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E4. Tamoxifen and gynaecological side-effects: an update

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1. Introduction

Tamoxifen is still the treatment of choice in the adjuvant setting in pre- and post-menopausal women with breast cancer and also the first choice in the palliative treatment of women with metastatic breast cancer [1]. This update considers the side-effects of tamoxifen on the female genital tract in pre- and post-menopausal women.

2. Results

Tamoxifen has oestrogen agonistic and antagonistic effects on gynaecological tissues and organs, depending on the ambient oestradiol concentration [2].

In *pre-menopausal* tamoxifen users, ovarian cysts occur in over 80%, resulting in high serum levels of oestradiol, while serum levels of FSH and LH are only minimally influenced [3]. Oligo- and amenorrhoea occur in half of the patients. Tamoxifen has an antagonistic effect on the endometrium in pre-menopausal women [4]. Even in women with supraphysiological serum levels of oestradiol, the endometrial lining stays thin. Tamoxifen is associated with impaired sexual functioning and hot flushes. Tamoxifen might be teratogenic.

In *post-menopausal* women, tamoxifen has an oestrogen agonistic effect on the uterus. Tamoxifen can induce benign endometrial stromal hyperplasia and endometrial polyps. Tamoxifen-exposure up to five years increases the endometrial cancer risk by two- to three-fold [5]. There is no general consensus regarding endometrial surveillance in post-menopausal tamoxifen users. In Europe, opinions about endometrial surveillance vary from no screening to pre-treatment ultrasound and subsequent annual screening three years after the start of tamoxifen [6,7]. No trials exist on the efficacy of pre-symptomatic screening. Women with tamoxifen-induced endometrial cancer present with post-menopausal bleeding in the same way as non-users. Endometrial surveillance by ultrasonography has a high false-positive rate due to tamoxifen-induced characteristic sonographic changes of the post-menopausal endometrium, hampering its interpretation [8]. Endometrial sonographic screening in asymptomatic tamoxifen users is not likely to be effective in lowering morbidity or mortality from endometrial cancer. Instead, patients need to be educated to report vaginal bleeding immediately. In all cases of post-menopausal bleeding, histology of the endometrium is indicated. Tamoxifen can aggravate symptoms of hot flashes and sexual dysfunction [9]. No recommendations exist about irregular vaginal bleeding in *perimenopausal* women. The irregular cycles in these women hamper the signal function of vaginal bleeding and they should be advised to be seen by a gynaecologist to exclude endometrial cancer.

3. Conclusions

Despite its side-effects on the female genital tract and psychosexual functioning, of which patients need to be informed, the benefits of tamoxifen outweigh the risks. Patients need to be educated to report abnormal bleeding or discharge without delay.

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