Tamoxifen's Impact on the Management of Breast Cancer: Patient Perspectives

By Bonnie S. Reichman, MD

Tamoxifen citrate has been prescribed to millions of women with breast cancer and has been one of the most important advances in breast cancer treatment over the past 25 years. Because she is a female physician, the

Introduction

Physicians need to be acutely aware of and sensitive to those concerns and factors that affect quality of life in order to be able to communicate the necessary information to their patients. Physicians must be able to provide information to their patients and to place simplistic or incorrect media reports into perspective.

Patients need to be aware of the side effects and what can be done to minimize them. They should also realize that some side effects may be due to other processes, including natural or induced menopause.

As a group, women are sensitive to issues that affect body image; this is particularly true of breast cancer survivors. Therefore, weight gain while on tamoxifen may represent a major concern. Menopausal symptoms such as hot flashes, sleeplessness, and urinary and vaginal changes may be debilitating and long lasting. Sexual function in the cancer survivor is an issue that is rarely broached by oncologists. Depression can also occur.

Other risks associated with tamoxifen, such as uterine cancer and ocular toxicity, are rare, and the role of the drug in the pathology of these conditions needs to be further defined.

If physicians are aware of patient concerns, communication can be improved. When patients are adequately informed about the real benefits and risks of tamoxifen, they are unlikely to refuse treatment and are more compliant with treatment recommendations.

Tamoxifen is an effective treatment for many women with advanced or metastatic breast cancer. Recent studies of early-stage breast cancer have confirmed that tamoxifen, when given after initial surgery or radiation therapy as "adjuvant systemic therapy," can prevent or delay breast cancer recurrence.

These studies have also shown that tamoxifen decreases the chance of breast cancer occurring in the untreated (opposite) breast. Tamoxifen has also been shown to prevent breast cancer in laboratory experiments. Tamoxifen is also currently being studied as a preventive treatment for women who are at an increased risk for breast cancer for a variety of reasons, including family history, age, and previous history of lobular neoplasia (LCIS or lobular carcinoma in situ).

Tamoxifen is a hormonal medication that acts against breast cancer cells by preventing estrogen from binding to the special estrogen receptors that are present in many breast cancer cells. This interaction inhibits the growth of cancer cells. Most tumors are tested for estrogen receptors and their presence determines the likelihood of response to tamoxifen. There are other mechanisms through which tamoxifen interferes with cancer cells, some of which are not well understood. Like all medications, tamoxifen has advantages and disadvantages to its use. However, for most women with early-stage or operable breast cancer, the risks of tamoxifen are greatly outweighed by its benefits.

My experience with tamoxifen citrate has been gathered through practice as a physician. My patients tend to reveal personal concerns to me that they might not discuss with a male physician. This has put me in a position to evaluate the benefits and drawbacks of breast cancer treatments from the patient perspective.

Patient Communication

When patients are well-informed, they tend to understand both the benefits and risks of taking tamoxifen. They know what side effects to expect and feel a sense of control over their lives.
Providing educational materials such as handouts and videos and referring women to support groups or therapists are particularly helpful in preparing patients for treatment. The negative media attention tamoxifen has received lately has created hysteria in many medical offices. We have to actively debunk negative impressions patients have developed based on inadequate or misleading information obtained from the media. We must provide our patients with accurate information and discuss their concerns in detail in order to help the patient better manage both their disease and treatment.

**Benefits of Tamoxifen**

Patients easily recognize the benefits of tamoxifen in relation to breast cancer. I do not have problems explaining these benefits in discussing why breast cancer patients should take tamoxifen. Clinical trials have revealed an increase in overall survival as well as disease-free survival in both premenopausal and postmenopausal patients, particularly those with estrogen receptor (ER)-positive disease.[1] Data from adjuvant trials have also demonstrated a 39% reduction in the incidence of contralateral primary breast cancer with tamoxifen.[2]

Predictors of tamoxifen response include the presence of ER-positive disease, soft tissue rather than osseous or visceral metastases, older age, longer time to recurrence, indolent course of disease, and prior response to hormonal therapy.

Tamoxifen also has favorable secondary effects on bone mineral density in postmenopausal women and on the cardiovascular system that may not be as well recognized. The cardiovascular effects are possibly related to the observed 12% reduction in non-cancer-related mortality. These benefits may be significant to some women.

**Duration of Tamoxifen**

The scientific question of how long to give tamoxifen remains unresolved, but for the patient, it is often a more personal question. Many patients feel that continuing therapy makes them feel proactive and secure--"the tamoxifen security blanket."

For patients with node-negative breast cancer, it is relatively clear that there may be no further benefit in continuing tamoxifen beyond five years; however, for patients with node-positive disease--and within its various subgroups--the answer is less clear. Patients with node-positive breast cancer need to be handled on a case-by-case basis. To formulate the best plan for the individual patient, we use all the prognostic information that we have available including pathologic findings, tumor size, number and level of lymph node involvement, hormonal receptor status, patient age, and menopausal status. Of course, the patient’s preferences must also be considered. Because of the media’s inaccurate reporting, the public doesn't understand the full story about duration and doesn't make the distinction between node-positive and node-negative disease. Media reports often give the impression that five years of therapy is standard for all patients, when this is not the case. Such reports often raise unnecessary concern among patients.

**Quality of Life**

Side effects of any drug are important to patients in relation to quality of life, especially when the drug is taken for extended periods. Being aware of side effects and minimizing their impact are important factors in continued compliance, which is necessary for maximum effectiveness.

A preliminary investigation was made into the quality of life of tamoxifen patients participating in the National Surgical Adjuvant Breast and Bowel Project (NSABP) B-14 protocol (Table 1).[3] The results demonstrated that there was no major difference between tamoxifen and placebo in the quality of life: no negative impact on social activities or work habits, including housework and volunteer work. More patients receiving tamoxifen experienced hot flashes than those receiving placebo. Contrary to what I would expect, more placebo patients reported that they felt less feminine and had reduced sexual desire than tamoxifen patients. Clearly more quality of life studies with detailed analyses need to be conducted in breast cancer patients on tamoxifen.

Patients who realize that certain side effects can occur tend to deal with the side effects better than those who have not been informed prior to their occurrence. Uninformed patients may not recognize side effects or seek help. Some patients report that they feel like they are "losing their mind" and that the side effects are imaginary. Patients must recognize that the side effects are real.

**Side Effects of Tamoxifen**

Types of side effects of tamoxifen vary significantly as does their reported incidences. As is the norm, patients tend to talk about their negative experiences rather than their positive ones, so we are more likely to hear from patients having significant side effects. Discussions on the Internet and
in patient groups also tend to focus on negative experiences, although occasionally patients report after discontinuing tamoxifen that they had felt better while on the drug.

**Menopausal Symptoms**

Many of the symptoms reported by tamoxifen patients are similar to those experienced by women going through natural or chemotherapy-induced menopause, since these symptoms are due to loss of estrogen. Some younger women experience abrupt, premature menopause on tamoxifen or as a result of chemotherapy and are very distressed by their symptoms. However, older women seem to have just as much difficulty.

As do women undergoing menopause, many women on tamoxifen struggle with hot flashes as well as sleeplessness. Bloating, constipation, irregular menses, vaginal complaints (dryness, itching, and/or discharge), nonmenstrual bleeding, depression, memory loss, and hair thinning are also reported. In many cases it is hard to separate the etiology of the symptoms; the important thing is to listen and to alleviate symptoms if possible.

**Vasomotor symptoms** may be remedied by taking vitamin E, B6, or selenium. Prescription drugs include progestational agents, Bellargal, and clonidine, the latter two causing major side effects. Using a divided schedule of tamoxifen or taking it at different times of the day may help to decrease hot flashes. Incorporation of soy products into the diet several times a week may be helpful.

Although estrogens are generally contraindicated in breast cancer patients, some physicians prescribe them to treat estrogen deprivation-related symptoms. This use of estrogens needs further investigation in controlled clinical trials.

A wide variety of herbal and natural remedies have been used, many without significant clinical studies on their safety and efficacy. Products such as primrose oil, dong quai, cat's claw, blue cohosh, false unicorn root, fennel, thistle, anise, and shark cartilage have been reported as being used. With some herbs, we do not know why or if they really help, or if there is a placebo effect. The bioavailability among preparations may be different. Many of these types of remedies are reported from patient to patient. When you ask patients what medicines they are taking, they often do not report all of the additional agents; such remedies have to be queried about specifically.

**Weight Gain**

Physicians treating breast cancer patients need to be especially sensitive about the issue of weight gain. Interestingly, weight gain has been correlated with both menopause and hormone replacement therapy, as well as tamoxifen. Women in general are concerned about body image, and patients with breast cancer have just experienced relatively deforming surgery, regardless of conservation and/or reconstruction, that makes them even more sensitive to body image.

Weight gain is common in healthy postmenopausal women and is prevalent in breast cancer patients as a group, regardless of their particular treatment. My best approach is to tell women that they may gain weight, and I stress the importance of optimizing their overall health through maintaining good body weight and exercise, which may prevent osteoporosis and heart disease.

**Sexual Dysfunction**

New interest has been generated in a historically neglected issue: sexual function in the cancer survivor. The lack of estrogen with tamoxifen treatment causes vaginal dryness, and dyspareunia may result. Painful intercourse is likely to produce reduced desire and hence sexual avoidance in these women. In a 1994 abstract, 53% of tamoxifen patients in partnered relationships reported dyspareunia and 29% reported decreased sexual desire. A loss of ability to achieve orgasm was suggested by the study. Treatment with topical estrogens and the use of systemic hormone replacement therapy in this population is controversial. We recommend the use of a variety of nonhormonal lubricants (ie, Replens, Astroglide) for this condition. Vaginal dilators may also prevent or delay vaginal atrophy.

Treatment for reduced sexual desire is less straightforward. The late Dr. Helen Singer Kaplan attributed reduced libido and sexual responsiveness in breast cancer survivors, as well as postmenopausal women as a whole, to reduced circulating testosterone levels. She was able to reverse this condition with low, nonvirilizing doses of testosterone. In addition, many women are emotionally vulnerable and depressed after breast cancer diagnosis and surgery, and this has a major impact on sexual life. Antidepressants and counseling should be considered for these women.

**Other Effects**

Some reported side effects of tamoxifen are very infrequent, including dizziness, headache, thromboembolism, and visual changes. Recently, concern in the media has focused on risks of tamoxifen with respect to the development of other cancers in breast cancer patients treated with tamoxifen. These reports have raised concern and need to be discussed openly. It should be noted that a higher proportion of colon and endometrial cancers have been reported in breast cancer patients.
patients than among the general population. The actual risks need to be communicated to patients. When patients are informed about the real risk of developing uterine cancer, they are unlikely to refuse tamoxifen. Indeed, tamoxifen patients are now monitored more closely for gynecological symptoms. However, evaluation beyond annual Pap smears and investigation of nonmenstrual bleeding appear unwarranted.

In postmenopausal women, the benefits of tamoxifen in preserving bone mineral density is known, although some data imply that there may be bone loss in premenopausal patients. We should determine whether our patients have adequate calcium intake with vitamin D and if they are performing weight-bearing exercise on a regular basis. Bone density evaluation might be considered in some patients to determine whether further implementation would be beneficial.

Another rare concern is tamoxifen-associated ocular toxicity. The pathology of eye findings in tamoxifen patients is very unclear and its investigation is complicated by age-related eye disease and other medical illnesses. I recommend baseline eye exams in all my patients.

Conclusion

For women with breast cancer, the benefits of tamoxifen, in terms of the reduction in contralateral breast cancer and increased survival, clearly outweigh the risks and toxicity associated with the drug. Despite tamoxifen's demonstrated efficacy in breast cancer treatment, physicians need to be concerned about issues that have an impact on a patient's quality of life. Breast cancer patients are particularly sensitive about body image, and weight gain on tamoxifen may be a major issue. Menopausal symptoms such as hot flashes, sleeplessness, and vaginal changes may be prolonged. Physicians need to broach the subject of sexual function with breast cancer patients receiving tamoxifen and offer appropriate counsel and/or referral. In my experience, informing patients about what they can expect from tamoxifen has made a great deal of difference in their acceptance of treatment.

References:


