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Review Article

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Both Perimenopausal Vasomotor Symptoms and associated anxiety disorder be managed with Escitalopram : an experience at a tertiary care hospital

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ABSTRACT

BACKGROUND & OBJECTIVE: Perimenopausal vasomotor symptoms (VMS) are distressing and often trigger mood disorders. Selective Serotonin Reuptake Inhibitors (SSRIs) may improve both. This study evaluated the incidence and severity of anxiety in menopausal women with VMS and assessed the efficacy of Escitalopram in managing both conditions.

METHODOLOGY: An interventional, multicenter, observational study was conducted from January to July 2023 at Rai Medical College, Sargodha, and at private clinics. Women aged 30–75 years with VMS (per STRAW staging) and anxiety were included. Exclusions were HRT, prior SSRIs/NSRIs, hypersensitivity, certain neurological/psychiatric disorders, malignancy, and major systemic diseases. The Vasomotor domain of the MENQOL questionnaire was used for the Composite Symptoms Severity Index (CSSI), and anxiety was measured using the GAD-7 scale. Patients with GAD >4 or CSSI >50 received Escitalopram 10 mg daily. Scores were reassessed at 8 and 12 weeks. Data were analyzed using SPSS 25, chi-square, and Fisher's exact test.

RESULTS: A total of 346 patients were enrolled in the study. Baseline anxiety (minimal, mild, moderate, severe) varied across CSSI groups. By week 12, the proportion with minimal anxiety increased markedly (e.g., from 36% to 75% in one group), while moderate and severe anxiety declined across all groups. CSSI scores also showed consistent improvement from 8 to 12 weeks.

CONCLUSION: Escitalopram significantly reduced both anxiety and vasomotor symptom severity in perimenopausal women, with improvements evident by week 8 and sustained through week 12.

KEYWORDS: Menopause, Generalized Anxiety Disorder, Quality of Life, Patient Health Questionnaire, Selective Serotonin Reuptake Inhibitors, Anxiety.

INTRODUCTION

The well-known vasomotor symptoms of hot flashes and sweating , often disturbing sleep, may occur during the transition to menopause (~35 to ~55 years) and may present for the first time long after the cessation of menstrual cycles. These symptoms are caused by fluctuating and declining estrogen levels and can significantly affect quality of life.

It is surprising that, in a Mayo Clinic survey, even residents in internal medicine, family medicine, and obstetrics/gynaecology were more than half unaware of appropriate therapy, and 30 to 50% were not prepared to prescribe for menopausal symptoms [1]. Penn Ovarian Ageing Study reported a median duration of Vasomotor Symptoms (VMS) of 10.2 to 11.6 years [2]. A Study of Women's Health Across the Nation reported a late perimenopausal transition to have an overall prevalence of approximately 70% [3]. According to the Study of Women's Health across the Nation (SWAN), presenting patterns vary [4].

Hot flushes (HF) are the most common, disruptive, and depressive for Quality of Life (QoL) [5]. The World Health Organization ranks depression among the leading causes of years lived with disability (YLD) and as the most prevalent serious psychiatric disorder. The decision to use HRT is based on the patient's preferences, severity index, contraindications , and CHD risk factors [6]. One patient may suffer from both anxiety and depression simultaneously, along with menopausal distressing symptoms necessitating a holistic management approach [7-9].

The Latest 2023 statement of the North American Menopause Society (NAMS) still recommends Hormone Replacement

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Therapy (HRT) as the first priority and Selective Serotonin Reuptake Inhibitors(SSRIs) and Non- Selective Serotonin Reuptake Inhibitors (NSRIs) where the risk-benefit ratio of HRT is not favorable [10-12]. These are the most prescribed drugs with documented efficacy (up to 70%) [13].

METHODOLOGY

This study was conducted between January and July 2023 on females with VMS & Anxiety between 30-75 years of age, presenting at Rai Medical College teaching hospital and private clinics at Sargodha. Approval from the ethical review committee was granted under RMCS/ERC 07.2023. The sample size of 346 female patients was calculated using the WHO sample size calculator with a 95% confidence level and a 5% margin of error, assuming the 95% of post-menopausal women experience vasomotor symptoms.

In the inclusion criteria, the number of perimenopausal women with Vasomotor symptoms, as per the STRAW staging system, aged 30-75 years, were invited to volunteer. (The usual age range for menopause is defined between 35 and 55 years, but up to 60 is not uncommon. There are anecdotal and isolated medical reports of women menstruating up to age 60–65, but these are exceptional and not the norm; vasomotor symptoms may occur during the transition and well beyond.

RESULTS

In the exclusion criteria, females on HRT, SSRIs, or NSRIs were excluded. Also excluded were those with a history of hypersensitivity, gabapentin or pregabalin use, clonidine, bipolar disease, uncontrolled seizures, suicidal thoughts, major psychiatric illness, malignancies, or major end-organ or endocrine disease [4].

Informed consent was sought. The Vasomotor domain of the Menopause-Specific Quality of Life (MENQOL) questionnaire was used to quantify the Composite Symptoms Severity Score (CSSI) [14,15]. Patients scoring >50 on the CSSI were invited to undergo a GAD-7 assessment [7,11].

Individuals scoring greater than 4 on the GAD scale or greater than 50 on the CSSI scale were invited to initiate treatment. Tablet Escitalopram 5 mg orally after breakfast was given and increased to 10 mg if no unwanted effects were observed at the end of the first week. CSSI and GAD-7 scores were evaluated at follow-up visits at 8 and 12 weeks. Data were analyzed using SPSS Version 25, and chi-square analysis and Fisher's exact test were used to check the significance of the study.

The study included 346 patients comprising 4% in the 4th decade (30-40 years), 36% in the 5th decade (41-50 years), 47% in the 6th decade (51-60 years), and 13% in the 7th decade (61-70 years). The majority of patients were in the 5th and 6th decades, indicating that menopausal symptoms are most prevalent in these age groups. The distribution of the Composite Symptom Severity Index (CSSI) over time is provided in Table- I.

Table-I: CSSI Scores at Baseline, 8 Weeks, and 12 Weeks (N = 346).

Time Point	CSSI <50 n(%)	CSSI 51-100 n(%)	CSSI >100 n(%)
Baseline	127 (36.70)	162 (46.82)	57 (16.47)
8 Weeks	184 (53.17)	139 (40.17)	23 (6.64)
12 Weeks	244 (70.52)	93 (26.87)	9 (2.60)

Table-II: CSSI and GAD at Baseline (N = 346).

CSSI Group	Minimal Anxiety (GAD 01-04) n(%)	Mild Anxiety (GAD 05-09) n(%)	Moderate Anxiety (GAD 10-14) n(%)	Severe Anxiety (GAD 15-21) n(%)	Total
CSSI <50	16 (12.56)	26 (20.47)	36 (28.35)	49 (38.58)	127
CSSI 51-100	13 (8.02)	34 (20.99)	62 (38.27)	53 (32.72)	162
CSSI >100	1 (1.74)	0 (0)	16 (28.07)	40 (70.18)	57
Total	30	60	114	142	346

The proportion of patients with severe symptoms (CSSI >100) decreased from 16.47% at baseline to 2.60% at 12 weeks, while the proportion of patients with mild symptoms (CSSI <50) increased from 36.70% to 70.52%. This indicates a significant reduction in symptom severity over time.

Table-III: CSSI and GAD at 8 Weeks (N = 346).

CSSI Group	Minimal Anxiety (GAD 01-04) n(%)	Mild Anxiety (GAD 05-09) n(%)	Moderate Anxiety (GAD 10-14) n(%)	Severe Anxiety (GAD 15-21) n(%)	Total
CSSI <50	46 (36.22)	41 (32.28)	25 (19.67)	15 (11.81)	127
CSSI 51-100	38 (23.46)	49 (30.25)	65 (40.12)	10 (6.17)	162
CSSI >100	16 (28.07)	32 (56.14)	5 (8.78)	4 (7.02)	57
Total	100	122	95	29	346

Table-IV: CSSI and GAD at 12 Weeks (N = 346).

CSSI Group	Minimal Anxiety (GAD 01-04) n(%)	Mild Anxiety (GAD 05-09) n(%)	Moderate Anxiety (GAD 10-14) n(%)	Severe Anxiety (GAD 15-21) n(%)	Total
CSSI <50	96 (75.59)	25 (19.69)	2 (1.57)	4 (3.15)	127
CSSI 51-100	68 (41.98)	79 (48.77)	8 (4.94)	7 (4.32)	162
CSSI >100	39 (68.42)	11 (19.30)	4 (7.02)	3 (5.26)	57
Total	203	115	14	14	346

The trend analysis of CSSI scores over time revealed that the proportion of patients with severe symptoms (CSSI > 100) decreased from 16.47% at baseline to 2.60% at 12 weeks, while the proportion with mild symptoms (CSSI <50) increased from 36.70% to 70.52% during the same period. For anxiety levels, severe anxiety in the CSSI <50 group fell from 38.58% at baseline to 3.15% at 12 weeks; in the CSSI 51-100 group, severe anxiety decreased from 32.72% to 4.32%; and in the CSSI >100 group, severe anxiety dropped from 70.18% to 5.26% over 12 weeks.

These results indicate a significant association between CSSI groups and anxiety levels at all time points, suggesting that the severity of menopausal symptoms was closely related to the level of anxiety experienced by patients. The intervention (Estalopram) was effective in reducing both the severity of menopausal symptoms and associated anxiety levels. Furthermore, the proportion of patients with severe symptoms and severe anxiety decreased significantly over the 12-week period, while the proportion of patients with mild symptoms and minimal anxiety increased. The statistical analyses of the study data are shown in Table -V.

Table-V: Chi-square Test Results.

Time Point	Chi-square (χ^2)	p-value
Baseline	34.660	< 0.001*
8 Weeks	34.96	< 0.001*
12 Weeks	41.374	< 0.001**

*p-value calculated using chi square

**p-value calculated using Fisher's exact test

These statistical results revealed the effectiveness of Estalopram in managing menopausal vasomotor symptoms and associated anxiety. The significant reduction in CSSI scores and anxiety levels over time highlights the potential benefits of this intervention for menopausal women experiencing VMS and anxiety. Further studies with larger sample sizes and longer follow-up periods are recommended to confirm these findings and explore the long-term effects of the treatment.

DISCUSSION

Incidence of anxiety in the general population increases from around 6% to 37% in patients experiencing VMS. Similarly, a temporary rise in BP was documented during VMS [16,17]. Antidepressants showed significant improvement in both anxiety and depressive symptoms (≥50% from baseline). In another systematic review of 36 articles, the efficacy and safety of SSRIs and NSRI were documented in both [10,11].

Vasomotor and psychological factors have the worst impact on QoL. The incidence and presentation vary widely across studies, cultures, ethnicities, and socioeconomic and educational backgrounds [18,19]. In another local study, 44% had mild hot flashes and sweating episodes, 23% had severe symptoms, 45% of women had mild sleep issues. 36% were suffering from mild depression, and 30% had no symptoms [20]. In a Pakistani study conducted on females serving a jail sentence, it was reported that 91.6% were aware of menopause, but only 8.3% had an educated idea of its health effects [21].

Zulfiqar E reported that 22% of females experienced VMS, noting that housewives reported far more frequent hot flushes and night sweats compared to working women. In a separate study focused on illiterate women, 79% were aware of menopausal symptoms, which contrasts with another group of educated women, among whom only 21% had a reasonable working knowledge of menopause and its effects on health. In a further study involving menopausal women from different educational backgrounds, 44 (91.6%) perceived menopause as a natural process. Reports on the frequency of various menopausal symptoms included 62.5% with insomnia, 54% with wide mood swings and impaired short-term memory, 54% with back pain, 65% with chronic fatigue, and 56% with unexplained nausea. Typical vasomotor symptoms, as well as unexpected symptoms like fever, a feverish feeling, and night sweats, were reported by 41.6% of these participants [22].

A remarkable improvement in the VMS scale was observed at 12 weeks, with the proportion of females experiencing mild CSSI increasing from 36% to 70% and the proportion experiencing severe symptoms decreasing from 16% to 2%. With treatment in CSSI, with mild symptoms, 75% were experiencing minimal anxiety, and only 4% were still suffering from severe anxiety. A similar trend was observed in CSSI, with a medium score; 42% and 49% fell within the comfortable zone of minimal to mild anxiety. In high CSSI, 68 19% were in the comfortable zone of minimal to mild anxiety. Escitalopram helped these patients in both reducing the severity of VMS symptoms, which contributed to the relief of anxiety, due to the unpleasant experience of VMS or anxiety per se getting worse with VMS.

CONCLUSION

In this study, a clear trend of decreasing anxiety scores was observed in all three CSSI groups. At 12 weeks, the majority showed a reduction in CSSI score and anxiety. This study strongly points out the need to evaluate GAD in this selected population, as both anxiety and VMS can be successfully managed by Escitalopram to improve the QoL.

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Mohammad Mohsin Rana: Substantial contributions to the conception and design of the work.

Nauman Khalid: The acquisition and analysis of data for the work.

Asifa Alia: Interpretation of data for the work..

Qasim Rauf: Drafting the work.

Um-A-Aiman: Reviewing it critically for important intellectual content.

Nadia Zulfiqar: Final approval of the version to be published.

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