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**Original Article**

**Concurrent Paclitaxel and Radiotherapy for Node Positive Breast Cancer**

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**Abstract**

**Background:** Concurrent chemo–radiotherapy in breast cancer (BC) may yield better local control with minimal toxicity in node positive patients. The feasibility of paclitaxel with radiotherapy was assessed for tolerability, cosmetic outcome as well as local control.

**Methods:** A prospective feasibility study on forty–three female breast cancer with stage II–III was conducted after definite surgery (modified radical mastectomy and breast conservative surgery). Adjuvant chemotherapy given was 4 cycles AC (Doxorubicin 60mg/m²+ cyclophosphamide 600mg/m²) followed by 4 cycles of Paclitaxel 60mg/ m² weekly for 12 weeks concurrent with 3D Conformal radiotherapy in a dose of 45Gy/20ttt/4wks to the whole breast and supraclavicular nodal region. Boost of 10Gy/5ttt was given to the tumor bed in conservative cases. Evaluation of lung function was done by carbon monoxide diffusion. Radiotherapy toxicity and breast cosmesis were assessed by the RTOG and Harvard criteria respectively. The cosmesis was assessed and scored at the beginning and end of RT and every 6 months thereafter. This was done by patient (subjective score) and physician (objective score) by comparing it with the contralateral untreated breast.

**Results:** After a median follow up of 36 months, the overall survival and disease–free survival were 95% and 92.5% respectively with no local relapse or radiation pneumonitis. There was no significant change in carbon monoxide diffusion after radiotherapy (p: 0.55). There was 15% delay in radiotherapy mainly due to acute GIII skin toxicity (10%), followed equally by mucositis and wound gap (2.5%). The volume of the irradiated breast was correlated with acute cosmetic effect (p = 0.057) but not on the late skin toxicity (p = 0.56). At the last follow up, the majority of patients declared excellent score in 62.5%, good in 20%, fair in 10% and poor in 7.5%. Subjective patient’s satisfaction for the shape, color and size of the treated breast was 93%.

**Conclusion:** Concurrent chemo–radiotherapy with weekly paclitaxel minimized the treatment duration with acceptable tolerance, cosmesis and good local control.

**Keywords:** Paclitaxel, chemo–radiotherapy, breast cancer, node positive

**Introduction**

Taxanes has been incorporated in the adjuvant setting of chemotherapy in early breast cancer with improve survival. This is usually following an anthracycline regimen [¹]. Local radiotherapy improved the local control on both node positive and high–risk node negative breast cancer patients undergoing breast conservative breast surgery. However, this did not affect the overall survival.

Concurrent chemo–radiotherapy in breast cancer started early by the CMF regimen. There was reasonable local toxicity and 4% local recurrence after 94m of follow up. [²]

This was followed by two multicenter trials comparing concurrent with sequential treatment. The first is the Acrosein trial using 6 cycles CNF (cyclophosphamide, novantrone, fluorouracil with radiotherapy. The second is a French trial using epirubicin instead of novantrone. They both showed increase in the local control with no effect on DFS or OS. [³,⁴,⁵,⁶]

Thereafter Paclitaxel was introduced in the concurrent regimen either weekly or every three weeks with increased toxicity. [⁷]

Combining Paclitaxel with radiotherapy was studied by Brustein et al (2006) on 40 patients. It compared the weekly paclitaxel in a dose of 60mg/m² versus the...
175mg/m² every 21 days (16 vs 24 patients). The three weekly regimens were more tolerable with less incidence of pneumonitis (8% vs 25%) [7]. Another study by Chen et al (2012) using the three weekly regimens showed no cases of pneumonitis and grade III skin toxicity in 4.7% of cases. [8]

The benefit of combining taxanes with radiotherapy comes from having a sensitizing effect. It acts as a mitotic inhibitor arresting the cells in G2/M phase which is radiosensitive. This may be a new pattern in locally advanced breast cancer as it is associated with higher response rates. [9].

In developing countries there is increase in the number of breast cancer patients with high burden on the radiotherapy machines leading to delay in starting radiation with possible poor monitoring of patients due to overcrowdings. Concurrent chemoradiotherapy shortens the treatment time, schedule radiotherapy early preventing delay, allows good monitoring of the patient. Most of all it increases the local control.

This is a prospective phase II feasibility study conducted at Kasr Al-Ainy Center of Clinical Oncology and Nuclear Medicine (NEMROCK) aimed to assess the feasibility and tolerance to concurrent chemo-radiotherapy with special emphasis on the Cosmetic outcomes of the patients.

**Patients and Methods**

Forty–three female patients with node positive breast cancer underwent breast conservative surgery or modified radical mastectomy and were planned for adjuvant chemotherapy and postoperative radiotherapy were recruited in this study at Kasr Al Ainy Center of Clinical Oncology and Nuclear Medicine (NEMROCK) during the period from July 2014 to August 2016.

Female breast cancer patients were eligibility if they were ≥ 18 years with histo–pathologically confirmed adenocarcinoma requiring loco–regional irradiation. This included stage II – III, pathologic T1– T4, N1– N3. Both mastectomy and conservative breast surgery were included. Participants with intact breast cancer should have negative margins without extensive intra–ductal component. All patients should have ECOG performance 0–2 and should be aware of the neoplastic nature of her disease. Informed consent was given by all patients.

Patients were excluded from the study if they were metastatic, previously irradiated, having history of other malignancy or collagen disease or not having adequate hematological reserve. Also, pregnant or nursing patient or those unable to lie on their backs and raise their arms above their heads in the treatment planning position for radiotherapy were omitted. Females with a clinically unstable or life–threatening medical condition such as congestive heart failure, acute or chronic renal failure, severe chronic obstructive pulmonary disease, or patients with stroke were not included. Other contraindications to chest wall irradiation included severe collagen vascular disease and previous chest wall irradiation.

All patients were subjected to full History and physical examination. Baseline complete blood count, kidney and liver function as well as electrolytes were done. Also, baseline cardiac assessment (ECG, Echocardiography), pulmonary function test was done before the timing of radiotherapy and after 4 cycles AC then repeated 6 months after finishing of radiotherapy.

**Chemotherapy protocol**

The Chemotherapy regimen consists of 4 cycles of doxorubicin (60mg/m²), cyclophosphamide (600mg/m²) then followed by 4 cycles of paclitaxel (60mg/m²) delivered every week for 12weeks.

After the third cycle of chemotherapy all patients screened to be included in the study and prepared to start radiotherapy with the first week’s paclitaxel chemotherapy.

**Radiotherapy**

All patients received 3D conformal RT to the whole breast or chest wall consisting of a dose of 45 Gy in 20 fractions over 4 weeks to chest wall & supraclavicular nodal region. A boost of 10Gy/5 fractions was added to the tumor bed in breast conservative surgery.

Patients were planned by a CT simulator and immobilized in the supine position on a chest board. The ipsilateral hand was raised above the head grasping the middle column of the board. The supraclavicular lymph node was given at a depth of 3 cm. the boost was defined by CT imaging and the inserted surgical clips.

LASER lines and tattoo was used to define a reference point for reproducibility. CT cuts were taken every 5 mm from the chin to upper abdomen. All cuts were transferred to the treatment planning system.

The breast was treated isocentrically using 2 tangential beams with selective multi–leaf blocking to protect risk structures (heart and lungs). Digitally reconstructed radiographs (DRRs) were generated for all treatment Portals and for 2 simulation portals for easy anatomical judgment using gantry angles of 0 and 90 degrees. All plans used 6 MV photons and the 100% isodose surface was prescribed to receive a total dose of 45Gy in 20 equal daily fractions for 4 weeks (2.25Gy/day). The acute and
late toxicities of chemo—radiation was recorded and assessed according to RTOG criteria during the treatment course and reevaluated after finishing of radiotherapy by one and 6 months. \[10\]

All Plans had to be approved by both physician and physicist. This was based on the homogeneity of dose distribution inside the target volume(s) where the PTV received a dose between 95% and 107% of the prescribed dose. Also, the volume of the lung that received at least 20Gy (V 20 Gy) was not allowed to exceed 31%. In addition, the volume of the heart receiving at least 40Gy (V40 Gy) did not exceed 30%.

Plan verification with Electronic portal images (EPI) was used to verify setup reproducibility and was done at least once weekly. Differences of 0—4.9 mm were acceptable. Patients had weekly follow up during radiotherapy treatment in order to provide patient reassurance, determine tolerance and toxicity of the treatment, and manage complications.

Time and causes of radiation treatment interruption was recorded.

Acute toxicity on the heart function, lung function, neurological sensory and skin changes was evaluated using the RTOG toxicity grading ranging from grade 0 to 4. \[10\]

Late lung and cardiac toxicity were assessed clinically, and by chest x—ray. Also, pulmonary function and echocardiography were repeated at the end of the study.

Evaluation of local recurrence and cosmesis were done. Local recurrence was calculated from the date of surgery until the date of loco—regional recurrence or the date of death. It was assessed by clinical examination and mammo—sonography.

Breast cosmesis was assessed and scored before and after radiotherapy and every six months thereafter. This was evaluated by two scores. The first was objective done by the oncologist using the contralateral, untreated breast as the reference and scoring the patient according to Harvard criteria \[11\]. This included excellent, good, fair and poor. The second score was subjective by the patient; if satisfied or not by the shape, color and size of the treated breast.

Monitoring chemotherapy toxicity included haematological and non—hematological toxicity. Hematological toxicity included anemia, neutropenia and thrombocytopenia. Non—hematological included hypersensitivity reaction, acute skin toxicity, dysphagia, nausea and vomiting, late skin toxicity, late subcutaneous toxicity, cardiac toxicity and pulmonary toxicity.

### Statistical Analysis

Data were statistically described in terms of range, mean, standard deviation, frequencies (number of cases) and relative frequencies (percentages) when appropriate. Comparison of quantitative variables between the study groups was done using T—Test for paired samples. A probability value (p value) less than 0.05 was considered statistically significant. All statistical calculations were done using computer package SPSS version 16 (Statistical Package for the Social Science; SPSS Inc., Chicago, IL, USA) statistical program for Microsoft Windows.

### Results

This is a prospective Phase II feasibility study conducted at Kasr Al—Ainy Center of Clinical Oncology and Nuclear Medicine (NEMROCK) during the period from August 2014 to August 2016.

The study included forty patients who underwent breast surgery followed by adjuvant adriamycin, cyclophosphamide then subjected to concomitant weekly paclitaxel with radiotherapy using 3D conformal technique to the chest wall or whole breast, tumor bed and peripheral lymphatics. Forty—three patients fulfilled the inclusion criteria. However, three patients were excluded from the study. The first case manifested severe hypersensitivity of paclitaxel. The second case showed poor pulmonary function after the three cycles of anthracycline before starting chemo—radiotherapy. While the third patient withdrawn her consent and refused to continue the treatment protocol. Forty patients continued the study and were included in the analysis after a median follow up of 36 months (ranging from 15 to 44 months).

The clinico—pathological data of the patients is shown in Table 1. The mean age of the patients was 50 years (31—70). The majority were postmenopausal (57.5% vs 42.5%). They were all invasive duct carcinoma grade II (100%). The tumor site was mostly UOQ (72.5%), T2 (70%) with N1 & N2 (75%). Concerning the molecular subtypes, luminal A (37.5, 15/40) was the most common followed by luminal B (32.5%), HER 2/neu (22.5%) and lastly Basal like (7.5%). Regarding their immuno—histo—chemical profile, ER status represented 80% (32/40), PR 72.5% (29/40), and overexpressed Her-2/neu (22.5%) and lastly Basal like (7.5%). Regarding their immuno—histo—chemical profile, ER status represented 80% (32/40), PR 72.5% (29/40), and overexpressed Her-2/neu (22.5%) and lastly Basal like (7.5%). Regarding their immuno—histo—chemical profile, ER status represented 80% (32/40), PR 72.5% (29/40), and overexpressed Her-2/neu (22.5%) and lastly Basal like (7.5%). Regarding their immuno—histo—chemical profile, ER status represented 80% (32/40), PR 72.5% (29/40), and overexpressed Her-2/neu (22.5%) and lastly Basal like (7.5%). Regarding their immuno—histo—chemical profile, ER status represented 80% (32/40), PR 72.5% (29/40), and overexpressed Her-2/neu (22.5%) and lastly Basal like (7.5%). Regarding their immuno—histo—chemical profile, ER status represented 80% (32/40), PR 72.5% (29/40), and overexpressed Her-2/neu (22.5%) and lastly Basal like (7.5%). Regarding their immuno—histo—chemical profile, ER status represented 80% (32/40), PR 72.5% (29/40), and overexpressed Her-2/neu (22.5%) and lastly Basal like (7.5%). Regarding their immuno—histo—chemical profile, ER status represented 80% (32/40), PR 72.5% (29/40), and overexpressed Her-2/neu (22.5%) and lastly Basal like (7.5%). Regarding their immuno—histo—chemical profile, ER status represented 80% (32/40), PR 72.5% (29/40), and overexpressed Her-2/neu (22.5%) and lastly Basal like (7.5%). Regarding their immuno—histo—chemical profile, ER status represented 80% (32/40), PR 72.5% (29/40), and overexpressed Her-2/neu (22.5%) and lastly Basal like (7.5%). Regarding their immuno—histo—chemical profile, ER status represented 80% (32/40), PR 72.5% (29/40), and overexpressed Her-2/neu (22.5%) and lastly Basal like (7.5%). Regarding their immuno—histo—chemical profile, ER status represented 80% (32/40), PR 72.5% (29/40), and overexpressed Her-2/neu (22.5%) and lastly Basal like (7.5%). Regarding their immuno—histo—chemical profile, ER status represented 80% (32/40), PR 72.5% (29/40), and overexpressed Her-2/neu (22.5%) and lastly Basal like (7.5%). Regarding their immuno—histo—chemical profile, ER status represented 80% (32/40), PR 72.5% (29/40), and overexpressed Her-2/neu (22.5%) and lastly Basal like (7.5%). Regarding their immuno—histo—chemical profile, ER status represented 80% (32/40), PR 72.5% (29/40), and overexpressed Her-2/neu (22.5%) and lastly Basal like (7.5%). Regarding their immuno—histo—chemical profile, ER status represented 80% (32/40), PR 72.5% (29/40), and overexpressed Her-2/neu (22.5%) and lastly Basal like (7.5%). Regarding their immuno—histo—chemical profile, ER status represented 80% (32/40), PR 72.5% (29/40), and overexpressed Her-2/neu (22.5%) and lastly Basal like (7.5%).
**Dosimetric data**

The clinical target volume (CTV) coverage in gray showed a D95% of 43.3 +/- 1.7, Dmax of 48.2 +/- 1.1 and the Dmin of 42.2 +/- 1.5. The Supra–clavicular lymph nodes Planning target volume (SCLN–PTV) coverage in gray showed a D95% of 45.2 +/-1.5, Dmax of 49.7 +/- 1.7 and the Dmin of 41.1 +/- 1.7.

The doses received by organs at risk were evaluated. This included the heart, lung, contralateral breast, and skin dose. The dose to the heart was 1.4 +/-2.2, 1.34 +/-0.61 and 3.01 +/- 1.91 for the V40 Gy, D50% and Mean heart dose respectively. As for the ipsilateral lung the V20 Gy was 16.4 +/- 4.5. The mean volume receiving 5Gy (V5 Gy) was 0.79 +/- 0.42. The mean skin dose was 35.2 +/- 4.6. The treatment plan for the patients is shown in Figures 1 and 2.

**Table 1: Clinico–pathological features for the patients**

<table>
<thead>
<tr>
<th>Item/Patients</th>
<th>(No = 40)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age (years) Mean ± SD</strong></td>
<td>50±11.17</td>
</tr>
<tr>
<td><strong>Range</strong></td>
<td>(31–70)</td>
</tr>
<tr>
<td><strong>WHO Performance status</strong></td>
<td>ER</td>
</tr>
<tr>
<td>0</td>
<td>27 (67.5%)</td>
</tr>
<tr>
<td>1</td>
<td>13 (32.5%)</td>
</tr>
<tr>
<td>2</td>
<td>0 (0%)</td>
</tr>
<tr>
<td><strong>Menopausal status</strong></td>
<td>Positive</td>
</tr>
<tr>
<td>Premenopausal</td>
<td>17 (42.5%)</td>
</tr>
<tr>
<td>Postmenopausal</td>
<td>23 (57.5%)</td>
</tr>
<tr>
<td><strong>Surgery</strong></td>
<td>Positive</td>
</tr>
<tr>
<td>2</td>
<td>16 (40%)</td>
</tr>
<tr>
<td>3</td>
<td>24 (60%)</td>
</tr>
<tr>
<td><strong>Pathology</strong></td>
<td>Positive</td>
</tr>
<tr>
<td>IDC</td>
<td>40 (100%)</td>
</tr>
<tr>
<td>Site– Quadrant</td>
<td>Ki67</td>
</tr>
<tr>
<td>UOQ</td>
<td>29 (72.5%)</td>
</tr>
<tr>
<td>Retro areolar</td>
<td>6 (15%)</td>
</tr>
<tr>
<td>LOQ</td>
<td>2 (5%)</td>
</tr>
<tr>
<td>UIQs</td>
<td>3 (7.5%)</td>
</tr>
<tr>
<td>Grade</td>
<td>High</td>
</tr>
<tr>
<td>II</td>
<td>40 (100%)</td>
</tr>
<tr>
<td><strong>Intraductal Component</strong></td>
<td>DM</td>
</tr>
<tr>
<td>no.</td>
<td>37 (92.5%)</td>
</tr>
<tr>
<td>&lt; 25 %</td>
<td>2 (5%)</td>
</tr>
<tr>
<td>&gt; 25 %</td>
<td>1 (2.5%)</td>
</tr>
<tr>
<td>T</td>
<td>Family History</td>
</tr>
<tr>
<td>1</td>
<td>6 (15%)</td>
</tr>
<tr>
<td>2</td>
<td>26 (70%)</td>
</tr>
<tr>
<td>3</td>
<td>5 (12.5%)</td>
</tr>
<tr>
<td>4</td>
<td>1 (2.5%)</td>
</tr>
<tr>
<td><strong>Nodes</strong></td>
<td>Range</td>
</tr>
<tr>
<td>N1</td>
<td>15 (37.5%)</td>
</tr>
<tr>
<td>N2</td>
<td>15 (37.5%)</td>
</tr>
<tr>
<td>N3</td>
<td>10 (25%)</td>
</tr>
</tbody>
</table>

**SD** Standard Deviation

**T** Tumor

**N1** = 1–3 positive nodes

**N2** = >9 positive nodes

**PR** Progesterone Receptor

**MMRM** Modified Radical Mastectomy

**UOQ** Upper Outer Quadrant

**UIQ** Upper Inner Quadrant

**WHO** World Health Organization

**HTN** Hypertension

**IDC** Invasive Duct Carcinoma

**N** Nodal status

**ER** Estrogen Receptor

**HER2** Her2 receptor

**BCS** Breast Conservative Surgery

**LOQ** Lower Outer Quadrant

**LIQ** Lower Inner Quadrant

**DM** Diabetes mellitus

**Figure 1:** 3D planning: showing axial, coronal and sagittal sections as well as a 3D reconstructed image of a 3D plan. Shows the dose distribution in CW PTV and DVH for the 3D–CRT plan which display the doses to the targets and the organs at risk.

**Figure 2:** 3D planning: showing axial, coronal and sagittal sections as well as a 3D reconstructed image of a 3D plan. Shows the dose distribution in CBS PTV and DVH for the 3D–CRT plan which display the doses to the targets and the organs at risk.
After a median follow-up of 36 months, there was no recurrent local disease detected. The overall survival (OS) was 95% and the disease-free survival (DFS) was 92.5%. (Fig. 3 and 4). Three patients died. Two patients died without disease (5%). One patient died by car accident and the other declared sudden death. Another three patients developed disease metastasis. Two patients developed distal metastasis and the third had contralateral breast cancer.

Clinical Results and Treatment Compliance

Radiotherapy treatment interruption occurred in 15% (6/40) of patients due to dysphagia and skin toxicity grade 3. There was hypersensitivity reaction to paclitaxel in 7.5% (3/40). There were all grade I–II except one patient who had grade III requiring discontinuation of treatment. The others were re-challenged successfully with slower rates of infusion.

Toxicity and Cosmetic Outcome

Both acute locoregional and acute systemic toxicities were moderate during concomitant chemo–radiotherapy.

Cosmetic Outcome

Most of the patients (62.5%) declared excellent score at the last follow up. This was followed by good (18.75%), fair (12.5%) and poor (6.25%) according to the Harvard score. (Fig 5). Subjective assessment done by the patients themselves revealed satisfaction by most of the patients (87.5%, 14/40). Only two patients were not satisfied (12.5%).

Compliance to treatment

Hematological toxicity

Grade III toxicity developed in a minority of the patients. This was anemia (2/40, 5%) followed equally by neutropenia (1/40, 2.5%) with no fever and thrombocytopenia (1/40, 2.5%). There was no grade 4 hematological toxicity. All patients had recovered spontaneously. There was no treatment related infection (Table 2).
Non-hematological toxicity

Severe hypersensitivity reactions developed in three patients (7.5%) in the form of palpitation, chest tightness with one patient stopping chemotherapy after the second dose. Two patients continued treatment after decreasing the rate of infusion and the third one stopped chemotherapy.

Grade III toxicity was encountered in few cases in the form of acute skin toxicity (10%) and dysphagia (2.5%), late skin toxicity 16 (40%), late subcutaneous tissue toxicity 8 (20%) (Table 2). Treatment delay and interruption occurred in 15% (6/40) of patients. This was due to wet desquamation (10%, 4/40), wound gaping (2.5%, 1/40) and dysphagia (2.5%, 1/40). The mean days of treatment interruption was 4 (range: 3–5).

<table>
<thead>
<tr>
<th>Toxicity</th>
<th>Number of patients (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Grade I/II</td>
</tr>
<tr>
<td>Acute skin toxicity</td>
<td>36 (90%)</td>
</tr>
<tr>
<td>Dysphagia</td>
<td>8 (20%)</td>
</tr>
<tr>
<td>Late subcutaneous tissue toxicity</td>
<td>8 (20%)</td>
</tr>
<tr>
<td>Cardiac toxicity</td>
<td>6 (15%)</td>
</tr>
<tr>
<td>Pulmonary toxicity</td>
<td>4 (10%)</td>
</tr>
<tr>
<td>Nausea and vomiting</td>
<td>9 (22.5%)</td>
</tr>
<tr>
<td>Anemia</td>
<td>23 (57.5%)</td>
</tr>
<tr>
<td>Neutropenia</td>
<td>24 (60%)</td>
</tr>
<tr>
<td>Thrombocytopenia</td>
<td>15 (37.5%)</td>
</tr>
<tr>
<td>Febrile neutropenia</td>
<td>0 (0%)</td>
</tr>
</tbody>
</table>

Table 2. Toxicity induced by concurrent chemo-radiotherapy among 40 patients

Late subcutaneous tissue toxicity was all grade I and II (12.5% and 7.5% respectively). There was no grade III–IV toxicity. At Mann–Whitney test only the diabetes was found to be statistically significant with the occurrence of late skin toxicity (p = 0.0283).

Cardiac toxicity

The change of ejection fraction before and after radiotherapy was insignificant (0.65±0.5 vs 0.64±0.43, P value 0.345). By the end of this study, RTOG Cardiac Toxicity Grading was grade I–II in 15% (6/40) with no grade III toxicity.

Pulmonary toxicity

By the end of this study only 10% (4/40) of the patients showed grade I & II pulmonary function changes. None of the patients showed grade III toxicity. The reduction of the pulmonary functions before and after treatment was not significant. The Forced Expiratory Volume1 (FEV1) and Forced Vital Capacity (FVC) were 84±5.3 versus 83±4.7, P value 0.973.

Discussion

Concurrent administration of Paclitaxel with irradiation is well tolerable, with good cosmetic outcome and minimal toxicity. The overall survival and the disease–free survival were 95% and 92.5% respectively with no local recurrence. The delay of radiotherapy occurred in 15% of cases with maximum 5 days of interruption. Grade III skin toxicity developed in 10% of cases (4/40). By the end of this study, the majority of patients declared excellent/good score in 81.25% with only 6.25% having poor score. Subjective patient’s satisfaction was 87.5%. None of the patients showed cardiac or pulmonary dysfunction of grade III.

The improve in local control was similar to a meta–analysis conducted by Huang et al (2017) in operable breast cancer after undergoing conservative surgery. The study assessed the local and overall survival in the adjuvant setting between concurrent and sequential chemo–radiotherapy[12]. There was significant increase in the 5 years local recurrence free survival (OR: 0.39, 95% CI: 0.2–0.75, P=0.005) with no significant difference in the overall survival (OR: 0.62, 95% CI: 0.35–1.11, P=>0.05), acute skin toxicity (OR: 1.73, 95% CI: 0.98–3.04, P=>0.05) and late skin toxicity (OR: 1.27, 95% CI: 0.88–1.83, P=>0.05).

Grade III skin toxicity was significantly higher in diabetic (p = 0.0283) accounting for 10%, with treatment interruption in 15% of cases. This was in accordance with Kumar et al (2016) showing skin toxicity and delay of radiotherapy in 28% and 22.7% respectively. They studied concurrent paclitaxel with radiotherapy in the adjuvant setting of conservative breast cancer. The radiation dose was 50Gy to the whole breast in addition to 16 Gy boost. This was given concurrent to 5 weekly paclitaxel at a dose of 60mg/m2. Acute grade III skin toxicity was also more severe in diabetic (P value: 0.03) [13].

In the same study Kumar et al (2016) analyzed and compared his results with the other 5 studies using paclitaxel with radiotherapy in breast cancer. Burstein et al (2006) used the same dose of paclitaxel (60mg/m2) and had no grade III skin toxicity [7]. Two other studies used paclitaxel in a dose of 175mg/m2. Hanna et al (2002) showed 25% grade III skin toxicity leading to 4
 Concurrent Paclitaxel in Breast Cancer, Asmaa Ali Hassan, et. al.

days interruption in all cases [14]. Whereas Ellerbroek et al (2003) showed 8 days interruption in 33% of cases with no grade III skin toxicity [8]. Formenti et al (2003) used a twice weekly dose of 30mg/m2 with 7% grade III skin toxicity [15].

Algizawy et al (2016) studied concurrent docetaxel in a dose of 30 mg/m2 weekly for 9 weeks with radiotherapy in locally advanced breast cancer. Grade III skin dermatitis occurred in 8% of cases [16].

Mandilaras et al (2015) reviewed all trials using concurrent chemoradiotherapy in locally advanced breast cancer. The study showed superior results for triple negative and HER 2 positive breast cancer. Twice weekly Paclitaxel concurrent with radiotherapy gave optimistic results. Most of the trials showed acceptable skin toxicity and minimal pneumonitis [9].

A similar study was conducted by Chen et al (2012) in node positive breast cancer after conservative therapy. The 5–yr DFS was 88% and the OS was 93%. There was no significant change in the diffusing capacity of carbon monoxide after treatment with grade III toxicity in 4.5% [8].

Severe radiation pneumonitis requiring treatment was not encountered in the study which was different than earlier studies by Burstein et al. [7]. This may be due to good dose homogeneity with conformal radiotherapy techniques. Also, none of the patients received separate axillary irradiation.

The study was limited by the small sample size not allowing stratifying the patients’ outcome according to risk factors. Also, the follow up period was relatively short and longer period is needed to confirm our results.

Conclusion

In the current study, concurrent adjuvant paclitaxel with radiotherapy in node positive breast cancer was well tolerable with minimal toxicity. This resulted in good cosmetic outcomes and good local control. There were few cases of skin toxicity with acceptable interruption of treatment with no significant lung toxicity. This shortened the treatment duration leading to decrease in the patient visit. Also, all cases had easy access to medical care and rapid management of any side effects. The patient’s visits also decreased. This limited the financial load and patient burden especially in developing countries. As the patient is scheduled early, there was no delay in the timing of radiotherapy.

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Ethical statement

The study has been reviewed and approved by the ethical committee of The Kasr Al-Any Center of Clinical Oncology and Nuclear Medicine (NEMROCK), faculty of medicine, Cairo university in Egypt. It has been performed in accordance with the ethical standards laid down in an appropriate version of the 1964 Declaration of Helsinki. All patients have given an informed consent prior to the inclusion in the study.

References


