RESEARCH ARTICLE

A STUDY OF TWO DIFFERENT DOSE FRACTIONATION SCHEDULES OF POST MASTECTOMY CHEST WALL IRRADIATION IN CARCINOMA BREAST PATIENTS

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ABSTRACT

Background: Breast cancer is the most frequently diagnosed cancer and the leading cause of cancer death in women.
Aims & Objective: To compare two different dose fractionation schedules in terms of overall treatment, locoregional control, acute and late toxicities and patient compliance.
Material and Methods: Patients of postmastectomy non metastatic breast cancer were randomized in two arms: Arm A (45) Arm B (46) according to dose fractionation schedule of external radiation given to chest wall and draining lymphatics. Arm A was given 50 Gy in 25 fractions and Arm B was given 40 Gy in 17 fractions. After completion of radiation patients were kept on follow up.
Results: Median follow up was 20 months. In arm A & B the median overall treatment time was 40 and 27 days with respective ranges of 36-47 days and 22-33 days .The patients in both the arms tolerated radiation well, skin reactions were most common followed by nausea and vomiting .Grade II and III acute reactions were comparable in both arms. There was non-significant increase in both late skin and subcutaneous skin toxicities in arm B. Result of treatment of both arms are, chest wall failure 5% v/s 9% ($p > 0.05$), nodal failure 8% v/s 7% ($p > 0.05$) and distant metastasis 25% v/s 28% ($p > 0.05$).
Conclusion: Both the studied dose fractionation schedules are equally efficacious in terms of locoregional control, acute and late toxicities. The shorter schedules in Arm B gives an added advantage of decreased overall treatment time giving better compliance and reduces work load of overburdened department.
Key-Words: Breast Cancer; Radiation; Dose Fractionation Schedules

Introduction

Breast cancer is the most frequently diagnosed cancer and the leading cause of cancer death in women, accounting worldwide for 23% of total new cancer cases and 14% of total cancer deaths in 2008.[1] It is the second most common leading site among women in India and incidence varies from 7 to 28 per 1 lakh women in various parts of India and treated with multimodal approach like surgery, radiotherapy, chemotherapy, hormonal therapy and immunotherapy.[2,3] Surgery is the treatment of choice which should be followed by postoperative radiotherapy and adjuvant systemic treatment.[3] There is no general agreement in literature regarding dose of radiation therapy which should be delivered to a patient after mastectomy.[4-6] The doses, ranging from 32.5 Gy/3 weeks to 60 Gy/10 to 14 weeks have been given.[4-8] Adjuvant radiotherapy has shown to improve local control and overall survival, with a 70% proportional reduction of the risk of recurrence[9] and a 9%–12% proportional reduction of the risk of death[10-13]. Despite this established role of radiotherapy, there are considerable disparities in the receipt of radiotherapy that are attributable to various factors such as limited availability of treatment centers, geographical distance, long waiting times, and costs.[14-16] Since developing countries are dependent on cobalt 60 teletherapy units for radiotherapy and though our centre has linear accelerator but more no of patients coming from rural background cannot afford treatment cost . The disparities can further be compounded by the long schedules required with conventional radiotherapy, since the schedules that were evaluated in clinical trials and were found to be associated with improved survival are based on conventional fractionation of 1.8-2.5 Gy/fraction, delivering treatment over 5 to 7 weeks.[10,13,17,18] Many researches are actively investigating

alternative approaches. Intraoperative radiotherapy (IORT) or accelerated partial breast irradiation (APBI) provide the shortest schedules.[19-21] However, IORT and APBI are limited to selected cases.[22] Whole breast radiotherapy with a hypofractionated schedule delivering 42.5 Gy in 16 fractions over 22 days has been shown by the Ontario randomized trial to be comparable with a conventional schedule of 50 Gy in 25 fractions over 35 days.[23] Therefore, we have conducted a study comparing two radiation dose schedules in post mastectomy carcinoma of the breast.

Materials and Methods

The study has been conducted on 91 histopathologically proved breast cancer patients in a tertiary care center for radiotherapy after modified radical mastectomy. Patients of postmastectomy non metastatic breast cancer were randomized in two arms: arm A (45) Arm B (46) according to dose fractionation schedule of external radiation given to chest wall and draining lymphatics. Arm A was given 50 Gy in 25fractions in 5 weeks and Arm B was given 40Gy in 17 fractions in 3.2 weeks. The postoperative radiation therapy was given to chest flap and drainage areas in all patients. Radiation therapy was given on a Co 60 teletherapy machine using tangent pair technique for chest wall irradiation. After completion of radiation patients were kept on regular follow up. The patients included in the study were; all patients surgically treated with modified radical mastectomy, radiotherapy and chemotherapy naive patients, having karnofsky performance status (KPS) >70. Patients with distant metastasis, inoperable cases, peaud orange, fixed inoperable nodes, any surgery other than modified radical mastectomy and Karnofsky performance status (KPS) <70 were excluded. All relevant investigations were done. Adjuvant chemotherapy schedule was similar in both the groups. All node positive patients were given CAF regimen (24). All post-menopausal patients received hormonal treatment in form of Tamoxifen 10 mg BD. Radiation reactions were carefully noted during treatment. The patients were advised regular follow up. At every follow up, patients were assessed for radiation reactions and status of disease. The radiation reactions and response were graded as per WHO criteria.[25]

Results

Median follow up was 20 months. In arm A &B the median overall treatment time was 40 and 27 days with respective ranges of 36-47 days and 22-33 days. The median age at presentation was 46 years (range 31-70 years). 56% patients in Group A and 60 in Group B were postmenopausal. All the patients in both groups presented with painless lump in breast and axillary mass present in 44% of patients in Group A and 50% of patients in Group B. Infiltrating duct carcinoma was the most common histopathology in both groups (84% in Group A and 87% in Group B). The other less common histopathological types were; colloid carcinoma, medullary carcinoma, lobular carcinoma etc. The most common stage at presentation was stage III (58% in Group A and 57.4% in Group B).

Table-1: Carcinoma of the Breast: Stages at Presentation

Stage	Group A N (%)	Group B N (%)
Stage I	2 (4%)	3 (5.5%)
Stage II	17 (38%)	17 (37%)
Stage III	26 (58%)	26 (57.4%)
Total no. of patients	45 (100)	46 (100)

Table-2: Post Mastectomy Radiation Therapy: Radiation Reactions

Radiation Effects		Group A N (%)	Group B N (%)
Skin Reaction	Grade 0	9 (20)	5 (10)
	Grade I	14 (30)	9 (20)
	Grade II	20 (45)	23 (50)
	Grade III	2 (5)	9 (20)
	Grade IV	0	0
Difficulty in swallowing		33 (74)	40 (76)
Nausea/vomiting		6 (13)	7 (12)
Infection		3 (7)	2 (5)
Lymphedema ARM		1 (2)	3 (7)
Lt. shoulder restriction		1 (2)	1 (2)
Brachial plexus involvement		0	0

Table-3: Post Mastectomy Radiation Therapy: Status at Last Follow Up

Status at Last Follow Up	Group A N (%)	Group B N (%)
No evidence of disease	28 (62)	26 (56)
Chest wall failure	2 (5)	4 (9)
Axillary lymph node failure	4 (8)	3 (7)
Distant metastasis	11 (25)	13 (28)
Total no. of patients	45 (100)	46 (100)

The results of treatment of 91 patients (45 of Group A and 46 of group B) were: The patients in both the groups tolerated radiation well. Skin

reactions were most common radiation reactions followed by difficulty in swallowing and nausea/vomiting.

Results of treatment in Group A versus Group B were as follows; chest wall failure 5% v/s 9 % (p> 0.05), axillar lymph node failure 8% v/s7% (p> 0.05), distant metastasis 25% v/s 28% (p> 0.05). Most of the patients in both the groups had no evidence of disease at last follow-up i.e. 28/45 (62%) in Group A and 26/46 (56%) in Group B. There was no statistically significant difference in local control and efficacy of these two radiation schedules in post mastectomy carcinoma of the breast.

Discussion

Surgery and radiotherapy are important for locoregional control in carcinoma breast.[3,26] Surgical treatment is mandatory for cure of breast carcinoma.[27] Three types of surgery practised are; conservative surgery (lumpectomy, quadrantectomy, tylectomy, partial mastectomy or segmental mastectomy etc.), moderate surgery (modified radical matsectomy, simple mastectomy with axillary clearance etc.) and radical surgery (Halsted mastectomy, Extended radical mastectomy and supraradical mastectomy etc.).[27] Modified radical mastectomy is the most common form of mastectomy performed now a days.[3] This was the operation done in all our patients included in the present study. Modified radical mastectomy includes removal of breast with axillary nodal dissection but with preservation of pectoralis major muscle.[27] Radiation after surgery decreases loco-regional recurrence.[28] There are several reasons or end points that might justify the use of postmastectomy radiotherapy (PMRT) for patients with invasive breast cancer. These include a reduction in the risk of local-regional failure (LRF), with its potential physical and psychological morbidity, as well as a reduction in the risks of distant relapse and death. In the cancer research campaign trial of 2248 evaluable patients with clinical stage I and breast cancers, the patients were randomly assigned to treatment with simple mastectomy alone or simple mastectomy combined with irradiation.[3] A threefold greater incidence of local recurrence was noted in control group (30% with simple mastectomy alone and 10% with simple mastectomy and irradiation.

After modified radical mastectomy external radiotherapy is delivered to chest flap and drainage areas which include ipsilateral supraclavicular fossa, axilla and internal mammary nodes.[3] External radiotherapy is delivered by tangent pair technique which spares lungs. This has been followed in our institute. There is no general agreement in literature regarding dose of radiation therapy which should be delivered to a patient after mastectomy.[4-6] The doses, ranging from 32.5 Gy/3 weeks to 60 Gy/10 to 14 weeks have been given.[4-8] Post mastectomy breast irradiation in our study showed that there is no significant difference between 50 Gy in 25 fractions and 40 Gy in 17 fractions, so 40 Gy in 17 fraction regimen are more convenient for the patients by limiting the number of treatment attendances. Moreover, the reduced resource use in terms of personnel and machine time is advantageous for radiotherapy departments and translates into lower treatment costs. In order to formally validate this therapeutic approach from a societal perspective, however, cost-effectiveness evaluations weighing long-term outcome against the societal costs incurred until many years after treatment are needed.[29,30] Treatment of women with breast cancer, confirm the safety and efficacy of schedules using fraction sizes of >2 Gy, provided the correct downward adjustments to total dose are made.[31] Hypofractionated radiation therapy offers the advantage of a more efficient and productive use of radiotherapy departments resources; whether machine time, staffing of treatment units, lower expenses in addition to far better patients convenience.[32] As our hospital is largest hospital in our state and patients from all our state as well as from nearby states come to our department and breast cancer is common cancer among females and most females presenting in our department are cases of breast carcinoma ,and due to longer treatment time in conventional fractionation many patients cannot get radiotherapy timely due to overburdened department, so this hypofractionated regimen is very advantageous for overburdened departments like our department. On the other hand,

hypofractionation, with larger radiation dose per fraction increases the possibility of late normal tissue damage.[33,34] However, the linear-quadratic model predicts that the normal tissue toxicity is not increased when the fraction dose is modestly increased and the total dose is reduced.[31] This is confirmed by results of many trials where hypofractionated radiotherapy protocols are as effective as the conventional radiation of 50 Gy in 25 fractions, regardless of disease stage or type of breast surgery.[35-37]

Our results of chest wall recurrence, axillary failure and distant metastasis as 5/50 (10%), 3/50 (6%) and ;16/50 (32%) in group A versus 3/54 (5.6%), 4/54 (7%) and 15/54 (28%) in Group B. Main side effects noted were reversible cutaneous reactions, difficulty in swallowing and nausea/ vomiting.

Conclusion

Our study justifies the routine use of HF for adjuvant radiotherapy in women with breast cancer. Hypofractionated radiation therapy resulted in OAS rate comparable to that of conventional fractionation (50 Gy/ 25 fractions/ 5 weeks) without evidence of inferior local tumour control or higher adverse effects. This therapy can be recommended as safe and effective alternatives to Conventional fractionation for postmastectomy chest wall radiotherapy: Both the studied dose fractionation schedules of 50 Gy /25 fractions/ 5 weeks, and 40 Gy/17 fractions /3.2 weeks are equally efficacious in terms of locoregional control, acute and late toxicities. The shorter schedules in Arm B gives an added advantage of decreased overall treatment time, which in turn can result in better patient compliance and decrease the work load of overburdened department.

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