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III.2 Saline Infusion Sonography (SIS) or Office Hysteroscopy: Which One is the Best? A Prospective Randomised Study

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A high proportion of asymptomatic tamoxifen-treated postmenopausal breast cancer patients have endometrial pathology (polyps, hyperplasia and cancer). Thick endometrium, as measured with ultrasound, is associated with pathology. Transvaginal sonography (with saline infusion sonography (SIS), if indicated) may be more effective and acceptable than office hysteroscopy for detecting these endometrial abnormalities. However, the value of endometrial surveillance in asymptomatic patients has not been proven, because this would require a prospective randomised trial including several thousands of tamoxifen-treated breast cancer patients, using mortality from endometrial cancer as an end-point. © **1998 Elsevier Science Ltd. All rights reserved.**

THE BENEFITS of adjuvant tamoxifen treatment clearly outweigh the potential risks [1]. However, it is now well-established that tamoxifen is associated with endometrial polyps, endometrial hyperplasia and endometrial cancer [2–4]. These polyps can display a wide variety of different appearances [5]. Currently, conflicting advice regarding gynaecological follow-up of patients on long-term tamoxifen treatment exists. Several authors have recommended some form of endometrial monitoring. Both the use of office hysteroscopy [2, 6] and transvaginal sonography [7, 8] have been advocated for this purpose. The aim of this randomised, cross-over study was to compare the effectiveness and acceptability of the two techniques that have been proposed for endometrial monitoring in tamoxifen-treated postmenopausal breast cancer patients [9]. Transvaginal sonography (TVS) (with saline infusion sonography (SIS) if the endometrial thickness was > 4 mm) was compared with office hysteroscopy.

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53 consecutive asymptomatic breast cancer patients gave informed consent to participate in this study. These patients were referred to our unit for endometrial monitoring. They had taken tamoxifen (20 or 40 mg/day) for at least 6 months. Patients were randomised to undergo either TVS or hysteroscopy as their initial test using a system of sealed envelopes. Group I first underwent TVS, combined with SIS if indicated, and office hysteroscopy within 30 min. Group II first underwent office hysteroscopy and TVS within 30 min, combined with SIS if indicated. After the second test the patients were asked which examination they would prefer, if both techniques were equally effective from a medical point of view. The gold standard used in this study was the histological result of resected polyps and endometrium at operative hysteroscopy.

25 patients had a positive screen result by both techniques; 8 patients and 2 patients had a positive result only by TVS or by office hysteroscopy, respectively. 33 patients underwent surgery (4 hysterectomy). 2 patients had endometrial cancer (1 primary, 1 breast secondary), both only detected by

TVS. 26 patients had at least one polyp (total 47, all benign). The sensitivity and specificity of TVS were 85 and 100%, respectively. The corresponding values for office hysteroscopy were 77 and 92%. The low sensitivity of office hysteroscopy was the result of 10 failed procedures because of the presence of cervical stenosis or intrauterine adhesions. SIS failed in 6 of these patients. Significantly more patients preferred TVS to office hysteroscopy ($P < 0.001$). This last finding is in agreement with a report comparing SIS and office hysteroscopy in patients presenting with abnormal uterine bleeding [10].

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III.3 Tamoxifen and Endometrium: Preliminary Results of a Follow-up Study

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SINCE 1992, we have studied the prospective effect of tamoxifen on the endometrium. We compared 2 groups: a group of 381 patients exposed to tamoxifen and a control group of 814 women without breast cancer, never exposed to tamoxifen and without hormone replacement therapy. The main duration of tamoxifen treatment was 14 months. The screening test used to evaluate the endometrium was an endovaginal ultrasonography (US). The endometrial thickness was considered abnormal if equal or superior to 8 mm. The patients with abnormal US were explored by diagnostic hysteroscopy and endometrial biopsy. Treatment by hysteroscopic endometrial ablation or classical surgery was performed if indicated. The compliance to assessment in the control group was worse than in the exposed group. Statistical results were corrected for compliance. Abnormal US was seen at first observation in 166 of the 381 treated patients (prevalence = 43.6%) and in 112 of the 814 controls (prevalence = 13.8%), with relative risk (RR) of 3.2 (2.6–3.9); $P < 0.001$. The mean thickness of the endometrium was 8 mm in the tamoxifen group versus 3 mm in the control group ($P < 0.001$). At first observation, the prevalence of endometrial pathology, confirmed by biopsy was 11.5% in the treated group and 4.1% in the control group. The RR is 2.8 [1.8–4.3] ($P < 0.001$). During the follow-up, within the tamoxifen group, 48 new cases of abnormal US have been observed. These results show an incidence rate (IR) of 22.9 for 100 person-year. Within the control group, 21 new cases of abnormal US occurred (IR = 4.8 for 100 person-year) with a RR of 4.8 (3.02–7.56) ($P < 0.001$) for the tamoxifen group. During the follow-up, 18 new cases of endometrial pathologies occurred in the exposed group. In the control group, 8 new cases were observed. The corrected RR to develop a pathology is 2.3 ($P < 0.05$) for treated versus control group. We observed that the cumulative risk increased regularly. Chi square for trend was significant ($P < 0.001$). No peak of annual incidence seemed to appear. The types of pathology observed by the group during the whole study, were respectively, in the treated group versus the control group: 6 cystic atrophia versus 5; 3 stromal hypertrophia versus none; 43 polyps versus 12; and 9 hyperplasia versus 5. Two well differentiated endometrial adenocarcinomas occurred in the treated group versus 1 in the control group. The 2 patients with endometrial carcinoma were treated with 40 mg of tamoxifen daily. Five seropapillary carcinomas of the ovaries and/or of the peritoneum