



## C-Gyn 12

# Tamoxifen and the Endometrium

Tamoxifen is the endocrine treatment of choice for selected patients with breast cancer, and has been shown to have a preventative role in healthy women at increased risk of developing breast cancer. Although Tamoxifen functions as an antioestrogen, it also has weak and variable oestrogenic effects.

Because of its weak oestrogenic activity, Tamoxifen produces a number of side effects on the female genital tract. These may include:

- oestrogen-like changes in the vaginal epithelium of some patients.
- stimulation of endometriosis, with worsening of symptoms in some patients. There has been one case report of an endometrioid carcinoma arising from an ovarian endometriotic focus.
- stimulation of the growth of benign fibroids.
- an increased incidence of benign endometrial polyps.
- an increase of benign endometrial proliferation. In postmenopausal women, it would seem that the incidence of atrophic endometrium is about 36% in women on Tamoxifen, compared to 73% in control patients, while the incidence of proliferative endometrium is about 20% (10% in controls), endometrial polyps 11% (3% in controls) and endometrial hyperplasia 6% (0.6% in controls).
- a two to three fold increased incidence of endometrial carcinoma. The stage and grade of tumours found in women on Tamoxifen is comparable to those tumours found in women not taking Tamoxifen.
- there have been isolated reports of uterine sarcoma occurring in women taking Tamoxifen.

Opinions vary widely in the literature and amongst clinicians on the surveillance of patients on Tamoxifen therapy who have an intact uterus. Transvaginal ultrasonography is relatively non-invasive and will detect a relatively high proportion of abnormalities. Detection rates may be further improved with the addition of saline infusion sonohysterography. Many of the ultrasonographic abnormalities are in fact located in the myometrium, and not in the endometrium as suggested by ultrasound. Biopsy of these lesions has produced a wide range of mainly benign pathologies.

Outpatient hysteroscopy and/ or endometrial biopsy are more invasive and less well tolerated in postmenopausal women. Withdrawal bleeding following administration of progestogens is another possible method of screening asymptomatic women for endometrial proliferation. The

specificity, sensitivity, and cost effectiveness of these various methods of monitoring are presently unknown.

Because the incidence of endometrial carcinoma is very low (2-3/1000 women per year) during or after Tamoxifen therapy, and because there is no convincing evidence that the stage or grade of these tumours differs from that seen in the general population, there are no data to support active investigation of asymptomatic women at the present time.

It is recommended that:

- All women taking Tamoxifen should be informed of its potential side effects, including specifically the two to three fold increased incidence of endometrial cancer.
- They should be warned of the possible symptoms of endometrial cancer, including intermenstrual or post-menopausal bleeding, abnormal vaginal discharge, or pelvic pain.
- All women on Tamoxifen should have a baseline pelvic examination. This should include a speculum examination to determine the presence or absence of a cervix and to take a pap smear (if appropriate), and a bi-manual examination to evaluate the size of the uterus and the adnexa.
- Routine screening of asymptomatic women taking Tamoxifen, using either ultrasound or endometrial biopsy, is not recommended.
- Any woman complaining of symptoms should be actively investigated immediately.
- If an individual patient expresses particular concern about the possibility of developing endometrial cancer, or is felt to be at additional risk because of a family history of breast, ovarian, endometrial or bowel cancer, the patient should be referred to a gynaecologist and offered investigation at the discretion of the gynaecologist.
- When indicated, a vaginal ultrasound should be performed by a skilled gynaecological ultrasonographer. This would seem to be the least invasive and most useful initial investigation. It should be recognised that interpretation of vaginal ultrasound may be difficult and at times may be misleading, especially in the asymptomatic patient. Ultrasonography may select out those women with bleeding who have an atrophic or inactive endometrium from those with possible pathology (who may require further intervention).
- Because of the absence of data establishing the sensitivity, specificity, clinical value and cost effectiveness of active investigation of asymptomatic women such research should be encouraged and supported.
- These recommendations, which apply to both the therapeutic and prophylactic use of Tamoxifen, will be reviewed regularly in the light of any new evidence which may emerge.

## References

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