

Poor response of breast cancer to tamoxifen

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Summary: Fifty eight (58) patients with early breast cancer (mean age 78.3 years) and 37 patients with advanced breast cancer (mean age 65.9 years) were treated with tamoxifen orally 20 mg daily or twice daily. The mean follow-up time was 19.1 months in the early group and 18.4 months in the late group. The drug was extremely well tolerated. All patients had cytological or histological evidence of breast cancer. A complete or partial response was found in only 36% of the patients with early breast cancer and only 13% in the advanced group. We conclude that tamoxifen was disappointing as a primary therapy in our patients. Although because of its lack of toxicity it can be seen as initial therapy for patients with breast cancer, it may have to be supplanted rapidly by other forms of therapy in the substantial proportion of patients in whom a response will not occur.

Introduction

In recent years tamoxifen has become an established treatment for breast cancer as both adjuvant and primary therapy. Most of the published experience has been in elderly patients.

In early breast cancer response rates between 60–73% have been reported.^{1–3} In locally advanced disease the response appears poorer with a remission rate of 40%⁴ but even in advanced disease a response rate of 57% has been reported.⁵

More recently doubt has been expressed about the real efficacy of tamoxifen. In a randomized controlled trial of tamoxifen versus mastectomy⁶ the authors concluded that surgery was the treatment of choice in the elderly. In this review we report our experience with tamoxifen as initial therapy for breast cancer.

Methods

Patients were included in this retrospective study if they had cytological proof of malignancy and a minimum follow up of 6 months. No data on oestrogen receptors was available for this study. The early breast cancer group received 20 mg tamoxifen daily as did 21 out of 37 of the late breast cancer group. The remaining 16 received 20 mg twice daily. There were 58 patients with early breast cancer (T = 1–2, N = 0–1) (mean age 78.3 years:

range 59–94). Two patients were treated with tamoxifen because they were unfit for surgery and a further two refused to undergo an operation. The mean follow-up time (or to death) was 19.1 months in this group.

There were 37 patients with advanced breast cancer (T = 3–4, N = 1–2, M = 0–1) (mean age 65.9 years; range 34–93). The mean follow-up time (or to death) was 18.4 months.

Complete and partial responses were defined in accordance with the UICC criteria.⁷ A complete response was the disappearance of palpable tumour and a partial response being a 50% reduction after 6 months of tamoxifen. The subsequent clinical course of the patients was noted with regard to surgery, chemotherapy or radiotherapy. Side effects were documented.

Results

Early breast cancer

Table I shows the results in the 58 patients with early breast cancer (T = 1–2; N = 0–1; M = 0). Only 10 (17%) had complete remission of their disease and the mean duration of this response was 23.4 months. One of these patients subsequently had a course of radiotherapy to the breast. This was a 79 year old patient with a 5 cm tumour which had regressed entirely at the 6 month assessment but by the twenty-second month was measured at 7 cm.

There were a further 10 (17%) patients who had a partial response with a mean duration of 25.2

Table I Response to tamoxifen of 58 patients with early breast cancer

	At 6 months	Mean duration of response	Subsequent course			
			Chemo-therapy	R/T	Surgery	Died
Complete response	10 (17%)	23.4 months	0	1	0	0
Partial response	10 (17%)	25.2 months	0	0	1	0
Static response	20 (34%)	14.0 months	0	1	1	2*
Non responders	18 (31%)	---	0	3	11	2

*1 died of non-related cause

months. Only one patient had other treatment and this was a wide excision in an 84 year old whose partial remission was maintained after 9 months of treatment. She requested surgery even though she was responding reasonably.

The remaining 38 patients (65%) had no decrease in palpable tumour size. Four died during the period of follow-up, 3 due to progression of disease; 4 required radiotherapy and 12 had a mastectomy.

Advanced breast cancer

Table II shows the results in 37 patients with advanced breast cancer (T = 3-4; N = 1-2; M = 0-1). These patients presented with either an inoperable primary tumour and/or lymph node or distant metastases. Table III details the pattern of disease in the patients presenting with advanced breast cancer.

There were two patients in this group whose breast lumps disappeared altogether on tamoxifen initially. In one there was local recurrence after one year of treatment at the same time as the emergence of distant metastases. She required radiotherapy and chemotherapy but died 15 months after first treatment with tamoxifen. The second patient had a complete remission of her breast tumour but not her nodal disease. She died of brain secondaries 37 months after treatment with tamoxifen.

There were 3 patients (8%) in the advanced breast cancer group who had a partial response maintained for a mean duration of 12 months. Two

Table III Pattern of late breast cancer at presentation (n = 37)

	Inoperable primary tumour (A)	Distant metastases (B)	(A) and (B)	Fixed nodes and (A)
Responders (complete or partial)	1	1	1	2
Non-responders	17	2	6	7

of the patients have subsequently died of their disease.

Thirty-two patients (87%) had no objective response to tamoxifen. Of these patients, 20 had died by the end of the study and 8 required surgery to control the chest wall disease.

Side effects

Three patients complained of nausea and/or vomiting. Other side effects were fluid retention, headache and flushing in three patients. Side effects appeared more common in the group taking tamoxifen 20 mg twice daily.

Discussion

Tamoxifen is well tolerated and because there are no serious side effects it is an attractive option in

Table II Response to tamoxifen of 37 patients with advanced breast cancer

	At 6 months	Mean duration of response	Subsequent course			
			Chemo-therapy	R/T	Surgery	Died
Complete response	2 (5%)	16.5 months	1	1	0	2
Partial response	3 (8%)	12.0 months	2	0	1	2
Static response	8 (22%)	9.3 months	2	3	3	4
Non responders	24 (65%)	---	12	13	5	16

selected patients with breast cancer. In a recently published randomized trial⁸ it was concluded that disease-free survival and local relapse rates were the same in a group of early breast cancer patients treated with tamoxifen 20 mg daily as in a comparable group treated by local excision. However, the relapse rate in the surgical arm of the trial was higher than would normally be expected.⁹

Our own experience with tamoxifen has been disappointing. We have shown that only 34% of early breast cancers respond at all. In advanced disease our finding of an overall response rate of only 13% is disappointingly low compared with previous studies. Also we found no pattern of disease at presentation of the late breast cancer patients that predicted a response.

There may be a place for higher doses of tamoxifen to show a response when 20 mg or 40 mg has failed. This has been suggested recently to produce stabilization if not regression of disease in some patients.¹⁰

Of course, survival and its quality are important in breast cancer and for many patients the continuing reminder of an unresponsive lump in the breast may diminish that quality.

Although the present study is not controlled it seems likely that the enthusiasm which first greeted tamoxifen may not now be justified. Perhaps we should see tamoxifen as an initial treatment that may have to be modified quite rapidly in many of the patients as it becomes clear that they are not going to respond.

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