximize treatment outcomes. Psychosocial and lifestyle factors also influence the severity of vasomotor symptoms. Aspects such as stress, lack of exercise, and an unbalanced diet can worsen symptoms. Therefore, a holistic approach involving lifestyle modification and psychological support is highly recommended. Non-pharmacological interventions such as physical exercise, relaxation techniques, and stress management may help reduce the frequency and severity of hot flashes. Supplements such as phytoestrogens and vitamins are also under study to assess their benefits.[37-39]

Obstacles and Challenges in the Development of New Therapies

The development of new pharmacological therapies faces several obstacles, including the need for long-term studies, high research costs, and the risk of unexpected side effects. In addition, individual response variability poses challenges in determining optimal doses and risk profiles. [40-42]

Another challenge is to ensure that new therapies have advantages over existing therapies, both in terms of efficacy and safety. Technological advances in neuropharmacology and genetics are expected to accelerate the development of safer and more effective agents.[40-42]

4. Conclusion

Overall, non-hormonal pharmacological interventions show great potential in the management of vasomotor symptoms in menopausal women. However, further studies are needed to assess the long-term

Table 3. Comparative Summary of Non-Hormonal Pharmacological Interventions for Vasomotor Symptoms in Menopausal Women[29]

Drug Class	Example Agents	Mechanism of Action	Effectiveness	Duration of Effect	Regulatory Status
SSRIs	Paroxetine, Escitalopram	Inhibit serotonin reuptake→ modulate hypothalamic thermoregulation	40–60% reduction in hot flashes	Daily dose; stable effect	Paroxetine FDA-approved for VMS; others off-label
SNRIs	Venlafaxine, Desvenlafaxine	Inhibit serotonin & norepinephrine reuptake → stabilize thermoregulatory response	45–60% reduction in hot flashes	Optimal response in 2–3 weeks	Used off-label; clinically recommended
Gabapentin	Gabapentin	Modulates calcium channels in CNS →reduces neuronal excitability in temperature center	50% reduction in hot flashes	6–8 hours (requires 3x/day dosing)	Off-label; approved for epilepsy & neuropathic pain
NK3R Antagonists	Fezolinetant, Elinzanetant	Block neurokinin B receptor → normalize KNDy neuron activity in hypothalamus	70% reduction in hot flashes	Consistent with once-daily dosing	Fezolinetant FDA-approved (2023); others under investigation

effects and ensure the safety of widespread use of these agents. A multidisciplinary approach combining pharmacological therapy, lifestyle modification, and psychosocial support will provide the best results in improving patients' quality of life.[40-42]

Based on the literature review that has been conducted, it can be concluded that non-hormonal pharmacological interventions, such as SSRIs, SNRIs, gabapentin, and NK3R antagonists, show significant effectiveness in reducing the frequency and severity of vasomotor symptoms in menopausal women. The side effects that appear are generally mild to moderate and can be managed with close monitoring. In particular, NK3R antagonists such as fezolinetant show great potential as a promising alternative with a rapid onset of action and an efficacy profile comparable to hormone therapy, although long-term studies are still needed to assess the safety and sustainability of their use.

The use of non-hormonal therapies is an important option for menopausal women who have contraindications to hormone therapy, as well as for those who want safer and more effective symptom management. An individualized approach to therapy and monitoring for potential side effects should remain part of clinical practice. Thus, non-hormonal pharmacological interventions are a feasible and promising solution to improve the quality of life of menopausal women, but further research is needed to ensure long-term safety and optimize dosage and delivery methods

References

1. McNeil MA, Merriam SB. Menopause. Ann Intern Med. 2021 Jul;174(7):ITC97–112.
2. Nappi RE, Siddiqui E, Todorova L, Rea C, Gemmen E, Schultz NM. Prevalence and quality-of-life burden of vasomotor symptoms associated with menopause: A European cross-sectional survey. Maturity. 2023 Jan;167:66–74.
3. Talaulikar V. Menopause transition: Physiology and symptoms. Best Practice Res Clin Obstet Gynaecol. 2022 May; 81:3–7.
4. Koysombat K, McGown P, Nyunt S, Abbara A, Dhillo WS. New advances in menopause symptom management. Best Practice Res Clin Endocrinol Metab. 2024 Jan; 38(1):101774.
5. Khan SJ, Kapoor E, Faubion SS, Kling JM. Vasomotor Symptoms During Menopause: A Practical Guide on Current Treatments and Future Perspectives. Int J Women's Health. 2023 Feb; 15:273–87.
6. Stute P, Cano A, Thurston RC, Small M, Lee L, Scott M, et al. Evaluation of the impact, treatment patterns, and patient and physician perceptions of vasomotor symptoms associated with menopause in Europe and the United States. Maturity. 2022 Oct; 164:38–45.
7. Mehta J, Kling JM, Manson JE. Risks, Benefits, and Treatment Modalities of Menopausal Hormone Therapy: Current Concepts. Front Endocrinol (Lausanne). 2021 Mar 26;12:564781.
8. Madsen TE, Sobel T, Negash S, Shrout Allen T, Stefanick ML, Manson JE, et al. A Review of Hormone and Non-Hormonal Therapy Options for the Treatment of Menopause. Int J Women's Health. 2023 May; 15: 825–36.
9. Pertynska-Marczewska M, Pertynski T. Non-hormonal pharmacological interventions for managing vasomotor symptoms-how can we help: 2024 landscape. Eur J Obstet Gynecol Reprod Biol. 2024 Nov; 302:141–8.
10. Eke AC, Gebreyohannes RD, Fernandes MFS, Pillai VC. Physiologic Changes

During Pregnancy and Impact on Small-Molecule Drugs, Biologics (Monoclonal Antibody) Disposition, and Response. J Clin Pharmacol. 2023 Jun 14; 63(S1):S34–50.
11. Chu A, Wadhwa R. Selective Serotonin Reuptake Inhibitors. [Updated 2023 May 1]. In: StatPearls. Treasure Island (FL): StatPearls Publishing; 2025 Jan.
12. Edinoff AN, Fort JM, Woo JJ, Causey CD, Burroughs CR, Cornett EM, et al. Selective Serotonin Reuptake Inhibitors and Clozapine: Clinically Relevant Interactions and Considerations. Neurol Int. 2021 Sep 1; 13(3):445–63.
13. Radosavljevic M, Svob Strac D, Jancic J, Samardzic J. The Role of Pharmacogenetics in Personalizing the Antidepressant and Anxiolytic Therapy. Genes (Basel). 2023 May 16 ;14(5):1095.
14. Kim J, Kim TE, Lee SH, Koo JW. The Role of Glutamate Underlying Treatment-resistant Depression. Clin Psychopharmacol Neurosci. 2023 Aug 31; 21(3):429–46.
15. Zakaraya Z, Abu Assab M, Tamimi LN, Karameh N, Hailat M, Al-Omari L, et al. Pharmacokinetics and Pharmacodynamics: A Comprehensive Analysis of the Absorption, Distribution, Metabolism, and Excretion of Psychiatric Drugs. Pharmaceuticals. 2024 Feb 22; 17(3):280.
16. David PS, Smith TL, Nordhues HC, Kling JM. A Clinical Review on Paroxetine and Emerging Therapies for the Treatment of Vasomotor Symptoms. Int J Women's Health. 2022 March; Volume 14:353–61.
17. Lagerberg T, Fazel S, Sjölander A, Hellner C, Lichtenstein P, Chang Z. Selective serotonin reuptake inhibitors and suicidal behavior: a population-based cohort study. Neuropsychopharmacology. 2022 Mar 24; 47(4):817–23.
18. Azizi M, Khani S, Kamali M, Elyasi F. The Efficacy and Safety of Selective Serotonin Reuptake Inhibitors and Serotonin-Norepinephrine Reuptake Inhibitors in the Treatment of Menopausal Hot Flashes: A Systematic Review of Clinical Trials. Iranian J Med Sci. 2022 May; 47(3):173–93.
19. Blumenfeld Z, Bera K, Castrén E, Lester HA. Antidepressants enter cells, organelles, and membranes. Neuropsychopharmacology. 2024 Jan 2; 49(1):246–61.
20. Mota A de AR, Pereira Vilhena do Nascimento G, Martins Pereira G. Acupuncture as a Complementary Alternative in The Treatment of Anxiety: A Literature Review. J Heal Technol - JHT. 2022 Sep 12; 1(2):e1216.
21. Gosmann NP, Costa M de A, Jaeger M de B, Frozi J, Spanemberg L, Manfro GG, et al. Incidence of adverse events and comparative tolerability of selective serotonin reuptake inhibitors, and serotonin and norepinephrine reuptake inhibitors for the treatment of anxiety, obsessive-compulsive, and stress disorders: a systematic review and network meta-analysis. Psychol Med. 2023 Jul 6; 53(9):3783–92.
22. Fanelli D, Weller G, Liu H. New Serotonin-Norepinephrine Reuptake Inhibitors and Their Anesthetic and Analgesic Considerations. Neurol Int. 2021 Oct; 13(4):497–509.
23. Rapkin AJ. Vasomotor symptoms in menopause: physiologic condition and central nervous system approaches to treatment. Am J Obstet Gynecol. 2007;196(2):97–106.
24. Robinson C, Dalal S, Chitneni A, Patil A, Berger AA, Mahmood S, et al. A Look at Commonly Utilized Serotonin Noradrenaline Reuptake Inhibitors

(SNRIs) in Chronic Pain. Heal Psychol Res. 2022 May 30; 10(2):32309.
25. Radkhah H, Esfandbod M, Khadembashiri MA, Eslami M, Etesam F, Shahi F, et al. Comparative Study of the Effects of Duloxetine and Venlafaxine on Acute Symptomatic Taxane-induced Neuropathy in Breast Cancer Patients: a randomized clinical trial. J Community Hosp Intern Med Perspect. 2024 Jan 10; 14(1):18–24.
26. Grover S, Sarkar S, Avasthi A. Management of Systemic Medical Emergencies Associated with Psychotropic Medications. Indian J Psychiatry. 2022 May; 64 (Suppl 2): 252–80.
27. Lee SR, Cho MK, Cho YJ, Chun S, Hong SH, Hwang KR, et al. The 2020 Menopausal Hormone Therapy Guidelines. J Menopausal Med. 2020 Aug ; 26 (2): 69.
28. Somirathne D. SSRI & SNRI over Menopausal Hormone Therapy (MHT) - Would be more practical to initiate due to its free availability and affordable price under this economic crisis of Sri Lanka. Sri Lanka J Menopause . 2023; 4(1):10–2.
29. Yoon SH, Lee JY, Lee C, Lee H, Kim SN. Gabapentin for the treatment of hot flushes in menopause: a meta-analysis. Menopause. 2020 Apr; 27(4):485–93.
30. Shan D, Zou L, Liu X, Shen Y, Cai Y, Zhang J. Efficacy and safety of gabapentin and pregabalin in patients with vasomotor symptoms: a systematic review and meta-analysis. Am J Obstet Gynecol. 2020 June; 222 (6):564-579.e12.
31. Edinoff AN, Nix CA, Hollier J, Sagrera CE, Delacroix BM, Abubakar T, et al. Benzodiazepines: Uses, Dangers, and Clinical Considerations. Neurol Int. 2021 Nov 10; 13(4):594–607.
32. Shrestha S, Palaian S. Respiratory concerns of gabapentin and pregabalin: What does it mean for the pharmacovigilance systems in developing countries? F1000Research. 2021 Feb 25; 9:32.
33. Rusciano D. Molecular Mechanisms and Therapeutic Potential of Gabapentin with a Focus on Topical Formulations to Treat Ocular Surface Diseases. Pharmaceuticals. 2024 May 11; 17(5):623.
34. Davari M, Amani B, Amani B, Khanijahani A, Akbarzadeh A, Shabestan R. Pregabalin and gabapentin in neuropathic pain management after spinal cord injury: a systematic review and meta-analysis. Korean J Pain. 2020 Jan 1 ;33(1):3–12.
35. Kling JM, Stuenkel CA, Faubion SS. Management of the Vasomotor Symptoms of Menopause: Twofers in Your Clinical Toolbox. Mayo Clinic Proc. 2024 Jul ;99(7):1142–8.
36. Hassan F, Saleem A, Samuel SS, Sarfraz Z, Sarfraz A, Sarfraz M, et al. Neurokinin 1/3 receptor antagonists for menopausal women: A current systematic review and insights into the investigational non-hormonal therapy. Medicine (Baltimore). 2023 Jun 9; 102(23):e33978.
37. Gompel A, Stuenkel CA. Neurokinin 3 receptor antagonists for menopausal vasomotor symptoms, an appraisal. Cell Reports Med. 2023 June; 4(6):101076.
38. González-García I, López M. Fezolinetant for menopausal hot flashes and night sweats. Trends Pharmacol Sci. 2023 Sep; 44(9):635–6.
39. Depypere H, Timmerman D, Donders G, Sieprath P, Ramael S, Combalbert J, et al. Treatment of Menopausal Vasomotor Symptoms With Fezolinetant, a Neurokinin 3 Receptor Antagonist: A Phase 2a Trial. J Clin

Endocrinol Metab. 2019 Dec 1;104(12):5893–905.

40. Pinkerton JAV, Redick DL, Homewood LN, Kaunitz AM. Neurokinin Receptor Antagonist, Fezolinetant, for Treatment of Menopausal Vasomotor Symptoms. J Clin Endocrinol Metab. 2023 Oct 18; 108(11):e1448–9.
41. Lederman S, Ottery FD, Cano A, Santoro N, Shapiro M, Stute P, et al. Fezolinetant for treatment of moderate-to-severe vasomotor symptoms associated with menopause (Skylight 1): A phase 3 randomized controlled study. Lancet. 2023 April; 401(10382):1091–102.
42. Prague JK, Abbara A, Comninos AN, Jayasena CN, Higham CE, Adaway J, et al. Neurokinin 3 Receptor Antagonists Do Not Increase FSH or Estradiol Secretion in Menopausal Women. J Endocr Soc. 2020 Feb 1; 4(2):1–10.
43. Fraser GL, Lederman S, Waldbaum A, Kroll R, Santoro N, Lee M, et al. A phase 2b, randomized, placebo-controlled, double-blind, dose-ranging study of the neurokinin 3 receptor antagonist fezolinetant for vasomotor symptoms associated with menopause. Menopause. 2020 Apr; 27(4):382–92