TO ASSESS THE QUALITY OF LIFE OF PACITAXEL BASED DOSE DENSE AND CONVENTIONAL NEOADJUVANT CHEMOTHERAPY IN LOCALLY ADVANCED FEMALE BREAST CANCER PATIENTS

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ABSTRACT

BACKGROUND
Breast cancer has become one of the most common cancers in women all over the world. It is a heterogeneous disease. Locally advanced breast cancer most commonly is diagnosed after a palpable mass is detected within the breast.

The aim of this study is to assess the quality of life of paclitaxel-based dose dense and conventional neoadjuvant chemotherapy in locally advanced female breast cancer patients.

MATERIALS AND METHODS
This observational study design was done between January 2011 and November 2012. A total of hundred locally advanced female breast cancer patients randomly selected from Department of Oncology, Government Medical College, Thiruvananthapuram. Fifty patients received paclitaxel 200 mg/m² and doxorubicin 50 mg/m² (4 course) every three weeks and other fifty patients received paclitaxel 80 mg/m² weekly (10 course) along with doxorubicin 50 mg/m² (4 course) every three weeks. Chemotherapy-induced toxicities and the quality of life of patients evaluated weekly (Total 10 weeks) by using Karnofsky Performance Status, Hamilton Depression scale, FACT-B (Functional Assessment of Cancer Therapy of Breast) and FACT-Taxane. Patients underwent modified radical mastectomy after the 4th week of chemotherapy and received adjuvant chemotherapy (Fluourouracil 500 mg/m², doxorubicin 50 mg/m², cyclophosphamide 500 mg/m² four course), external beam radiotherapy (dose of 50 Gy in 25 fractions using co-radioactive isotope) and hormone therapy for those who have receptor status positive.

RESULTS
Weekly patients had more problems regarding physical and social well-being, significantly less functional and emotional well-being, significantly more additional chemotherapy related problems and Taxane toxicity than three weekly patients. Based on Karnofsky Performance Status, three weekly patients had better performance status. Hamilton Depression Scale shows more depression in weekly patients.

CONCLUSION
This study shows that the quality of life during neoadjuvant chemotherapy in locally advanced female breast cancer patients was better in three weekly arm. Patients in three weekly arm have significantly more functional and emotional well-being. Patients in weekly arm had more depression which may be due to the physical problem, poor performance status, frequent hospital visits and change in life pattern.

KEY WORDS
Quality of Life, Neoadjuvant Chemotherapy, Locally Advanced.

Study Period
10 weeks (During neoadjuvant chemotherapy).

Inclusion Criteria
1. Patients should have locally advanced female breast cancer.
2. Breast cancer should be biopsy proven.
3. Patients age between 25 and 65.
4. Patients should have normal Haemoglobin (More than or equal to 10 gm%), WBC count (5000 - 11000/mm³), platelet count (70000 - 300000/ mm³), liver function test and renal function test.

Exclusion Criteria
1. Any previous cancer treatment.
2. Uncompensated congestive heart failure, renal failure and diabetes mellitus.
3. Supraclavicular lymph nodes and distant metastasis from breast cancer.
5. Poor performance status.

Sample Size
Sample size was calculated for convenience.

Study Procedure
In our Department, locally advanced female breast cancer patients receiving different types of paclitaxel containing neoadjuvant chemotherapy. In one pilot study, it had been observed that weekly Paclitaxel improves pathologic complete remission in locally advanced female breast cancer patients when compared with Paclitaxel once every 3 weeks, but quality of life is better in patients receiving 3 weekly Paclitaxel. In our study, we selected the locally advanced female breast cancer patients receiving dose dense (weekly) and conventional (three weekly) were selected and compared their quality of life during paclitaxel based neoadjuvant chemotherapy. This study was approved by the Ethics Committee. The aim of the research and interview method was explained to the participants. All patients signed an informed consent. Patients who refused to enter the study were also excluded.

Fifty patients treated with paclitaxel 200 mg/m² and doxorubicin 50 mg/m² (4 course) every three weekly and other fifty treated with paclitaxel 80 mg/m²2 weekly (10 course) along with doxorubicin 50 mg/m² (4 course) every three weekly. Patients received desamethasone 8 mg, diphenhydramine 50 mg and ranitidine 50 mg intravenously as paclitaxel premedication at 12 hours and 30 minutes before starting chemotherapy. Antiemetic- ondansetron 8 mg given intravenously in both arms before starting chemotherapy followed by tablet ondansetron 8 mg and tablet ranitidine 150 mg given morning and evening for 3 days. In all patients, neoadjuvant chemotherapy completed at the end of 9th week. Prophylactic growth factor support was given after 72 hours of paclitaxel in all patients.

Total Cumulative Dose Weekly Patients-
Paclitaxel- 80 mg/m² × 10 course weekly= 800 mg/m²
Doxorubicin- 50 mg/m² × 4 course three weekly= 200 mg/m²
Total Cumulative Dose Three Weekly Patients:
- Paclitaxel: 200 mg/m² × 4 course three weekly= 800 mg/m²
- Doxorubicin: 50 mg/m² × 4 course three weekly= 200 mg/m²
- Cumulative dose 800 mg/m² Paclitaxel and 200 mg/m² Doxorubicin in both arms.

Quality of Life - Assessment
Chemotherapy induced toxicities, common and serious clinical problems that is adversely affecting the quality of life of patients evaluated weekly by clinical examination and interview (Started after the first week of chemotherapy and completed at the end of tenth week) and compared average mean scores on different domains of quality of life between weekly arm and three weekly arm by using FACT-B, Karnofsky Performance Status and Hamilton Depression scale.

FACT-B (Functional Assessment of Cancer Therapy of Breast). FACT-B comprised of subscales assessing Physical Well-Being (PWB), Social/ Family Well-Being (SWB), Emotional Well-Being (EWB), Functional Well-Being (FWB) and Additional concerns (short of breath, dressing, swollen or tenderness of arms, sexually, hair loss, effect of stress, change in weight, pain, chance of spread to family members etc.) and FACT-Taxane (Functional Assessment of Cancer Therapy-Taxane). FACT-Taxane is a self-report instrument that was developed to measure the health related quality of life of patients receiving taxane containing chemotherapy.

Performance status of patients assessed by using Karnofsky Performance Status. Patients were clinically examined and interviewed regarding their ability do daily activities and performance. The scoring was done weekly. 1000 assessments were done in both groups (500 in each group).

Hamilton Rating Scale for Depression
Hamilton rating scale for depression is a multiple-choice questionnaire, that is clinically used to rate the severity of a patient’s major depression. The question which is designed for adult patient and is in the public domain rate the severity of symptoms observed for adult patient and is in the public domain rate the severity of symptoms observed in depression such as low mood, insomnia, agitation, anxiety and weight loss. Although, the HAM-D form lists 21 items, the scoring is based on the first 17. It generally takes 15 - 20 minutes to complete the interview and score the results. Eight items are scored on a 5-point scale ranging from 0= not present to 4 = severe. Nine are scores from 0 - 2.

Sum the Score:
0-7 = Normal
8-13 = Mild Depression.
14-18 = Moderate Depression.
19-22= Severe Depression.
≥22 = Very Severe Depression.

All statistical calculations were performed using the SPSS 17.0 statistical software. Quantitative variables were expressed as mean and standard deviation. Qualitative variables were expressed as frequency and percentage. Comparison of quantitative variables between two groups were analysed by unpaired t-test and that of qualitative variables were analysed by Chi-square test. A p-value < .05 was considered as statistically significant.

Patients underwent modified radical mastectomy and axillary daceeance after the 4th week of neoadjuvant chemotherapy. Adjuvant chemotherapy (FAC-fluorouracil 500 mg/m², doxorubicin 50 mg/m², cyclophosphamid 500 mg/m² four courses) was given after the two weeks of surgery and external beam radiotherapy dose of 50 Gy in 25 fractions, 5 days/ week total of 5 weeks using co-radiative isotope (average energy of 1.25 MeV) with medical and lateral tangential beams and supraclavicular on field. Adjuvant hormone therapy (Premenopausal patients-Tamoxifen, Post-Menopausal patients- Letrozole/ Anastrozole) given after radiation those who have receptor status positive.

RESULTS
performance status to 80 was 17% in weekly group and 7% in three weekly group.

<table>
<thead>
<tr>
<th>Hamilton Depression Score</th>
<th>Category</th>
<th>3 Weekly</th>
<th>Weekly</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No.</td>
<td>%</td>
<td>No.</td>
<td>%</td>
</tr>
<tr>
<td>Mild 8 - 13</td>
<td>23</td>
<td>46</td>
<td>15</td>
<td>30</td>
</tr>
<tr>
<td>Moderate 14 - 18</td>
<td>25</td>
<td>50</td>
<td>31</td>
<td>62</td>
</tr>
<tr>
<td>Severe 19 - 22</td>
<td>2</td>
<td>4</td>
<td>4</td>
<td>8</td>
</tr>
<tr>
<td>Total</td>
<td>50</td>
<td>100</td>
<td>50</td>
<td>100</td>
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</table>

Table 3. Hamilton Rating Scale for Depression

<table>
<thead>
<tr>
<th>Hamilton Depression Score</th>
<th>Category</th>
<th>No.</th>
<th>Mean</th>
<th>Standard Deviation</th>
<th>T</th>
<th>P</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>3 Weekly</td>
<td>50</td>
<td>14.82</td>
<td>2.760</td>
<td>1.562</td>
<td>0.122</td>
</tr>
<tr>
<td></td>
<td>Weekly</td>
<td>50</td>
<td>14.04</td>
<td>2.204</td>
<td></td>
<td></td>
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</table>

Box plot diagram describing the depression score of weekly and 3 weekly chemotherapy given patients. Lower and upper end of the whisker of the box plot represents the minimum and maximum score in each category respectively. Lower and upper border of the box represents first quartile (25th percentile) and third quartile (75th percentile) of the depression score respectively. Line of separation of the two-coloured rectangles is the median score. Means value in weekly group is 14.82 with minimum value 9 and maximum value 20. Means value in three weekly group is 14.04 with minimum value of 10 and maximum value of 19.

<table>
<thead>
<tr>
<th>Qualities</th>
<th>No.</th>
<th>Mean</th>
<th>Standard Deviation</th>
<th>T</th>
<th>P</th>
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<tr>
<td>Physical</td>
<td>weekly</td>
<td>50</td>
<td>10.5</td>
<td>1.8</td>
<td>0.845</td>
</tr>
<tr>
<td></td>
<td>3 weekly</td>
<td>50</td>
<td>10.3</td>
<td>1.3</td>
<td></td>
</tr>
<tr>
<td>Social/Family</td>
<td>weekly</td>
<td>50</td>
<td>15.4</td>
<td>2.5</td>
<td>2.749</td>
</tr>
<tr>
<td></td>
<td>3 weekly</td>
<td>50</td>
<td>14.3</td>
<td>1.5</td>
<td></td>
</tr>
<tr>
<td>Functional</td>
<td>weekly</td>
<td>50</td>
<td>9.1</td>
<td>1.6</td>
<td>3.263</td>
</tr>
<tr>
<td></td>
<td>3 weekly</td>
<td>50</td>
<td>10.3</td>
<td>2.1</td>
<td></td>
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Average physical well-being mean score among the weekly patients was 10.5 ± 1.8 and that among the three weekly patients was 10.3 ± 1.3. The observed difference in score among the two groups was not statistically significant.

Average social well-being mean score among the weekly patients was 15.4 ± 2.5 and that among the three weekly patients was 14.3 ± 1.5. The observed difference in score among the two groups was statistically significant (p= 0.007).

Average functional well-being mean score among the weekly patients was 9.1 ± 1.6 and that among the three weekly patients was 10.3 ± 2.1. The observed difference in score among the two groups was statistically significant (p=0.007).

Average emotional well-being mean score among the weekly patients was 11.8 ± 2.7 and that among the three weekly patients was 10.6 ± 1.5. The observed difference in score among the two groups was statistically significant (p=0.006).

Average additional concerns regarding breast chemotherapy means score among the weekly patients was 22.92 ± 5.2 and that among the three weekly patients was 20.34 ± 3.06. The observed difference in score among the two groups was statistically significant (p= 0.003).

Average taxane toxicity during breast chemotherapy, mean score among the weekly patients was 35.04 ± 8.56 and that among the three weekly chemotherapy patients was 31.12 ± 5.52. The observed difference in score among the two groups was statistically significant (p= 0.008).

**DISCUSSION**

Breast cancer is the most common type of tumour and the leading cause of cancer deaths in women. There are several therapeutic approaches to treat these patients. Each has its own particular effects and complications, which can determine a patient’s survival and quality of life. Neoadjuvant chemotherapy has been used to treat women with locally advanced breast cancer in an attempt to render the tumour operable. Anthracycline and taxane-based regimens are the backbones of most neoadjuvant chemotherapy protocols for breast cancer. A study by Green et al demonstrated weekly administration of paclitaxel is associated with an improved response rate and time to tumour progression when compared to the standard three-weekly treatment.

Hürny et al have reported a significant relationship between chemotherapy and the quality of life of women with breast cancer. Stein et al showed that women with breast cancer treated with radiotherapy and chemotherapy suffered from poor sleep quality and had lower quality of life. Hatam et al observed a vast increase in side effects such as constipation, nausea, stomatitis, fatigue and alopecia during chemotherapy. Mohadesi et al have concluded that fatigue was the most common complication caused by treatment in patients with breast cancer.
Abdel Halim and M El Ashri conducted a study in metastatic breast cancer. That study showed that after adjuvant anthracycline treatment, weekly paclitaxel 80 mg/m² (And every 4 weekly paraplatin AUC5) seems less toxic and more efficient compared with 3 weekly paclitaxel 175 mg/m² (And paraplatin AUC5 every 3 weeks).

Comparison of the mean quality of life scores both arms were done. Chemotherapy-induced toxicities are common and serious clinical problems that adversely impact both the quality of life and the ability of patients to continue treatment for their cancer. This study has shown that at the end of neoadjuvant chemotherapy, quality of life in both groups deteriorated as a result of the side effects and reveals the difference from the initial results.

Weekly patients had more physical problem than three weekly due to chemotherapy-induced toxicities (Haematological, neurologial-paraesthesia), lack of energy, body pain, frequent hospital visit etc., but not statistically significant. Physical well-being increases as total score decrease.

Weekly patients have significant more social/family well-being than three weekly patients. Patients are satisfied with family communication about their illness and get support from their friends. Social well-being increases as total score increases.

Weekly patients have significantly less functional well-being than the three weekly patients, mainly due to physical problems. Functional well-being like able to work at home, enjoy life and sleeping are better in three weekly patients. Functional well-being increases as total score increases. Based on Karnofsky performance status, three weekly patients had better performance status than weekly patients. Weekly patients have significantly less emotional well-being than the three weekly patients due to depression, feeling of sad, fear of death and recurrence. Emotional well-being increases as total score decreases. Hamilton Rating Scale for Depression and Box plot diagram describing the depression score of weekly and 3 weekly patients. Both arm patients had depression after diagnosis. Moderate and severe depression is more in weekly arm than three weekly arm. There is no statistically significant difference between two arms. Weekly patients have significantly more additional chemotherapy-related problems (Short of breath, dressing, swollen or tenderness of arms, sexually, hair loss, effect of stress, change in weight, pain and chance of spread to family members etc.) than three weekly patients. Additional chemotherapy-related problems increase as total score increases.

Weekly patients have significantly more Taxane toxicity (Numbness of hands and feet (peripheral neuropathy), joint pain or muscle cramps etc.) than three weekly patients.

**CONCLUSION**

Stress, pain and fatigue can severely diminish quality of life during and after cancer treatment. This study show that the quality of life was better in three weekly neoadjuvant chemotherapy patients due to significantly more functional and emotional well-being, less chemotherapy related toxicity and physical problem. Promote physical therapy, accepting illness, maintain regular sleep, manage hair loss by wig, coping strategies or addressing spiritual concerns, emotional support from family and friends, reading books, using laptop and music player and deep breathing or guided imagery to reduce stress. A team of doctors, nurses and other health care professionals working together with the patient, their family and caregivers to understand the patient’s goals, explain treatment options and provide good general hygiene, comfortable clothes, hydration and management of toxicity to increase quality of life before and after chemotherapy.

**REFERENCES**


