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	Double Spacing
Title (type in CAPITAL LETTERS)	ASSESSMENT OF TAMOXIFEN EFFECTS ON UROGENITAL TRACT USING VAGINAL AND URINARY CYTOLOGY AND COLOR DOPPLER EVALUATION OF PERIURETHRAL VESSELS (PREVIOUS NOTE).

**Aims of study:** Estrogen plays an important role in urinary continence influencing the factors responsible for intraurethral pressure: urethral epithelium, connective tissue, periurethral musculature and urethra's submucous vascular plexus. After menopause, the relative lack of estrogen can lead to a complex of symptoms, including urinary incontinence. Hormone replacement results in improvement of genuine stress incontinence in postmenopausal women<sup>1</sup>.

Recent studies assessed the submucous vascular plexus using color doppler, showing that the technique can be utilized in urethral and incontinence investigation.<sup>2,3</sup>

Tamoxifen is a non-steroidal antiestrogen that has complex and incompletely understood biological actions. It behaves as an antiestrogen in some tissues, as the breast, but in others (as cardiovascular and skeletal systems) it has weak agonist properties. The studies referring evaluation of vaginal smears are not conclusive for estrogenic or antiestrogenic effect of tamoxifen.

Two investigations have mentioned actions of tamoxifen in urinary tract. The first showed that neonatally administered tamoxifen causes abnormalities in urogenital tract of female mice<sup>4</sup>; and the second, the NSABP B-14 project<sup>5</sup> found three cases of bladder cancer among 1419 women using tamoxifen, although it doesn't mean an increased risk of bladder cancer in this group.

The present investigation has two objectives: a) to study the effects of tamoxifen use in dopplervelocimetric parameters of periurethral vessels in postmenopausal women and b) to verify the effects of this drug on the maturation of vaginal squamous epithelium and on urinary sediment cells.

**Methods:** Twenty menopausal women with breast cancer underwent color doppler examination of periurethral vessels and vaginal and urinary cytology. Written consent was obtained from all patients. Eight of them had been using 20 mg/d of tamoxifen for at least three months (group tamoxifen). Twelve patients were not receiving drug therapy (control group). Women with vascular disease and hypertension were excluded.

The number of periurethral vessel, systolic peak, minimum diastolic values, pulsatility and resistance indexes were assessed using an ATL – HD 2000 ultrasound equipment. An intravaginal high frequency transducer (5-9 MHz) was placed horizontally in the subclitoridian area and a sagittal image of the urethra was obtained. The vessel chosen for analysis was the one closest to the lumen in the medium third of the anterior urethral wall. Vaginal and urinary sediment smears were collected after color doppler examination and the maturation value was calculated.

**Results:** The groups were compared using Mann-Whitney non-parametric test. Significance was accepted at  $P < 0.05$ . There was no statistical difference between the two groups for number of periurethral vessels, systolic peak, minimum diastolic values, pulsatility and resistance indexes and for the maturation value of urinary sediment smears.

Patients receiving tamoxifen showed higher maturation values for vaginal smears in comparison to the non-treated group.

**Conclusions:** Until this moment, our study has not found evidence of tamoxifen effects on the female urethra's submucous vascular plexus nor in maturation value of vaginal smears, indicating an estrogenic effect.

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