Management of Postmenopausal Symptoms with Extended-Release Venlafaxine

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Abstract

Objective: *To examine the efficacy of extended-release venlafaxine for the treatment of postmenopausal symptoms, especially the vasomotor symptoms.*
Methods: *Twenty-eight postmenopausal women were recruited for this observational study and received treatment with open-label extended-release venlafaxine, 75mg daily for 6 weeks. Menopausal symptoms were evaluated with Green Climacteric Scale (GCS) and for inclusion a GCS total score > 20 was required.*
Results: *GCS mean scores declined for each subscale: Psychological Subscale mean score decreased over the 6 weeks of treatment from 14.4 to 8.9; Somatic subscale mean score decreased from 5.9 to 3.8; and Vasomotor Subscale mean score decreased from 5.3 to 3.1, a decrease with 41.5% from baseline. The most frequent adverse events were nausea and dry mouth.*
Conclusion: *Extended-release venlafaxine, 75 mg per day, appears to be effective for treating postmenopausal symptoms and thus may be a possible alternative to hormonal therapy for postmenopausal women.*
Keywords: *postmenopausal symptoms, venlafaxine, hot flashes.*

Introduction

The menopausal transition usually begins in the mid-to-late 40s and lasts about 4 years, with menopause occurring at a median age of 51 years. During the early menopausal transition, estrogen levels are generally normal or even slightly elevated; the level of follicle-stimulating hormone begins to increase but is generally in the normal range. As the menopause transition progresses, hormone levels are variable, but estrogen levels fall markedly and levels of follicle-stimulating hormone increase. After menopause, the ovaries do not produce estradiol or progesterone but continue to produce testosterone. A small amount of estrogen is produced by the metabolism of adrenal steroids to estradiol in peripheral fat tissue.

The most common problematic symptoms of menopause are vasomotor symptoms, such as hot flashes and night sweats. Other symptoms are mood disorders, irritability, sleep disturbances, difficulty concentrating, memory impairment, headaches etc. Vasomotor symptoms are characterized by the perception of intense heat (hot flash) and subsequent cooling by cutaneous vasodilatation (skin flushing), perspiration and chills[(1)]. Vasomotor symptoms occur in 70% of women within 3 months of menopause, with 50% of these women experiencing persistent symptoms during the first 5 years[(2,3,4)].

Most of these symptoms have a central nervous system component and can have a significant negative effect of a woman's quality of life. The basic hormonal change in menopause is loss of estrogen. This loss of estrogen alters the activity of the nonadrenergic and serotonergic systems[(5,6)] by affecting the levels of the neurotransmitters in the brain and thus it affects the hypothalamic thermoregulatory cen-

ter, causing hot flashes. There is a transient lowering of the hypothalamic temperature regulatory set point, but the mechanism by which this occurs is unknown. It is speculated that a combination of hormonal, metabolic and psychogenic factors play a role in the etiology of menopausal vasomotor symptoms.

Estrogen with or without progesterone has been the most commonly prescribed medication for the treatment of menopausal symptoms, especially vasomotor symptoms. However, there is significant, mounting evidence of the risk of hormone therapy, outweighing the benefits. Hormone therapy was associated with a higher risk of breast cancer, stroke and venous thromboembolism and it may increase the risk of heart disease[7]. Therefore, there has been great interest in finding alternative, nonhormonal strategies for the management of menopausal symptoms. Recent data suggest that selective serotonin reuptake inhibitor antidepressants (SSRI) and serotonin norepinephrine inhibitor antidepressants (SNRI) may be effective for this kind of symptoms.

Extended release Venlafaxine's mechanism of action is blockade of the reuptake of serotonin and norepinephrine (SNRI). At lower doses, it is primary involved in serotonin reuptake inhibition (like SSRI). Frequent adverse reactions are nausea, dry mouth, headache, insomnia or somnolence, anxiety, constipation, sweating, and decreased libidos.

The present study was an observational, uncontrolled, 6-week, outpatient study, conducted at Ward 3, Clinical Hospital of Psychiatry "Prof. Dr. Al. Obregia", Bucharest and its aim was to examine the possibility of treating posmenoupausal symptoms with extended release Venlafaxine.

Materials and Methods

Postmenopausal women (age between 40 and 60 years) were recruited for this study. Their postmenopausal symptoms must have been present for at least 1 month before study entry. Menopausal symptoms were evaluated with Green Climacteric Scale (GCS) and for inclusion a GCS total score >20 was required. Symptoms were evaluated with GSC at the end of week 2, 4, and 6.

The Greene Climacteric Scale provides a brief measure of menopause symptoms. It can be used to assess changes in different symptoms, before and after menopause treatment. It has 21 items, as follows: 1-heart beating quickly and strongly, 2-feeling tense or nervous, 3-difficulty in sleeping, 4-excitable, 5-attacks of panic, 6-difficulty in concentrating, 7-feeling tired or lacking in energy, 8-loss of interest in most things, 9-feeling unhappy or depressed, 10-crying spells, 11-irritability, 12-feeling dizzy or faint, 13-pressure or tightness in head or body, 14-parts of body feeling numb or tingling, 15-headaches, 16-muscle or joint pains, 17-loss of feeling in hands or feet, 18-breathing difficulties, 19-hot flushes,

Table 1

Demographic data at baseline

Age (mean, years)	51.77
Age at menopause (mean, years)	49.05
Years since menopause	2.77
Menopause type surgical/natural (n)	5/13

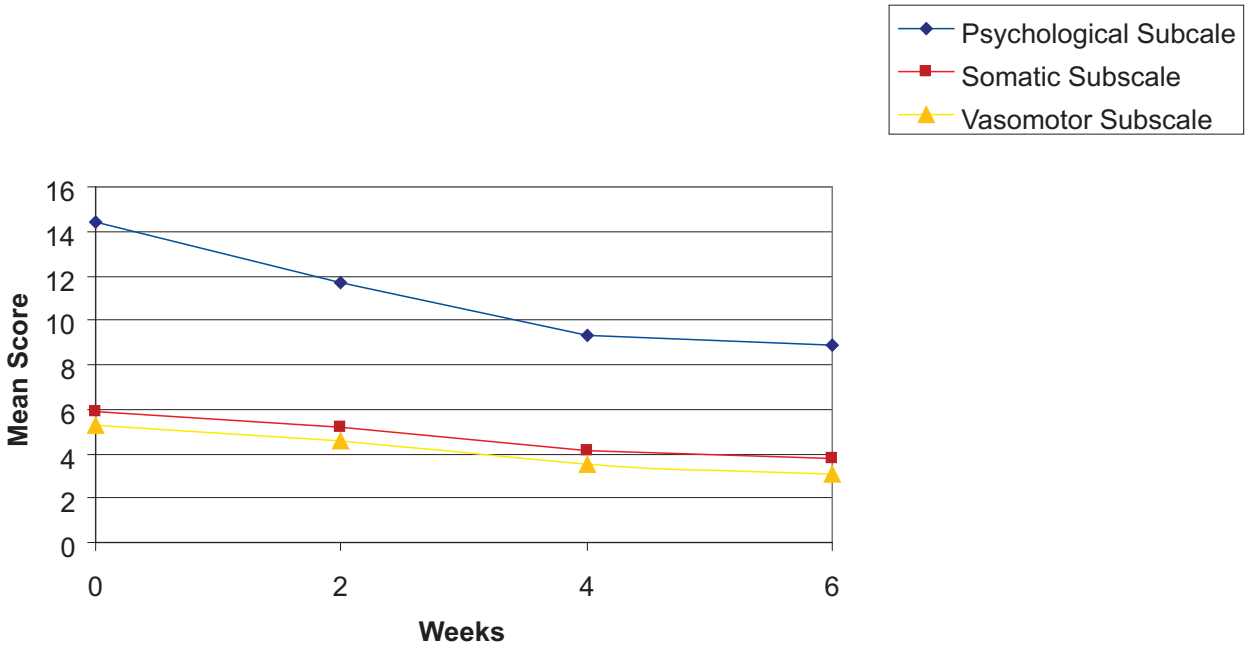

Figure. 1. Mean change over 6 weeks of treatment with Extended Release Venlafaxine for Psychological Subscale, Somatic Subscale and Vasomotor Subscale of the Green Climacteric Scale

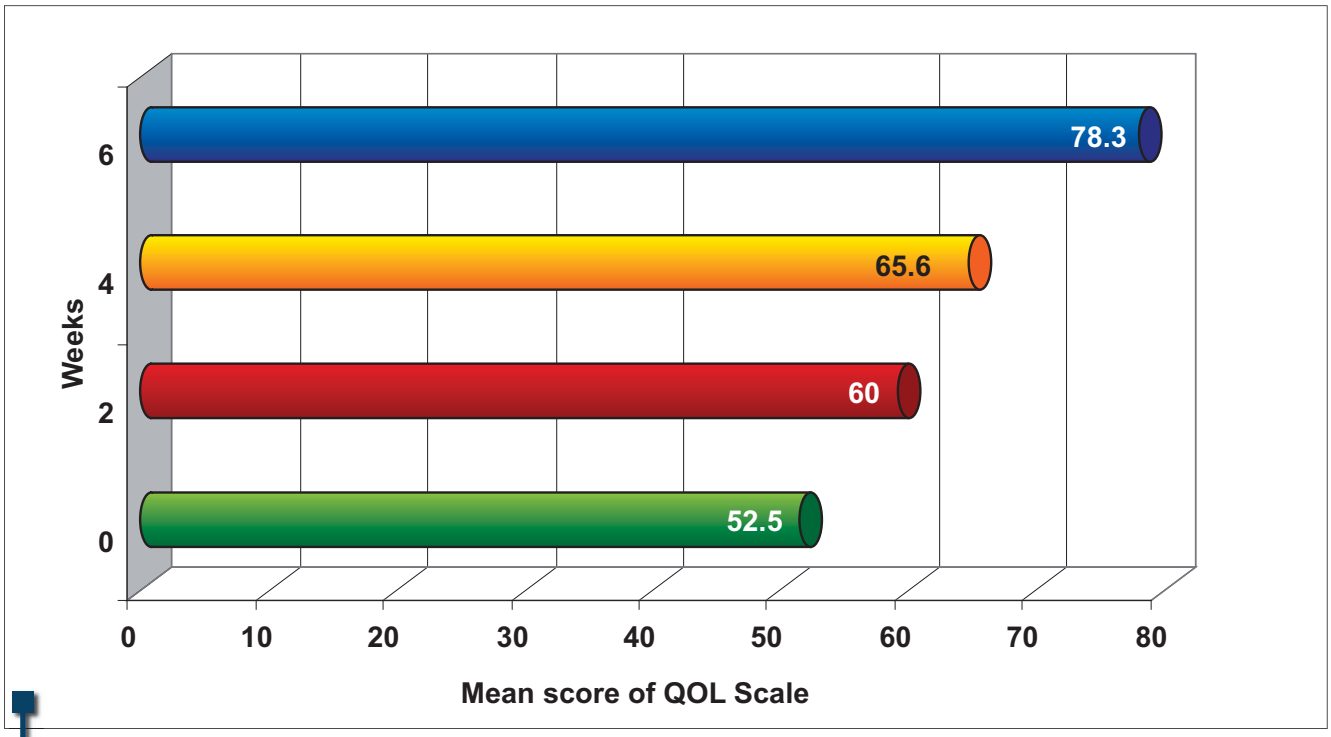

Figure 2. Mean score change over 6 weeks of treatment with Extended Release Venlafaxine in QOL Scale

Table 2

Reported adverse events

Adverse event	No. patients
Nausea	8
Dry mouth	6
Somnolence	4
Anxiety	2
Headache	2
Decreased libido	1

20-sweating at night, 21-loss of interest in sex. Patient can rate the severity of each item from 0 to 3 (none to severe).

The Scale yields three main independent symptom measures: one of Psychological Symptoms (sum of items 1 to 11), one of Somatic Symptoms (sum of items 12 to 18), and one of Vasomotor Symptoms (sum of items 19 and 20).

The Psychological SubScale can be further subdivided to give measures of: Anxiety (A) - sum of items 1 to 6; Depression (D) - sum of items 7 to 11. Symptom 21 is a probe for sexual dysfunction[5].

The recommended cut-off points are: clinically anxious - Anxiety Score of 10 or more; clinically depressed - Depression Score of 10 or more. For inclusion a score less than 10 was required for Anxiety Subscale and Depression Subscale.

In addition, patients completed Quality of Life Scale (QOL), a 16-items instrument, when they entered the study and at the end of week 2, 4, and 6.

Women receiving hormonal therapy or antidepressants were excluded.

All patients were required to give written informed consent.

Patients received treatment with open-label extended-release venlafaxine, 75 mg daily for 6 weeks. After the 6 weeks period, the patients could choose to continue treatment with venlafaxine.

Results

Twenty-four women were enrolled for this study. Six patients (25%) withdrew from the study. Reasons for withdrawing included nausea, anxiety, decreased libido or failure cu obtain relief with treatment (2 patients). The 6-week trial was completed by 18 women.

Table 1 lists the demographic data of patients (age, age at menopause, years since menopause and proportions with surgical versus natural menopause).

GCS mean scores declined for each subscale: Psychological Subscale mean score decreased over the 6 weeks of treatment from 14.4 to 8.9; Somatic subscale mean score decreased from 5.9 to 3.8; and Vasomotor Subscale mean score decreased from 5.3 to 3.1, a decrease with 41.5% from baseline (see Figure 1). The Psychological Subscale mean decrease corresponds to a 38.2% reduction of the score, and the Somatic Subscale mean decrease corresponds to a 35.6% reduction.

Mean score of QOL Scale increased from 52.5 when entering the trial to 78.3 over 6 weeks of treatment with extended release Venlafaxine (see Figure 2).

Over half (54%) of the women reported adverse effects. The most frequent were nausea and dry mouth (Table 2).

After 6 weeks of treatment with venlafaxine, 14 women of 18 (77.7%) who completed the study, decided to continue the treatment with venlafaxine.

Conclusions

The study indicates that Extended-release venlafaxine, 75 mg per day, could be effective for treating postmenopausal symptoms, improving quality of life for women at menopause. The effectiveness of venlafaxine could also be supported by the great number of women who choose to continue the treatment after 6 weeks.

Several theories tried to explain the cause of hot flashes, the dominant symptom of postmenopausal women. Freedman et al[6] tested the hypothesis that hot flashes are triggered by hypothalamus through the action of alfa2-adrenergic receptors on nonadrenergic neurons, which decreases the release of noradrenaline. He administrated clonidine (an alfa2-adrenergic agonist) and yohimbine (an alfa2-adrenergic antagonist) to postmenopausal women. Clonidine significantly decreased the number of hot flashes, and yohimbine had the opposite effect. But clonidine is not very much used for treatment because of its adverse effects profile.

Berendsen[5] has proposed a hypothesis for the role of serotonin (5-HT). Decreased levels of estrogen leads to decreased serotonin blood levels and an increased 5-HT2A receptor sensitivity in the hypothalamus. In response to stimuli (eg, stress), there is an increased release of 5-HT moduline, which lead to blockade of 5-HT1A receptors and subsequent increased release of serotonin. The increased levels of serotonin stimulate the 5-HT2A receptors in the hypothalamus and influence the hypothalamic thermoregulatory center.

Venlafaxine affects both serotonin and norepinephrine reuptake and addresses both of the theories and could be considered an option for treating postmenopausal symptoms. Further placebo-controlled studies are necessary for establishing the role of antidepressant in the treatment of women with post menopausal symptoms. ■

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Menopauza terapie naturală fără riscuri

Dr. Oana Gagionea

Menopauza este o perioadă fiziologică prin care fiecare femeie va trece la un moment dat. Simptomatologia psihică și vegetativă asociată menopauzei se datorează unei producții scăzute de hormoni ovarieni. Aceste modificări aduc adesea suferințe considerabile și afectează calitatea vieții pacientei. Medicul de multe ori este nevoit să înceapă un tratament medicamentos. Tratamentul de substituție hormonală are un efect pozitiv asupra simptomatologiei, însă, în mod frecvent, este tulburat de efecte secundare și riscuri crescute sau chiar și contraindicații. Din ce în ce mai mulți medici au o părere foarte rezervată despre terapia de substituție hormonală, având în vedere în special incidența crescută a tumorilor maligne hormon-dependente.

Tratamentul tulburărilor de climax cu medicamente non-hormonale poate fi indicat în pre-, peri- și port-menopauză timpurie, când ovarele încă mai produc cantități mici de hormoni.

În multe din aceste cazuri, Klimaktoplant oferă o alternativă non-hormonală, naturală, cu risc scăzut și fără contraindicații.

Klimaktoplant este un preparat homeopat standardizat, ce conține patru remedii, fiecare cu modul său diferit de acțiune, ce produc un efect sinergic asupra tulburărilor somatice și psihice ale menopauzei. Cimicifuga racemosa este un remediu utilizat pentru dereglări de natură ginecologică de peste 200 ani.

Autorii Jarry și Harnischfeger au demonstrat capacitatea diferitelor părți ale extractului de Cimicifuga de a se conecta la receptorii de estrogen și de a reduce selectiv concentrația în ser a hormonului pituitar LH.

Experiența clinică confirmă eficiența Klimaktoplant în tratamentul simptomelor complexe de deficiență de climacteriu în sfera somatică, psihică, neuro-vegetativă și organică. Raportul pozitiv între riscuri și beneficii (efecte secundare scăzute specifice substanțelor, fără contraindicații) desemnează de asemenea Klimaktoplant pentru terapia pe termen lung, fără hormoni și cu risc scăzut. ■

VAVIAN PHARMA

DHU Deutsche Homöopathie-Union