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III.1 Tamoxifen and the Uterus—the Hysteroscopic Approach

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All our hysteroscopic observations over the last 10 years strongly support that tamoxifen has an endometrial effect not seen with synthetic oestrogens. The development of small sized instruments, combined with an atraumatic insertion technique have made hysteroscopy a simple and safe procedure that can be performed on an outpatient base without any form of anaesthesia and with good patient compliance. In long-term tamoxifen users, hysteroscopy enables us to differentiate between atrophic endometria with glandulocystic changes in the underlying stroma and endometrial polyps mainly of the glandulocystic type. The diagnostic value of direct visualisation with the advantage of being able to guide endometrial biopsies is superior to any indirect technique like transvaginal ultrasonography (TVU). © **1998 Elsevier Science Ltd. All rights reserved.**

HISTORY SHOWS that hysteroscopy has only recently found the place it deserves in routine gynaecological practice. This delay was due to organ-specific problems such as difficult distension of the virtual cavity due to resorption (vascular, peritoneal) and loss (cervix, tubes) of distension medium and a very fragile endocervical and endometrial mucosa. Relatively large diameters of hysteroscopes resulted in a long learning curve and poor patient compliance compared to ultrasonography and TVU in particular. These problems were solved once small diameter hysteroscopes were developed (outer sheet maximum 3.5 mm) and following the introduction of the atraumatic insertion technique. This technique consists of introducing the scope under direct vision in a complete atraumatic way. Once in the uterine cavity the (12° or 30°) optic is slowly turned around its axis, thus visualising the whole uterine cavity without traumatic movements inside the cervical canal. In this way, hysteroscopy can be performed in a few minutes as an outpatient procedure without any form of anaesthesia. The following results clearly illustrate the tremendous progress hysteroscopy made during the last decade. Between 1982 and 1989 we performed a total of 4,204 consecutive outpatient hysteroscopies in our department. Using a 5 mm rigid scope and CO_2 as distension medium, 3,332 (79.2%) of all women reported no or minor discomfort. We had a 5.2% failure rate due to cervical stenosis, insufficient visualisation or major patient discomfort mainly in nulliparous and postmenopausal women. Using a 2.4 mm semi-rigid mini-fiberhysteroscope and Ringer lactate to distend the uterine cavity almost all procedures (97.7%) could be done without patient discomfort. A similar increase in feasibility was seen using a 3.5 mm rigid hysteroscope. In view of good patient compliance, low failure and complication rate with the technique, we undertook outpatient hysteroscopy to study the endometrial safety of tamoxifen in postmenopausal breast cancer patients.

In the two case–control studies [1] and in the one follow-up study [2] on the hysteroscopic appearance of the uterine cavity there was strong support for endometrial stimulation in the tamoxifen group. This effect seemed to be related to total dose and duration of treatment [3]. To evaluate the number of years one can safely leave the uterine cavity without screening, we evaluated the effect of duration of tamoxifen treatment on endometrial stimulation in another longitudinal hysteroscopic follow-up study. 57 postmenopausal women had at one stage a normal atrophic uterine cavity and the effect of tamoxifen on the endometrium was examined at regular intervals by hysteroscopy [4]. Endometrial stimulation or intra-uterine lesions were biopsied or removed. Patients were divided into three groups; tamoxifen less than 3 years, between 3 and 6 years and those using tamoxifen longer than 6 years. The majority of patients developed endometrial stimulation of some sort while an endometrial cancer was found in three women, all belonging to the group taking tamoxifen for more than 6 years. There was one polyp-cancer, one low grade and one high grade endometrial cancer. Comparing the groups up to 6 years versus more than 6 years tamoxifen, we found a trend towards developing clinical important intra-uterine lesions but this association was not significant ($P = 0.14$). In this study, in the 3 years following a normal baseline hysteroscopy, postmenopausal women using tamoxifen 20 mg daily did not develop endometrial hyperplasia or endometrial cancer. In this time period, however, benign endometrial polyps and atrophic glandulocystic endometria may appear. Finally, using hysteroscopy, we were able to describe the hysteroscopic appearance of frequently encountered tamoxifen-exposed endometrial lesions.

In conclusion, for those considering endometrial surveillance in women on tamoxifen, we suggest a baseline hysteroscopy before treatment followed by annual outpatient hysteroscopy with the first follow-up hysteroscopy 2 years after initiation of treatment.

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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