PERGAMON

European Journal of Cancer 36 (2000) S39–S46

European Journal of Cancer

www.ejconline.com

Monitoring for endometrial disorders in 406 breast cancer women treated by tamoxifen: a low aggressive strategy

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1. Introduction

The best endometrial surveillance strategy for women receiving tamoxifen is still unclear: should they be monitored or not, since cost-effectiveness is far from proven [1,2]? Which, if any, should be the best scheme?

2. Objectives

To assess our current, low invasive strategy of routine monitoring for postmenopausal breast cancer women treated by tamoxifen, to describe observed endometrial disorders in those women and to propose a monitoring scheme based on our findings.

3. Population and methods

Transvaginal ultrasonography (TVUS) was performed in 317 women with breast cancer included during the course of their tamoxifen therapy (group I), in 89 women with breast cancer at baseline assessment (group II) and in 823 healthy women (group III). Among women with breast cancer (group I and group II), hysteroscopy and biopsy were performed if endometrial thickness was above 8 mm. The mean outcome measures were ultrasonographic endometrial thickness, prevalence of hysteroscopic and/or histological endometrial pathology at first screening, relationship with length of intake and with total cumulated dose, incidence of new pathology during follow-up, compliance to protocol, cancer detection rate, positive predictive value.

4. Results

In group I, average endometrial thickness was 8.1 mm, compared with 4.4 mm in women of group II and 3.4 mm in women of group III ($P < 0.001$). Compliance to protocol was achieved in 58% of women of group I. Additional work-up in those patients showed 46 endometrial pathologies (14.5%), consisting of 32 polyps, 12 hyperplasia and 2 cancers while only 4 (4%) of women of group II presented endometrial pathology at baseline assessment. Significant association was found with duration of intake and cumulative dose of tamoxifen ($P < 0.001$). Follow-up of women with a normal endometrium at first assessment showed an incidence rate of new pathology of 3 for 100 person-years for women of group I and II, with an incidence rate of endometrial cancer of 5 for a thousand person-years in women of group I. No cancer was seen in women of group II. Both cancers appeared in women with more than 3 years of tamoxifen intake, and with a cumulative dose of more than 30 g. Sensitivity of ultrasonography was 80%, and the positive predictive value of our strategy for any endometrial pathology was 67%.

5. Discussion

We observed, as other authors, frequent modifications of endometrium in women taking tamoxifen [3–5]. Malignancies are uncommon, appear late and after a quite high cumulative dose of tamoxifen, and are possibly unrelated to benign pathology. In this context, and without any evidence of cost-efficacy, an aggressive surveillance strategy should be avoided. Our current low invasive strategy, with TVUS as first-line screening test, can achieve good results in terms of compliance, cancer detection rate, sensitivity and positive predictive value. Starting yearly follow-up 3 years after the start of

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PII: S0959-8049(00)00218-5

tamoxifen could still improve compliance and should not miss any cancers.

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Absence of correlation between risk factors for endometrial cancer and the presence of tamoxifen-associated endometrial polyps in postmenopausal patients with breast cancer

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Abstract

In order to investigate the presence of established risk factors for endometrial carcinoma in postmenopausal patients with breast cancer and with tamoxifen-associated endometrial polyps we compared a group of 25 patients with tamoxifen-associated endometrial polyps with 25 tamoxifen-treated patients without endometrial polyps. No significant differences were found between both groups of patients in age, parity, time after breast cancer and after menopause, duration and daily and total cumulative dose of tamoxifen intake, body mass index and serum levels of luteinising hormone (LH), follicle-stimulating hormone (FSH), oestradiol (E2), progesterone, sex hormone-binding globulin (SHBG), tamoxifen and CA125. So far there is no evidence that these polyps are premalignant lesions.

Keywords: Tamoxifen; Endometrium; Polyps; CA125; Oestrogen; Endometrial cancer

It is well established that tamoxifen can induce endometrial hyperplasia and polyps [1–4]. The possible association between tamoxifen and the occurrence of endometrial cancer has been reviewed [5]. It has been suggested that the risk of developing endometrial cancer may be associated with the oestrogen-agonist effect of tamoxifen on the endometrium and would, therefore, increase with the duration of tamoxifen intake and with higher cumulative tamoxifen doses [6]. However, the pathogenesis of tamoxifen-associated endometrial polyps is unclear. We report here the results from a prospective study based on a randomised trial comparing transvaginal ultrasound (with sonohysterography) and office hysteroscopy [7].

1. Materials and methods

Asymptomatic postmenopausal patients with breast cancer who had taken tamoxifen for at least 6 months were eligible unless they had undergone a hysterectomy. 53 consecutive patients agreed to participate. The daily tamoxifen dosage consisted of either 20 mg ($n=24$) or 40 mg ($n=29$). The histopathological findings combined

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0959-8049/00/$ - see front matter
PII: S0959-8049(00)00219-7