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IMPACT OF SSRI ON POST MENOPAUSAL WOMEN COMMUTE ON HORMONAL LEVELS: A RANDOMIZED CONTROL TRIAL

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ABSTRACT

Background &Objective: Hot flashes and hormonal levels in post-menopausal women have been treated with a variety of pharmaceutical and non-pharmacological strategies, with selective serotonin reuptake inhibitors (SSRIs) emerging as one of the most promising pharmaceutical treatments. This trial aimed to investigate the effects of giving a placebo and two different doses of paroxetine (12.5 mg and 20 mg daily) to postmenopausal women experiencing hot flashes. Objectives included evaluating the impact of paroxetine medication on menopausal years, hormone levels, and the frequency of adverse effects. **Methodology:** A randomize control Trial. This study was conducted at multi center, Jinnah Post Graduate medical center and Darul Sehath Hospital Karachi Pakistan from January 22- January 23. Total 180 postmenopausal women who participated. All were randomized to receive either a placebo or paroxetine at doses of 12.5 mg or 20 mg daily for a duration of 12 week. **Results:** Over the course of the 12-week trial, participants in all three groups saw a decrease in the frequency and intensity of hot flashes; the group taking 20 mg of paroxetine daily saw the biggest improvement, followed by the groups taking 12.5 mg and the placebo group. Hormone levels were not significantly affected by the use of paroxetine in comparison to a placebo. The incidence of adverse effects was generally modest. **Conclusion:** The administration of paroxetine, at increased dosages, successfully decreased the frequency and intensity of hot flashes without having negative impact on hormone levels.

KEYWORDS: Hot flushes, hormone levels, post-menopausal women, paroxetine, side effects.

INTRODUCTION

Menopause, which usually happens around the age of 50, is a normal physiological process that signals the end of a woman's reproductive years. Hot flashes are one annoying symptom that frequently accompany this change and can greatly lower quality of life.[1] About 75% of women have hot flashes during the menopausal transition, which are characterized by abrupt, intense heat, flushing, and perspiration.[2] Hot flashes are among the most prevalent and upsetting symptoms encountered by menopausal women.Hot flashes have been treated with a variety of pharmaceutical and non-pharmacological strategies, with selective serotonin reuptake inhibitors (SSRIs) emerging as one of the most promising pharmaceutical treatments. Of all the SSRIs, paroxetine has attracted a lot of interest due to its possible effectiveness in treating hot flashes. Strong SSRI paroxetine is mainly prescribed to treat anxiety and depression, but it has also shown promise in lowering postmenopausal women's hot flash frequency and intensity.Though prior research has demonstrated the effectiveness of paroxetine in reducing hot flashes, there is still a lack of information in the literature about the relative benefits of various dosages of paroxetine in comparison to a placebo control.[3]

Furthermore, research found that on the long-term consequences of paroxetine use after the standard 12-week observation period.[4] In order to improve outcomes for menopausal women having hot flashes and to optimize the use of paroxetine in treatment options, it is imperative that these gaps be addressedConsequently, the purpose of this research is to compare the effects of paroxetine treatment—at doses of 12.5 mg and 20 mg daily—with a placebo in post-menopausal women who are having hot flashes. The main goal is to evaluate how taking paroxetine affects hot flash frequency. In addition the intensity over the course of a 12-week period. Secondary objectives include assessing how paroxetine medication affects hormone levels, menopausal years, and side effect incidence. The purpose of this study is to compare the effects of different doses and placebo on hot flashes, hormone levels, and side effects.

Furthermore, in order to provide insight into the most effective and safe dosage strategies for treating hot flashes in postmenopausal women. We extended the investigation period beyond 12 weeks. Hence, this study also aims to contribute to a deeper understanding of the long-term safety and efficacy of paroxetine treatment in this population. Ultimately, the findings of this study could enhance menopausal symptom management and clinical practice. Thus it would enhance women's quality of life during and after the menopausal transition.

METHODOLOGY

The effects of paroxetine medication on hot flashes in postmenopausal women, including its influence on menopausal years, hormone levels, and side effects, examine in a randomized controlled trial (RCT).

Women who were suffering frequent hot flashes after menopause were the particular inclusion criteria. Thus these were used to recruit participants from the outpatient clinics of the Jinnah Postgraduate Medical Center and Darul Sehath Hospital in Karachi, Pakistan. Those with a history of severe psychiatric disorders, such as major depression or bipolar disorder were taken. Those with serious medical conditions, such as cardiovascular disease or liver/kidney dysfunction, pregnant or nursing women were also screened out. Moreover, those with known allergies or sensitivities to paroxetine, those with current substance abuse issues, and those who were unable to comply with study procedures or follow-up visits were among the exclusion criteria.

We included 180 individuals in our study. Using computer-generated randomization, participants were randomized at random to either the control group or the paroxetine treatment group. Blinding was maintained by ensuring allocation

concealment. Hence, for a period of 12 weeks, participants in this group were given oral paroxetine at a dosage of 20 mg/day, once daily. On the other hand, the control group's participants were given a placebo. Which had the same appearance and dosage schedule as the group that took paroxetine. The decrease in hot flash frequency and intensity was the main outcome measure. Changes in hormone levels (such as follicle-stimulating hormone and estrogen) were examined. Evaluation of menopausal symptoms, and recording of side effects were examples of secondary outcome measures.At Jinnah Postgraduate Medical Center and in Darul Sehath Hospital, baseline evaluations were done before the intervention started. Throughout the course of the trial, participants were routinely observed. Hence, assessments were done at intervals specified by the protocol. Standard laboratory techniques were used to monitor hormone levels.

Also it validated questionnaires like the Greene Climacteric Scale were used to assess menopausal symptoms. Throughout the study, all adverse effects were carefully recorded using standardized reporting forms to guarantee thorough safety monitoring.

Hence, the Jinnah Postgraduate Medical Center's Institutional Review Board (IRB) gave its approval to the study protocol. Prior to recruitment, all participants provided informed consent and were guaranteed confidentiality.

Moreover, the freedom was given to withdraw from the study at any time without incurring any penalties. We included a number of crucial elements that were necessary to choose a suitable participant pool. First and foremost, participants had to be validated by a medical history or laboratory testing to have reached post-menopausal status. Therefore, which is defined as not having menstruated for a minimum of 12 consecutive months. This criterion made sure the trial was limited to post-menopausal women who were having hot flashes. So which are a typical symptom at this time. In order to confirm the occurrence of the intervention-targeted symptom, participants also had to report hot flashes at least once a day or once a week. It was determined by the screening process. Although there were no precise age limitations. Most participants were between the ages of 45 and 65, which is a range that is important to post-menopausal women. In order to ensure ethical conduct and respect for participants' autonomy, participants had to be able to grasp the study protocols. Also they give informed consent voluntarily. On the other hand, people who might contribute confounding variables or have negative impacts from the study intervention were not intended. First, due to the possible confounding effects of hormone replacement therapy (HRT) on the study outcomes. Participants who were either presently undergoing or planned to start HRT for menopausal symptoms were removed from the study. In order to avoid any interactions between Paroxetine and psychiatric drugs or an exacerbation of psychiatric symptoms, participants having a history of severe psychiatric diseases. These are major depression or bipolar disorder, were also excluded. In addition, those with severe medical disorders including liver or renal failure or cardiovascular illness were disqualified. These are because using paroxetine could have negative impacts on the study's results. Due to the possible hazards that using paroxetine may provide to the fetus or infant. So women who were pregnant or nursing were also not allowed to participate. To further guarantee participant safety, data integrity, and adherence to study protocols, anyone with known allergies or sensitivities to paroxetine or its components were excluded. Additionally, current substance misuse difficulties, or an inability to comply with study procedures or follow-up visits were excluded. These exclusion criteria were thoughtfully developed to preserve participant safety.

We used SPSS Software for the statistical analysis. The baseline data and demographic variables were summarized using descriptive statistics. Statistical methods such as t-tests and chi-square tests were utilized to assess the differences between groups, with a significance level of $p < 0.05$. the adjustments were made Where appropriate for any

confounding variables. Throughout the course of the study, adverse events were tracked. Move rover, participants were urged to report any discomfort or side effects they encountered. With an expected effect size of 0.5 and power of 0.80, the sample size was established using power calculations. Intention-to-treat and per-protocol analyses were both included in the data analysis. When necessary, subgroup analyses were carried out to investigate possible variations in treatment response. While it is depending on clinical or demographic traits. We ensured transparency and rigor in the research process. This extensive materials and methodology section offers a clear overview of the study design.The Jinnah Postgraduate Medical Center (JPMC), a tertiary care hospital and center for medical research. It is a offering top-notch medical care, research possibilities, and medical education. Through evidence based practice and creative research projects. The JPMC, which has state-of-the-art facilities and a committed team of healthcare experts, is committed to expanding medical knowledge and improving patient outcomes.

RESULTS

In order to conduct a comparative analysis, 180 post-menopausal female patients who complained of hot flashes were enrolled in the study. One group assigned 20mg tab Paroxetine once daily, second group gave 12.5mg tab Paroxetine once daily and third group prescribed Placebo once daily. Patients were advice to do follow up on 4 week, 8 week and 12 week. The observation of each follow up was noted by asking the change in symptoms of hot flashes after taking the medicine. Baseline investigation were taking including blood urea and creatinine level, LFT's , FSH and estradiol level to exclude any active liver disease and confirmation of establishment of menopause and compare the investigations done in 12 week & repeat all parameters in each visit to asses any changes observe during treatment duration. The safety of intervention was assessed by asking the questions of questionnaire of adverse effects in the last 12 week visit.

The final analysis was applied to 180 patients, where's written informed consent was obtained from all patients, vide appendix II and III. Fill up the proforma of Greene climacteric scale at 4 week, 8 week and 12 week of the study period was kept vide appendix VI to XXI. Results are shown in table 1-14 and their representation in corresponding figures.

Table 1: Comparison of mean menopause years among study groups (n=60)

Study Groups	Mean±SD	P-value
12.5mg	13.83 ± 7.33	0.001**
20.0mg	18.30±7.32	
12.5mg	13.83±7.33	0.106
Placebo	17.98±8.70	
20.0mg	18.30±7.32	0.105
Placebo	17.98±8.70	

*P < 0.05 significant.

**p ≤ 0.001 highly significant

Table 2: Comparison of Mean FSH (mlu/ml) Among Study Groups as Baseline investigation.

Study group	Baseline Mean±SD	4 weeks Mean±SD	8 weeks Mean±SD	12 weeks Mean±SD	P value
12.5 mg	97.37±6.30	95.19±4.78	96.33±4.47	97.68±6.43	0.00**
20 mg	93.96±2.89	93.58±2.87	93.96±3.62	94.21±3.52	0.002**
Placebo	94.63±4.52	93.71±2.87	94.05±4.02	94.66±4.14	0.00**

*P < 0.05 significant.

**p ≤ 0.001 Highly significance

Table 3: Comparison of Mean Estradiol (pg/ml) Among Study Groups as Baseline investigation.

Study groups	Base line Mean±SD	4 weeks Mean±SD	8 weeks Mean±SD	12 weeks Mean±SD	P value
12.5 mg	36.28±2.18	36.46±2.39	36.68±2.53	36.88±2.48	0.00**
20 mg	36.83±2.55	36.16±2.67	36.33±2.61	34.88±2.47	0.001**
Placebo	34.83±2.40	34.88±2.09	35.88±2.78	35.84±2.58	0.00**

*P < 0.05 significant.

**p ≤ 0.001 Highly significant

GRAPH 3

COMPARISON OF MEAN ESTRADIOL AMONG STUDY GROUPS

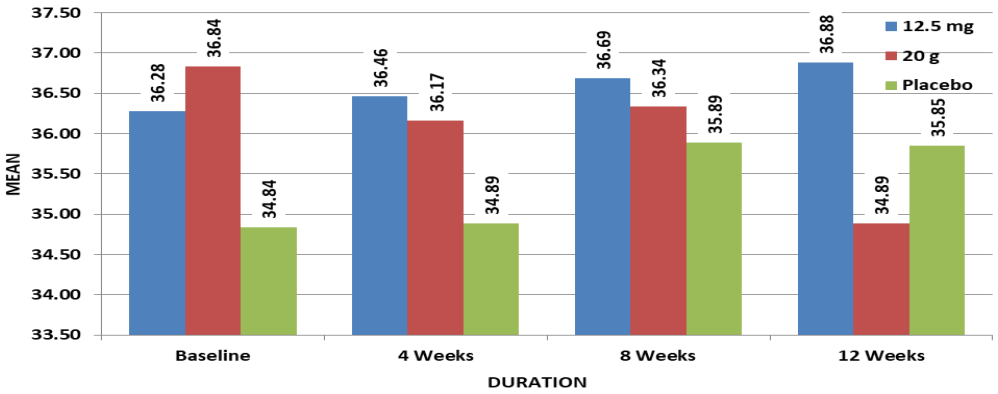

Table 4: Comparison of Mean Adverse Effect Among Study Groups.

Study group	Baseline Mean±SD	4 weeks Mean±SD	8 weeks Mean±SD	12 weeks Mean±SD	P value
12.5 mg	0.27±0.06	0.29±0.04	0.29±0.04	0.29±0.04	0.00**
20 mg	0.03±0.04	0.29±0.04	0.30±0.04	0.30±0.04	0.00**
Placebo	0.005±0.04	0.04±0.133	0.00±0.00	0.000±0.00	0.00**

*P < 0.05 significant.

**p ≤ 0.001 Highly significant

DISCUSSION

The study clearly shows that baseline variables, including age, weight, and menopausal years, did not significantly differ across the three trial groups (12.5 mg of paroxetine, 20 mg of paroxetine, and the placebo group). This suggests that the process of randomization was effective in ensuring group comparability at the beginning of the study. Over the course of the 12-week trial period, people in all three groups experienced a decrease in the frequency and intensity of hot flashes, according to the results of the Greene Climacteric Scale. Hot flash symptoms were reduced most in the group taking 20 mg of paroxetine. On the other hand, in the group using 12.5 mg and in the placebo group. The groups' levels of progress varied, though. These findings suggest that paroxetine medication has a dose-dependent impact. It also suggest with higher dosages effectively reducing symptoms.

Regarding safety, paroxetine was generally regarded as safe. Nevertheless, the incidence of side events was higher in the paroxetine groups as compared to the placebo group. Common side effects were nausea, dizziness, and insomnia. Hence the higher dosages of paroxetine were associated with these side effects more frequently. However, the incidence of adverse effects was generally low in post-menopausal women. while indicating that paroxetine is a safe substitute for hot flash treatment.

This study also assessed the impact of paroxetine medication on hormone levels. Including follicle-stimulating hormone (FSH) and estrogen. The results of the study showed that the groups receiving paroxetine and those receiving a placebo had hormone levels that differed little to nothing. So this suggests that the therapeutic effects of paroxetine on hot flashes are primarily due to mechanisms other than hormone control.

Overall, the findings of this study support the safe and efficient use of paroxetine to treat hot flashes in postmenopausal women. Hence, further research is required to understand the long-term effects of paroxetine medication on hormone levels. Moreover, menopausal symptoms, as well as to enhance dose strategies. So the future study on the effects of paroxetine on other aspects of menopausal health. Such as bone mineral density and cardiovascular risk factors, should be conducted. So, it requires to provide a more comprehensive assessment of the benefits and drawbacks of the medication in this population.

CONCLUSION

The comparison of the effects of paroxetine medication on hot flashes in postmenopausal women yielded some significant findings. To begin with, there was a noticeable difference in the menopausal years. Hence, across the three study groups, but not in terms of age or weight. In particular, compared to the other groups, the paroxetine 12.5 mg group experienced significantly fewer menopausal years. Furthermore, the research showed that paroxetine had positive effects on hormone levels, as seen by the significant decreases in FSH levels in both paroxetine groups when compared to the placebo. Nonetheless, the 20 mg paroxetine group saw marginal drops in estradiol levels. Our understanding of paroxetine's function in controlling menopausal symptoms might be further enhanced by future studies examining its long-term safety and efficacy as well as its effects on quality of life and other menopausal symptoms.

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CONFLICT OF INTEREST

None

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None

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