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The effect of tibolone versus 17β-estradiol on climacteric symptoms in women with surgical menopause: A randomized, cross-over study

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Abstract

Objective: To compare the effectiveness of tibolone and 17β-estradiol on climacteric symptoms, in a randomized, single-blind, cross-over study in surgically menopausal women.
Material and methods: Forty surgically menopausal women were divided randomly into two groups. Group A received treatment with tibolone for 6 months, while group B received 17β-estradiol. After 3 weeks washout period, treatment protocols were exchanged for another 6 months. The climacteric symptoms were assessed with Greene Climacteric Scale at baseline, during washout and after the treatments. Statistical analysis was done with the Wilcoxon's Sign Rank test.
Results: Both treatments significantly improved the scores of all subscales with respect to baseline. However, the improvement in psychological, somatic and sexual subscales were significantly superior in the tibolone group compared with 17β-estradiol group. Both treatments showed comparable improvements in the relief of vasomotor symptoms.
Conclusion: Our findings suggest that tibolone may improve mood, libido and somatic symptoms in surgically menopausal women to a greater extent than estrogen therapy alone.

Keywords: Surgical menopause; Tibolone; 17β-Estradiol; Greene Climacteric Scale

1. Introduction

The decline in circulating estrogen levels in the perimenopause results in climacteric symptoms. Hot flushes, sweating, changes in mood and libido are some important outcomes affecting the quality of life (QoL) during climacterium in women. Quality of life covers physical, functional, emotional, social and cognitive variables [1] and menopause-associated symptoms can impair these major aspects of QoL for many women.

After the results of The Women's Health Initiative (WHI) study, to improve the quality of life in women

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during the menopausal transition period is the main indication for estrogen plus progestin based hormone therapy (HT) [2]. Another issue is the quality of life in women undergoing surgical menopause. Since the circulating sex steroids abruptly decrease, the climacteric symptoms are more severe and disturbing in women undergoing bilateral oophorectomy. Estrogen replacement therapy (ERT) improves the complaints and in turn, quality of life. But ERT arm of the WHI study was terminated prior to the scheduled close-out interval, because of increased risk of stroke, and the likelihood that neither cardioprotection nor breast cancer risk would be demonstrated in the remaining intervention period [3]. As a result hormone therapies, estrogen plus progestin or estrogen alone, are appropriate for the relief of vasomotor symptoms, and primarily recommended for the prevention of menopausal symptoms for the shortest possible time. The effects of alternatives to HRT, such as tibolone, phytoestrogens or SERMs, need to be evaluated.

Tibolone is a tissue specific compound, structurally related to 19-nortestosterone derivatives, which exhibits weak estrogenic, progestagenic and androgenic activities [4]. In a number of studies, it has been shown that tibolone provided relief of vasomotor symptoms without stimulating endometrium and breast tissue [5]. The success of this relatively new compound, tibolone, in treating climacteric symptoms after natural/surgical menopause, has not been addressed by well-designed studies. Albertazzi et al. reviewed the studies in which tibolone was used for climacteric symptoms. According to them the problems with study designs were; the randomized double blind studies were not cross-over, in the cross-over studies there were no washout periods, and measurement of symptoms were not stated clearly [6].

The effect of tibolone versus estrogen on climacteric symptoms in women with surgical menopause was the subject of two previous studies [7,8], but both of them used the Blatt–Kupperman Indices to measure climacteric symptoms/complaints. The Blatt–Kupperman Index has severe limitations such as; the symptoms are highly selected, the scales have no psychometric properties and they are derived from biased samples. It is argued that this index should be replaced by standardized scales that have reported properties of reliability and validity [9].

The climacteric scale constructed by Greene, is based on factor analysis studies [10]. This scale independently measures psychological, somatic, vasomotor and sexual symptoms and is used as a quality of life measurement in estrogen replacement trials [11,12], and in a population-based study to obtain normative data for climacteric symptoms [13]. A recently published study by Lam et al. investigated the effect of tibolone on menopause symptoms, psychological well-being and dyadic relationships. In this randomized placebo-controlled crossover study the menopausal symptoms were assessed by Greene Climacteric Scale [14].

In the present study, we conducted a randomized cross-over trial to compare the effects of tibolone and 17β-estradiol on climacteric symptoms, in women with surgical menopause, with a standardized scale.

2. Material and methods

A randomized, controlled, cross-over trial was conducted at Department of Obstetrics and Gynecology, Duzce School of Medicine to compare the effects of tibolone and 17β-estradiol in climacteric symptoms in women with surgical menopause. The study protocol was approved by the Medical Ethics Committee of Duzce Medical School and conformed to the ethical guidelines of the 1975 Helsinki Declaration. Informed written consent was obtained from each woman before enrollment in the study.

2.1. Subjects

Forty women who had been subjected to hysterectomy and bilateral oophorectomy for benign gynecological conditions in our clinic were enrolled to the study. All of the patients were in the perimenopausal period before the operation and none of them had been treated with hormones for their climacteric complaints before the operation. The initial screening included medical history, physical and gynecological examination, measurement of systolic and diastolic arterial blood pressures, height and weight and a mammography if not performed during the previous 12 months. Complete blood count, urine analysis and blood biochemistry were done. All analysis was found to be in the normal range. Any women who had hypertensive