

ER and PR Positive Locoregional Breast Cancer in Elderly Women: Comparison of Response of Letrozole Alone and Letrozole Plus Surgery

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ABSTRACT

Introduction: Hormone sensitive breast cancer in elderly women with locoregional disease, treatment with Letrozole (aromatase inhibitors) is often recommended. Many a times these patients are subjected to surgery also. Aim of this study was to compare the response of Letrozole alone versus Letrozole followed by surgery in these patients.

Material and Methods: Neoadjuvant hormone therapy treatment was given to 40 postmenopausal breast cancer patients in form of Letrozole, who were Estrogen receptor (ER) positive and progesterone receptor (PR) positive. After Letrozole therapy, eligible patients underwent surgery, and those who were not candidates for surgery continued on Letrozole therapy. We retrospectively analyzed disease free survival at three years, and response with impact of surgery on outcome.

Results: Out of 22 patients who underwent adjuvant surgery after neoadjuvant letrozole therapy only 8 (36.3%) could be offered lumpectomy and rest had mastectomy. 18 patients continued on letrozole therapy alone. At completion of three years the surgery group patient showed 72.7% DFS whereas letrozole only group had 55.5% DFS.

Conclusions: The present study, also, shows a high response rate and disease free survival in patients having adjuvant surgery to neoadjuvant letrozole therapy.

Keywords: Neoadjuvant Letrozole, Adjuvant Surgery, Postmenopausal Elderly ER/PR Positive Breast Cancer.

INTRODUCTION

Breast cancer even in developing countries has become the commonest cancer among women in terms of incidence as well as cancer related death. It is related to the hormonal status of the women and depends upon the level and duration to the hormonal exposure of their life. Therefore in this management of breast cancer, regulation of the hormonal level in the women's body is of key importance.

Although the percentage incidence of the breast cancer varies in urban and rural areas mostly depending upon the period of breast feeding, age at first child birth, number of pregnancies, duration of estrogen exposure of the women etc. Management of breast cancer is done by sequential treatment modalities involving chemotherapy, hormone therapy, surgery, radiation therapy and targeted therapy depending on the stage, menopausal status, hormonal stratus, age etc.

In elderly postmenopausal locoregional breast cancer patients, neoadjuvant chemotherapy or hormone therapy followed by surgery is the standard treatment strategy, as it provides good disease control and downstaging of the tumours, enabling

surgery to be performed in initially unresectable patients and breast-conserving surgery in patients who would otherwise require mastectomy.^{1,2,3} Although neoadjuvant chemotherapy is recommended in the majority of cases, in elderly patients treatment-related toxicities and the presence of comorbidities make hormone therapy the neoadjuvant treatment of choice. Almost two third of the breast cancer in these elderly women are ER/PR positive and are highly responsive to hormone therapy.

Tamoxifen is a preferred treatment for premenopausal breast cancer patients as in these patients estrogen is produced mostly by their ovaries which is dealt very effectively by the anti-estrogen tamoxifen, but for post menopausal elderly patients estrogen is mainly produced in peripheral tissues of the body and at the site of cancer i.e. the adipose tissues of the breast.

Among the Non-steroidal Aromatase Inhibitors Letrozole has been proved to be more effective as neoadjuvant and adjuvant hormonal therapy in treatment of locoregional ER/PR positive elderly breast cancer patients than the other Aromatase Inhibitors.^{4,5,6,7,8}

Aim of this study was to compare the response of neoadjuvant Letrozole alone versus Letrozole followed by surgery in elderly patients having ER/PR positive locoregional breast cancers. And at three years, responses to be analysed retrospectively with regards to disease free survival.

MATERIAL AND METHODS

To achieve our aim a retrospective analysis regarding the same was done on the patients attending our department (Radiotherapy Department), Patna Medical College and Hospital (PMCH), Patna, 800004, India, between the periods 2004 to 2012. A total of 40 postmenopausal elderly patients, treated for ER/PR positive locoregional breast cancer were analyzed. Informed consent was already taken from all the patients before commencement of their treatment.

Records of all the 40 patients were analysed for clinical history and examination, haematological, radiological, histopathological and hormonal status.

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	Letrozole only group Total – 18 (100%)patients	Letrozole + Surgery Group Total – 22 (100%)patients
Disease Free Survival	10 (55.5%)	16 (72.7%)
Local Recurrence only	3 (16.6%)	0 (00.0%)
Nodal Recurrence only	0 (00.0%)	4 (18.1%)
Distant Metastasis only	0 (00.0%)	1 (4.5%)
Local Recurrence + Nodal Recurrence	2 (11.1%)	0 (00.0%)
Nodal Recurrence +Distant Metastasis	0 (00.0%)	1 (4.5%)
Local Recurrence + Nodal Recurrence +Distant Metastasis	3 (16.6%)	0 (00.0%)

Table-1: Comparative outcomes in two groups after completion of three years

Clinically all patients were in fair to good general condition, 27 patients were between 60-69 years of age and remaining 13 patients were between 70-76 years. Only the patients having primary tumour upto T2 (upto 5cm) and nodal status of N1, metastatic mobile ipsilateral nodes and all having ER/PR positive status were included.

All the patients had the neoadjuvant hormonal therapy with letrozole 2.5 mg orally daily for 6 months. 22(55%) patients were subjected to surgery; remaining 18 (45%) patients were subjected to further letrozole therapy.

After surgery all the 22 patients were again put on letrozole therapy.

RESULTS

At the end of neoadjuvant letrozole therapy 2 patients had complete response, primary tumor size as well as the size of the involved node was reduced more than half i.e partial response in 21 patients (52.5%). 10 (25%) patients had intermediate response to the hormone therapy as their disease size were similar to the initial T and N size of their disease i.e. stable disease.

7 (17.5%) patients though each having positive ER/PR hormonal status showed progression of local disease only, without any detectable metastatic disease.

Out of the 22(100%) patients who were subjected to surgery, lumpectomy could be done in 8 patients (36.3%) only and the remaining 14(63.6%) patients had mastectomy.

At three years 16 (72.7%) patients of the surgery group were disease free, 4 patients had nodal recurrence and 2 patients had distant metastasis of which one had both. (Table – 1)

Only 10 (55.5%) patients of letrozole only group were disease free after three years. Of the remaining 8 patients, 3 had only local recurrence, 2 patients had local recurrence with nodal involvement only and 3 had local recurrence at the primary site with nodal involvement and distant metastasis. (Table – 1)

DISCUSSION

For the treatment of ER/PR positive post menopausal elderly breast cancer patients, in this study the selection of letrozole hormonal therapy was based on results from various studies. This fact is also supported by a randomized double-blind multicenter study by Eiermann W et al⁴ who reported 55% disease free survival with letrozole alone treatment as compared to 36% disease free survival in Tamoxifen alone treated patients. At the end of three years in our study letrozole

therapy alone gave a disease free survival of 55.5%, which is comparable to the earlier study by Eiermann W et al.

A very good and elaborate study by Olivier Nguyen et al.¹⁰ Published in 2012 in which they concluded that hormonal therapy in ER/PR positive post menopausal elderly breast cancer patients should follow surgical treatment/resection even if the patient was inoperable at the time of diagnosis, this was because they found an enhanced survival and better response in those patients who underwent surgery after initial hormonal therapy than the patients who received the hormonal therapy alone. In our study also we got a clear difference of response and survival in favour of initial hormonal therapy followed by surgery. Letrozole therapy alone gave a disease free survival of 55.5% (10 out of 18 patients) whereas in patients receiving surgical treatment after initial letrozole therapy disease free survival was in 16 out of 22 patients i.e. 72.7%.

Now evidences are emerging that surgery after initial hormonal therapy in ER/PR positive post menopausal elderly breast cancer patients enhances the percentage of disease free survival of these cancer patients in comparison to the patients receiving hormonal therapy alone. The same conclusion and observation has been obtained and documented by an extensive multicentric study conducted by L. Cataliotti et. Al.,¹¹ similar results has been observed in our present study. Ellis MJ et al.⁵ has reported marked improvement in adjuvant surgery group patients, in our study also a disease free survival at three years was 72.7%, this shows that after hormonal therapy surgery improves the outcome of postmenopausal ER/PR positive elderly patients as the neoadjuvant letrozole therapy improves the operability, mainly breast conserving surgery, which is evident in our study also.

Olson JA Junior et al.⁹ reported a higher survival of 62% of the adjuvant surgery group patients after the neoadjuvant hormonal therapy, in our study the adjuvant surgery group had achieved a disease free survival of 72.7%. He also pointed out that the neoadjuvant hormonal therapy reduces the tumour burden; as a result the patients become a better candidate for surgery.

CONCLUSIONS

The present study, also, shows that in case of ER and PR positive breast cancer in elderly women with locoregional disease, letrozole only therapy does not provide very good response in terms of survival and longer duration to recurrence. When letrozole plus surgery therapy is given

the results are more promising and satisfactory in terms of providing disease free survival and prolonged duration to recurrence. Hence it is recommended that after letrozole therapy surgery should be done in these patients to get better response.

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