Original Article - Clinical Trial

Prospective, randomized, assessor-blind comparative trial of the effects of menopausal hormone therapy with levonorgestrel-releasing intrauterine systems and other regimens on mammographic density

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ABSTRACT

Aim of the study

This is a prospective, randomized, assessor - blind comparative trial of Continuous Combined Hormonal Therapy (CCHT) with Levonorgestrel-releasing Intrauterine System (LNG-IUS) and other regimens in women receiving postmenopausal HT, based on mammographic density (MD) measurements.

Methods

77 postmenopausal women with intact uterus who had climacteric complaints were evaluated prospectively for one year. The patients were randomised in three groups. The patients of Group 1 (n:23) were given oral combination of 0.625 mg conjugated equine estrogen (CEE) and 2.5 mg medroxyprogesterone asetate (MPA) daily; the patients in Group 2 (n:30) were given oral 0.625 mg/day CEE in conjunction with LNG-IUS, and the patients in Group 3 (n:24) were given oral 2.5 mg/day tibolon. Before the beginning of the medication protocol mammographic findings and endometrial biopsies were obtained and new samples were received 6 months later for comparison. The groups were compared for the parameters of MD changes, effectiveness, tolerability, and endometrial safety of each treatment.

Results

The follow up mammographies within 6 months of the HT showed that the mammographic density increased in 26.1% patients of Group 1 (n=6), 16.7% of Group 2 (n=5), and 16.7% of Group 3 (n=4), with no statistical significance in the above mentioned measurements. Also, there were no significant differences in terms of effectiveness, endometrial safety, and tolerance to the regimens.

Conclusions

Estrogen therapy combined with LNG-IUS seems to have the potential to become an alternative method to conventional medications for estrogen replacement therapy in postmenopausal women. Larger series as well as follow-up after 6 months will be needed for definitive decision making.

Keywords: Medicated intrauterine devices, estrogen replacement therapy, mammography, levonorgestrel, menopause.

Introduction

In prescribing a postmenopausal hormone therapy (HT) in women with intact uterus, progestins are essential to protect the endometrium from the development of unopposed estrogen effects. Recently, supplying the progestagenic component of therapy by intrauterine systems was introduced in clinical practice. Levonorgestrel intrauterine system (LNG-IUS) (Mirena®, Schering, Turku, Finland) has been widely used for hormonal contraception; recently its role was expanded in continuous combined HT (CCHT).[1-3] Intrauterine progestin administration ensures lower blood levels of progestins in comparison with levels measured in oral administration.[1-3] Up to date, mammographic density changes that may occur during CCHT with LNG-IUS have not been extensively studied.

This is a prospective, randomized, assessor - blind comparative trial of CCHT with LNG-IUS and other regimens in women receiving postmenopausal HT, based on mammographic density measurements.

Material and methods

Study design

For the trial of the compared methods 77 postmenopausal women with intact uterus and climacteric symptoms were tracked; all of them were registered patients in the Menopause Clinic of Reproductive Endocrinology Department of Obstetric and Gynecology Department, Cerrahpasa Medical School, Istanbul University, between June 2003 and February 2004. The study protocol was approved by the ethical committee of the medical school before the study was initiated, and the informed consents of the patients were obtained. The study was conducted in accordance with the basic principles of the Declaration of Helsinki. The trial was registered and approved by the Hospital Scientific Committee.

Eligibility criteria

Inclusion criteria of the study were: presence of climacteric complaints, intact uterus, amenorrhea for more than 6 months, no postmenopausal HT in the last 6 months, and absence of known HT contraindications (undiagnosed vaginal bleeding, history of tromboembolic disease, active liver disease, genital cancer, migrain headache, hypersensitivity to steroid hormones).

Study protocol

The patients enrolled in the study were randomly allocated into three treatment groups: Group 1 (n:23), daily oral 0.625 mg conjugated equine estrogen (CEE) plus oral 2.5