

Mammographic changes during postmenopausal hormonal replacement therapy with tibolone

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Summary

Purpose of investigation: To evaluate mammographic changes in postmenopausal women receiving hormonal replacement therapy (HRT) with tibolone.

Methods: 83 postmenopausal women aged 45-62 received the same dose of tibolone for a period of six months to five years without interruption. The women were examined mammographically every six to 12 months during the observation period.

Results: There was a low incidence of breast tenderness. Also, we did not observe any significantly increased mammographic density or neoplastic disease of the breast. As far as dysplastic changes are concerned, no remarkable aggravation in the mammographic picture was noted.

Conclusion: The new synthetic steroid tibolone, in contrast to conventional HRT, rarely causes breast pain. At least short-period tibolone therapy (less than 5 years) has good effects on climacteric disorders and does not cause breast changes (dysplasia or cancer). Our study is on-going.

Key words: Hormone replacement therapy; Tibolone; Mammographic density.

Introduction

Hormonal replacement therapy (HRT) in postmenopausal women improves their quality of life by ameliorating hot flashes and genital atrophy, by reducing the risk of cardiovascular disease and by preventing osteoporosis. Moreover, it does not seem to increase the risk of breast cancer.

Mammography is a unique screening method for the detection of breast cancer. Increase in breast density, multifocal disproportion, cysts and fibroadenomas are possible mammographic changes caused by HRT [1-3].

Tibolone is a new synthetic steroid combining the beneficial influences of estrogens, progestogens and androgens in one and only one substance. It relieves postmenopausal symptoms, preserves skeletal integrity and does not cause endometrial irritation. However, the effects of tibolone on breast cancer risk, as well as on mammographic density caused by its usage, have not been fully studied.

The aim of our prospective study was the evaluation of mammographic changes in postmenopausal women receiving HRT with tibolone.

Materials and Methods

Our study included 83 postmenopausal women from 45 to 62 years of age (median age 51 years), receiving tibolone therapy without interruption after menopause for a period of six months to five years. The treatment had begun within two years of menopause. All women on HRT were using the same dose of tibolone (the daily dose was 2.5 mg per os).

Menopause was defined as the absence of menstrual periods for one year for those with intact reproductive organs or the time of hysterectomy with bilateral salpingo-oophorectomy. In women with a prior hysterectomy without bilateral salpingo-oophorectomy, menopause was defined as the onset of hot flashes.

The women had a normal mammography before starting HRT. We repeated the mammographic examination every six to 12 months during the observation period and we evaluated the results of our study.

Results

During the women's follow-up by breast examination, the following points were noted:

- There was a low incidence of breast tenderness
- None of the examined women receiving tibolone presented a significant increase in mammographic density.
- No neoplastic disease of the breast developed.
- As far as dysplastic changes are concerned, no remarkable aggravation in the mammographic picture was observed.

Discussion - Conclusions

It is well known that breast cancer as well as endometrial cancer is hormone-related. Different investigators express controversial aspects on the effects of HRT, but the majority of them agree that there is only a limitedly increased risk of breast carcinoma by the reception of long-period and/or high doses of HRT (more than 10 years) [4, 5].

The new synthetic steroid tibolone has been used as an alternative HRT in postmenopausal women and combines weak estrogen, progestogen and androgen properties. In contrast to conventional HRT, women receiving tibolone rarely complain about breast pain. Preclinical studies have shown that there is no indication of cancer genesis by HRT with tibolone. Tibolone and its metabolites significantly inhibit the regional production of estradiol in breast tissue, a hormone that has been considered as a key-factor in the genesis of breast tumors [6, 7].

The results of our study based on the women's follow up show that at least short-period tibolone therapy (less than 5 years) has good effects on climacteric disorders and does not cause breast changes (dysplasia or cancer).

Our study is being continued considering that a greater number of women are receiving tibolone therapy and a greater follow-up period is necessary to establish our results. In spite of this, we believe that tibolone therapy is a safe HRT in postmenopausal women but its usage has to be individualized. Frequent clinical and laboratory controls are necessary as breast examination is of a great importance and must be applied to women receiving HRT.

References

- [1] Berkowitz J.E., Gatewood O.M.B., Goldblum L.E., Gayler B.W.: "Hormonal replacement therapy: mammographic manifestations". *Radiology*, 1990, 174, 199.
- [2] Erel C.T., Seyisoglu H., Senturk M.L., Akman C., Ersavasti G., Benian A. *et al.*: "Mammographic changes in women on hormonal replacement therapy". *Maturitas*, 1996, 25, 51.
- [3] Laya M.B., Gallagher J.C., Schreiman J.S., Larson E.B., Watson P., Weinstein L.: "Effect of postmenopausal hormonal replacement therapy on mammographic density and parenchymal pattern". *Radiology*, 1995, 196, 433.
- [4] McNicholas M.M.J., Heneghan J.P., Milner M.A., Tunney T., Hourihane J.B., MacErlaine D.P.: "Pain and increased mammographic density in women receiving hormone replacement therapy: a prospective study". *A.J.R. Am. J. Roentgenol.*, 1994, 163, 311.
- [5] Stomper P.C., Von Voorkis B.J., Ravnikar V.A., Meyer J.E.: "Mammographic changes associated with postmenopausal hormone replacement therapy: a longitudinal study". *Radiology*, 1990, 174, 487.
- [6] Cemal T.E., Koray E., Canan A., Gul E., Ayca A., Hakan S. *et al.*: "Mammographic changes in women receiving tibolone therapy". *Fertil. Steril.*, 1998, 69, 870.
- [7] Coelingh Bennink H. J. T.: "Clinical experience with tibolone, a tissue-specific hormone". *Gynecol. Endocrinol.*, 1997, 11 (suppl. 1), 57.

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