International Journal of Life Sciences, Biotechnology and Pharma Research Vol. 14, No. 2, February 2025 Online ISSN: 2250-3137
Print ISSN: 2977-0122

DOI: 10.69605/ijlbpr_14.2.2025.124

ORIGINAL RESEARCH

Efficacy of Non-Hormonal Therapies in Managing Menopausal Symptoms: A Randomized Controlled Trial

Dr. Prashant Pujara[1], Dr. Ruchi Gokani[2], Dr. Bhamini G Kadikar[3]

[1]Consultant Gynaecologist, Department Obstetrics and Gynaecology, Maa Women's Hospital, Viramgam, Gujarat, India
[2]Assistant Professor, Department Biochemistry, GMERS Medical College, Sola, Ahmedabad, Gujarat, India
[3]Associate Professor, Department of Obstetrics and Gynaecology, Nootan Medical College and Research Centre, Visnagar, Gujarat, India

Corresponding Author
Dr. Bhamini G Kadikar
Associate Professor, Department of Obstetrics and Gynaecology, Nootan Medical College and Research Centre, Visnagar, Gujarat, India
Email: drbhaminip@gmail.com

Received: 22 January, 2025 Accepted: 15 February, 2025 Published: 24 February, 2025

ABSTRACT

Background: Menopausal symptoms, including hot flashes, mood disturbances, and sleep disorders, significantly impact women's quality of life. While hormonal therapy is effective, concerns about its safety have led to increased interest in non-hormonal alternatives. This study evaluates the efficacy of non-hormonal therapies in alleviating menopausal symptoms. **Materials and Methods:** A randomized controlled trial was conducted with 120 menopausal women aged 45–60 years, divided into three groups (n=40 each): Group A received cognitive behavioral therapy (CBT), Group B was administered phytoestrogens, and Group C served as the control (placebo). The intervention lasted for 12 weeks. Symptom severity was assessed using the Menopause Rating Scale (MRS) at baseline, six weeks, and post-intervention. Statistical analysis was performed using ANOVA and post-hoc tests, with significance set at $p<0.05$. **Results:** At baseline, mean MRS scores were comparable across groups (CBT: 18.5±2.3, Phytoestrogens: 19.1±2.6, Control: 18.9±2.4, $p=0.78$). After 12 weeks, Group A showed a significant reduction in MRS scores (9.2±1.8, $p<0.001$), followed by Group B (12.1±2.2, $p<0.01$). The control group exhibited minimal improvement (18.3±2.1, $p=0.09$). Improvements in sleep quality and mood were more pronounced in the CBT group, while phytoestrogens were more effective in reducing vasomotor symptoms. **Conclusion:** Non-hormonal therapies, particularly cognitive behavioral therapy and phytoestrogens, effectively alleviate menopausal symptoms. CBT demonstrated superior efficacy in improving mood and sleep, whereas phytoestrogens provided significant relief from hot flashes. These therapies offer promising alternatives for women unable or unwilling to use hormone therapy.

Keywords: Menopause, non-hormonal therapy, cognitive behavioral therapy, phytoestrogens, menopausal symptoms, randomized controlled trial.

INTRODUCTION

Menopause is a natural biological transition that marks the end of a woman's reproductive phase, typically occurring between the ages of 45 and 55 years. It is characterized by a decline in estrogen levels, leading to various vasomotor, psychological, and genitourinary symptoms that can significantly impact quality of life (1). Hot flashes, night sweats, mood disturbances, sleep disorders, and cognitive changes are among the most commonly reported symptoms (2). While hormonal therapy (HT) remains the most effective treatment, concerns regarding its long-term safety, particularly the risk of breast cancer, cardiovascular diseases, and thromboembolic events, have limited its widespread use (3,4). As a result, there has been a growing interest in non-hormonal alternatives for managing menopausal symptoms.

Several non-hormonal therapies have been explored, including cognitive behavioral therapy (CBT), phytoestrogens, selective serotonin reuptake inhibitors (SSRIs), and lifestyle modifications (5). CBT has demonstrated efficacy in improving mood disturbances, reducing sleep disturbances, and enhancing overall well-being in menopausal women (6). Phytoestrogens, plant-derived compounds with estrogen-like properties, have been investigated for their potential in alleviating vasomotor symptoms, with mixed but promising results (7). Given the

DOI: 10.69605/ijlbpr_14.2.2025.124

increasing preference for non-hormonal approaches, further research is needed to compare the effectiveness of these interventions.

This randomized controlled trial (RCT) aims to assess and compare the efficacy of cognitive behavioral therapy and phytoestrogens in managing menopausal symptoms. The findings of this study could provide valuable insights into safer and effective non-hormonal alternatives for menopause management.

MATERIALS AND METHODS

Study Design and Participants

This randomized controlled trial (RCT) was conducted to assess the efficacy of non-hormonal therapies in managing menopausal symptoms. A total of 120 menopausal women aged 45–60 years, experiencing moderate to severe menopausal symptoms, were recruited from outpatient clinics. Participants were randomly assigned into three groups (n=40 each): Group A received cognitive behavioral therapy (CBT), Group B was administered phytoestrogens, and Group C served as the control group receiving a placebo. Written informed consent was obtained from all participants before enrolment.

Inclusion and Exclusion Criteria

Women who had not used hormone replacement therapy (HRT) or other pharmacological treatments for menopausal symptoms in the last six months were included. Participants with severe medical conditions, psychiatric disorders, or those using medications affecting menopausal symptoms were excluded.

Intervention

- **Cognitive Behavioral Therapy (CBT) (Group A):** Participants attended weekly structured CBT sessions for 12 weeks, focusing on stress management, cognitive restructuring, and behavioral modification strategies. Each session lasted 60 minutes and was conducted by a trained psychologist.
- **Phytoestrogen Supplementation (Group B):** Women in this group received 50 mg of standardized isoflavone supplements daily for 12 weeks.
- **Control Group (Group C):** Participants received an identical placebo capsule without active ingredients.

Outcome Measures

The severity of menopausal symptoms was assessed using the Menopause Rating Scale (MRS) at baseline, six weeks, and post-intervention (12 weeks). The primary outcome was the reduction in total MRS scores, while secondary outcomes included improvements in sleep quality, mood, and vasomotor symptoms.

Randomization and Blinding

Participants were randomized using a computer-generated allocation sequence. The phytoestrogen and placebo groups were double-blinded, while blinding was not feasible for the CBT group due to the nature of the intervention.

Statistical Analysis

Data were analyzed using **SPSS version 25.0**. Descriptive statistics were used to summarize baseline characteristics. Comparisons between groups were performed using **one-way ANOVA** and **post-hoc tests**, while within-group changes over time were analyzed using **paired t-tests**. A significance level of $p<0.05$ was considered statistically significant.

RESULTS

Baseline Characteristics

The study enrolled 120 menopausal women, equally distributed among the three intervention groups. At baseline, there were no significant differences in mean age, body mass index (BMI), menopause duration, or Menopause Rating Scale (MRS) scores among the groups ($p>0.05$), indicating a comparable starting point for all participants (Table 1).

Table 1: Baseline Characteristics of Participants

Characteristic	CBT Group (n=40)	Phytoestrogen Group (n=40)	Control Group (n=40)
Age (years)	52.3 ± 3.5	51.8 ± 3.2	52.1 ± 3.4
BMI (kg/m²)	26.4 ± 2.8	27.1 ± 2.5	26.8 ± 2.7
Menopause Duration (years)	4.5 ± 1.2	4.7 ± 1.4	4.6 ± 1.3
Baseline MRS Score	18.5 ± 2.3	19.1 ± 2.6	18.9 ± 2.4

Effect on Menopause Rating Scale (MRS) Scores

After 12 weeks of intervention, a significant reduction in MRS scores was observed in both the CBT and phytoestrogen groups compared to the control group ($p<0.001$). The CBT group showed the greatest improvement, with MRS scores decreasing from 18.5±2.3 at baseline to 9.2±1.8 at 12 weeks. The phytoestrogen group also demonstrated a significant reduction, from 19.1±2.6 at baseline to 12.1±2.2 at 12 weeks. In contrast, the control group exhibited minimal changes, with MRS scores remaining relatively stable (Table 2).

Table 2: Changes in Menopause Rating Scale (MRS) Scores Over 12 Weeks

Time point	CBT Group (n=40)	Phytoestrogen Group (n=40)	Control Group (n=40)
Baseline	18.5 ± 2.3	19.1 ± 2.6	18.9 ± 2.4
6 Weeks	12.8 ± 2.1	15.3 ± 2.4	18.5 ± 2.2

DOI: 10.69605/ijlbpr_14.2.2025.124

12 Weeks	9.2 ± 1.8	12.1 ± 2.2	18.3 ± 2.1

Symptom-Specific Improvements

- **Vasomotor Symptoms:** Participants in the phytoestrogen group reported a substantial reduction in hot flashes and night sweats compared to baseline ($p<0.01$).
- **Mood and Sleep Disturbances:** The CBT group showed the most significant improvements in psychological symptoms, including anxiety, depression, and sleep quality ($p<0.001$).
- **Overall Symptom Relief:** The CBT group demonstrated superior effectiveness in alleviating a broader range of menopausal symptoms compared to the phytoestrogen group.

These findings suggest that both non-hormonal therapies effectively reduce menopausal symptoms, with CBT being more beneficial for psychological and sleep-related issues, while phytoestrogens provide notable relief from vasomotor symptoms.

DISCUSSION

The findings of this randomized controlled trial suggest that non-hormonal interventions, specifically cognitive behavioral therapy (CBT) and phytoestrogens, are effective in alleviating menopausal symptoms, with CBT showing greater efficacy in improving mood and sleep disturbances. These results align with previous studies highlighting the benefits of non-hormonal approaches in managing menopause-related symptoms (1,2).

CBT has been well-documented as a psychological intervention that helps modify negative thought patterns and behaviors, leading to improved emotional well-being and sleep quality (3). Our study observed a significant reduction in Menopause Rating Scale (MRS) scores in the CBT group, consistent with previous trials where CBT demonstrated effectiveness in reducing anxiety, depression, and sleep disturbances in menopausal women (4,5). The underlying mechanism may involve cognitive restructuring and relaxation techniques that help manage stress-related hormonal fluctuations (6). Furthermore, CBT has been recommended as a first-line non-pharmacological approach for menopausal symptoms, particularly for women seeking alternatives to hormone therapy (7).

Phytoestrogens, plant-derived compounds with estrogen-like activity, have been extensively studied for their potential to alleviate vasomotor symptoms such as hot flashes and night sweats (8). In this study, participants receiving phytoestrogen supplementation exhibited a notable improvement in vasomotor symptoms, supporting previous meta-analyses that indicate their moderate efficacy in reducing menopausal discomfort (9,10). Isoflavones, a key component of phytoestrogens, bind to estrogen receptors and exert mild estrogenic effects, which may explain their effectiveness in symptom relief (11). However, the degree of response varies based on factors such as individual metabolism and gut microbiota composition (12).

Compared to the control group, both intervention groups showed significant improvements in symptom severity, reinforcing the potential of non-hormonal strategies as viable treatment alternatives (13). The minimal change observed in the control group suggests that the placebo effect alone is insufficient for meaningful symptom relief, further validating the efficacy of the interventions studied. Additionally, previous research has highlighted concerns regarding the safety of long-term hormone therapy due to its association with increased risks of cardiovascular disease and breast cancer (14,15). As a result, non-hormonal therapies such as CBT and phytoestrogens present promising options for menopausal women who prefer or require alternatives to hormonal interventions.

Limitations and Future Directions

Despite its strengths, this study has certain limitations. First, the relatively short follow-up period of 12 weeks limits the ability to assess long-term effectiveness and sustainability of symptom relief. Future studies should incorporate extended follow-ups to determine the durability of benefits. Second, individual variations in the metabolism of phytoestrogens were not assessed, which could impact the efficacy of supplementation. Further research should explore personalized approaches based on genetic and metabolic profiling. Lastly, while CBT was highly effective, its accessibility may be limited in certain settings due to the need for trained therapists. Investigating digital or self-guided CBT programs could offer wider applicability.

CONCLUSION

This study supports the effectiveness of non-hormonal therapies in managing menopausal symptoms, with CBT demonstrating superior improvements in mood and sleep quality, while phytoestrogens effectively reduced vasomotor symptoms. Given the growing concerns surrounding hormone therapy, these interventions offer safer and viable alternatives for symptom management in menopausal women. Future studies should focus on long-term efficacy, personalized treatment strategies, and wider accessibility of these therapies.

REFERENCES

1. Hunter MS, Smith M. Managing hot flushes with cognitive behavioral therapy: evidence from clinical trials. Menopause Int. 2013 Dec;19(4):157-63.
2. Ayers B, Smith M, Hellier J, Mann E, Hunter MS. Effectiveness of group and self-help cognitive behavioral therapy in reducing menopausal symptoms. Menopause. 2012 Jul;19(7):749-57.
3. Newton KM, Reed SD, LaCroix AZ, Grothaus LC, Ehrlich K, Guiltinan J. Treatment of vasomotor

DOI: 10.69605/ijlbpr_14.2.2025.124

symptoms of menopause with black cohosh, multibotanicals, soy, hormone therapy, or placebo. Ann Intern Med. 2006 Dec 19;145(12):869-79.
4. Sassarini DJ, Lumsden MA. Non-hormonal management of menopausal vasomotor symptoms. BMJ. 2015 Nov 23;351:h6036.
5. Reddy SY, Warner H, Guttuso T, Messing S, DiGrazio W, Thornbury J, et al. Gabapentin, estrogen, and placebo for treating hot flushes: a randomized controlled trial. Obstet Gynecol. 2006 Jul;108(1):41-8.
6. Manson JE, Kaunitz AM. Menopause management—getting clinical care back on track. N Engl J Med. 2016 Mar 3;374(9):803-6.
7. Franco OH, Chowdhury R, Troup J, Voortman T, Kunutsor S, Kavousi M, et al. Use of plant-based therapies and menopausal symptoms: A systematic review and meta-analysis. JAMA. 2016 Jun 21;315(23):2554-63.
8. Nelson HD. Menopause. Lancet. 2008 Mar 1;371(9614):760-70.
9. van Die MD, Burger HG, Bone KM, Cohen MM, Teede HJ. Hypericum perforatum with Vitex agnus-castus in menopausal symptoms: A randomized, controlled trial. Menopause. 2009 Jan-Feb;16(1):156-63.
10. Kim KH, Choi MS, Kim YJ, Jung UJ, Yeo J, Jeon SM, et al. Effects of daidzein-rich isoflavone aglycone on menopausal symptoms. Menopause. 2011 Oct;18(10):1130-5.
11. Hersh AL, Stefanick ML, Stafford RS. National use of postmenopausal hormone therapy. JAMA. 2004 Jan 7;291(1):47-53.
12. Genazzani AR, Gambacciani M. Effect of isoflavones on menopausal neuroendocrine function. Gynecol Endocrinol. 2006 Jan;22(1):1-7.
13. Rossouw JE, Anderson GL, Prentice RL, LaCroix AZ, Kooperberg C, Stefanick ML, et al. Risks and benefits of estrogen plus progestin in healthy postmenopausal women: principal results from the Women's Health Initiative randomized controlled trial. JAMA. 2002 Jul 17;288(3):321-33.
14. Lethaby A, Marjoribanks J, Kronenberg F, Roberts H, Eden J, Brown J. Phytoestrogens for menopausal vasomotor symptoms. Cochrane Database Syst Rev. 2013 Dec 10;(12):CD001395.
15. Hunter MS, Smith M. Cognitive-behavioral approaches for managing hot flushes and night sweats. J Psychosom Obstet Gynaecol. 2015 Mar;36(1):1-10.