RESEARCH COMMUNICATION

Effects of Tamoxifen on the Cervix and Uterus in Women with Breast Cancer: Experience with Iranian Patients and a Literature Review

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Abstract

Objective: Invasive breast cancer is the most common malignancy in women. Due to the declining mortality rate that is partly attributable to the use of screening mammography and effective adjuvant therapy, more women survive their breast cancers. The aim of this study was to evaluate the effects of tamoxifen on the genital tract with particular attention to the uterus and cervix. Methods: We investigated the relationship between tamoxifen and cervical or uterine cancer in Iran, reviewing all the studies performed by the Vali-Asr Gynecology Oncology Clinic in Tehran. In addition, the available data on Medline from 1980 until 2009 were reviewed. Results: A total of 182 articles showed associations with gynecologic malignancies. Although as many as 121 referred to links between the drug and endometrial abnormalities (polyps or cancers), 55 articles studied the relationship with changes of pap smears, four of which indicated isolated cervical metastasis followed tamoxifen use in patients with breast cancer. Conclusion: In spite of the significant relationship between tamoxifen and endometrial cancers, cervix is rarely involved in breast cancer patients. However, vaginal bleeding or abnormal vaginal discharge has been reported in all cases before the diagnosis was made. To rule out genital tract malignancy, it is necessary, therefore, to have an annual pelvic exam, pap smear and early endometrial with endocervical curettage for tamoxifen users following a breast cancer in those with abnormal uterine bleeding or persistent vaginal discharge.

Key Words: Tamoxifen - breast cancer - pap smear - cervical cancer - uterine cancer

Introduction

Breast cancer is the most common malignancy in American women. It afflicts one in 8 women and that is to say every women may catch it at the probability of 12.6% during her life (Jemal et al., 2007). It is also the most common malignancy among Iranian women, so that the incidence is 18.2/100000 persons (Mousavi, 2007). Due to mammography and other screening techniques along with adjuvant therapies, more women can survive their breast cancers nowadays (Berry et al., 2003). It is necessary to be aware of care to be taken during follow-up period of treatment. It is to be noted that the risk of endometrial cancer is increased by using tamoxifen after a breast cancer incidence (Berry et al., 2003; Jemal et al., 2007; Mousavi et al., 2008).

Tamoxifen, a nonsteroid anti-estrogenic drug, is used in all stages of a breast cancer. As a prevention to a secondary breast cancer in high-risk patients, tamoxifen serves to increase their survival rate (Early Breast Cancer Trialists’ Collaborative Group., 2005). Since it affects on estrogenic receptors, it can lead to some changes in genital organs (Gill et al., 1998; Abadi et al., 2000). As awareness of effective screening tests of cancer in breast cancer women and how tamoxifen affects cervical cytology or relates to with genital tract malignancies is very important.

The aim of this study is to evaluate pap smear changes due to using tamoxifen in Iranian breast cancer patients and to interpret different cervical abnormalities. The incidence of endometrial cancer, uterine sarcoma and cervical malignancies was studied in tamoxifen users following their breast cancer. The patients were all referred to the Gynecologic Oncology Clinic of Vali-Asr Hospital in Tehran, Iran.

Materials and Methods

As there was no recent review article about the association of tamoxifen with cervical/endometrial malignancies or cervical cytological changes in tamoxifen users, we searched and evaluated all medline articles between 1980 and 2008 by using tamoxifen, breast cancer, cervical cytology, cervical cancer, and uterine cancer as key words.

Therefore, all studies on breast cancer patients referred to Vali-Asr Gynecologic Oncology Clinic of Tehran, Iran from 1997 to 2009 were reviewed to verify the relationship of tamoxifen use with cervical/uterine malignancies.
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of progression in endometrial cancer.

The value of pap smear for breast cancer patients especially for tamoxifen users lies in an early diagnosis of endometrial abnormalities such as endometrial cancer or uterine sarcoma (Khatcheressian et al., 2006). The presence of endometrial or glandular cells can be indication of endometrial cancer in these patients (Khatcheressian et al., 2006; Emens LA et al., 2002). It is especially true about the cases suffering from vaginal bleeding or vaginal discharge resistant to treatment. So, all breast cancer cases using tamoxifen should undergo a vaginal sonography and a diagnostic curettage to rule out any endometrial cancer, if vaginal bleeding or resistant vaginal discharge occurs (Emens et al., 2002; Khatcheressian et al., 2006).

There are many articles on the association of tamoxifen with endometrial polyps, uterine body cancer and uterine sarcoma (Magriples et al., 1993; Bissett et al., 1994; Fisher et al., 1994; Sismondi et al., 1994; Mignotte et al., 1998; Deligdisch et al., 2000; Wickerham et al., 2002; Behtash et al., 2009), but only a few studies have been performed on pathological effects of tamoxifen on female genital organs (Ferrazzi et al., 1977; Boccardo et al., 1981; Eells et al., 1990; Fornander et al., 1991; Athanassiadou et al., 1992; Wolf et al., 1992; Cohen et al., 1994; Sonnendecker et al., 1994).

There is some experimental evidences indicating that high doses of tamoxifen can induce a cervical tumor. It should be also noted that a low dose of tamoxifen may stimulate cell growth (Ferrazzi et al., 1977; Fornander et al., 1991). Some studies determined the presence of estrogenic receptors on the squamous and columnar cells of the cervix in premenopause and post-menopause women (Ferrazzi et al., 1977; Boccardo et al., 1981; Fornander et al., 1991; Athanassiadou et al., 1992; Wolf et al., 1992; Cohen et al., 1994; Sonnendecker et al., 1994). It is not known if these receptors are affected by menstrual cycle or agonist–antagonist estrogenic factors (Boccardo et al., 1981). Eells et al. (1990) found out that in a few of menopausal women treated by tamoxifen, the metastasis of squamous cells was increased. Therefore, a review article was written by Fornanders et al. (1991) to report the effect of tamoxifen on female genital system and that there was no difference in cervical cancer incidence between the tamoxifen user and the non-user group.

Gill et al. (1998) reported that tamoxifen with or without chemotherapy led to the formation of atypical cells in the pap smear of 62% of cases half of whom were ASCUS and the rest were nondysplastic. It should be noted that none of the smears progressed to a malignant or precancerous lesion during the follow-up. Mousavi and Karimi Zarchi (2007) reported some isolated metastatic cervical cancers in breast cancer patients, especially tamoxifen users. However, cervical involvement following a breast cancer was rare; only 28 cases of cervical involvement were reported 4 of which were isolated type.

In conclusion, when using tamoxifen following a breast cancer, an annual pelvic examination and pap smear are needed as a part of gynecologic studies. It should be noted that tamoxifen does not have any significant effect on pap smear findings. If vaginal bleeding or discharge occurs, vaginal sonography as well as endocervical and endometrial curettage be helpful to rule out endometrial/cervical cancer in patients with breast cancer followed by tamoxifen.

References


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