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WHICH IS BETTER WEEKLY OR 3-WEEKLY PACLITAXEL? - IN COMBINATION CHEMOTHERAPY USING PACLITAXEL AND DOXORUBICIN IN METASTATIC CARCINOMA BREAST

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ABSTRACT

Introduction: Metastatic breast cancer (MBC) is known as an incurable disease with a median 5-year survival rate around 23.8–30%.Each physician maintains a hierarchy of goals for the treatment of patients — prolongation of survival, palliation of symptoms, minimization of toxicity, and rarely, in a small fraction of patients, the potential for cure.

Aim: The aim of this study was to compare the efficacy and toxicity of weekly paclitaxel, and 3-weekly paclitaxel in combination with doxorubicin in metastatic carcinoma breast.

Methods: This study was prospective randomised controlled trial. 30 patients were randomised to weekly paclitaxel as well as to 3-weekly paclitaxel in combination with doxorubicin after inclusion and exclusion criteria.

Combination chemotherapy in carcinoma breast

Arm A - Paclitaxel 75mg/m2 weekly (Day 1, 8 , 15)and doxorubicin 50mg/m2 3-weekly (Day 1).

Arm B – Paclitaxel 175mg/m2 3-weekly (Day1) and doxorubicin 50mg/m2 3-weekly (Day 1).

The treatment was planned for 2 cycles only. Appropriate premedication and supportive therapy was given as needed. The response to chemotherapy will be assessed at end of 3 weeks after 2nd cycle. Further treatment in non-responders was individualised as per standard guidelines. Statistical data were analysed using SPSS.

Results: The overall response rate of combination chemotherapy in this study was 40%. Arm A (43.3%) had better response rate than Arm B (36.7%).The quality of life was poor in 18.3% of the total study population. In Arm A 33.3% had good quality of life, which was better than Arm B (23.3%). Quality of life was moderate in 50% in Arm A and 56.7% in Arm B. In Arm A and Arm B, 16.7% and 20% had poor quality of life respectively. The incidence of toxicity such as neuropathy, neutropenia, vomiting, anorexia, anemia and thrombocytopenia was found to less in Arm A than Arm B. The incidence of fatigue, alopecia, nausea and nail changes was found to be less in Arm B than Arm A.

Conclusion: Weekly paclitaxel had better response rate than 3-weekly paclitaxel in combination with doxorubicin in metastatic carcinoma breast. The quality of life was better in weekly paclitaxel than 3-weekly paclitaxel.

KEYWORDS : carcinoma breast, doxorubicin , paclitaxel

INTRODUCTION

Metastatic breast cancer (MBC) is known as an incurable disease with a median 5-year survival rate around 23.8–30% [1].First-line chemotherapy for metastatic breast cancer has been the focus of ongoing controversy, a condition that partially reflects the imperfections of available therapy [2]. It also partially reflects not only the imperfections in our ability to monitor response, but also the disagreements among clinicians over the goals of therapy [2]. Each physician maintains a hierarchy of goals for the treatment of patients — prolongation of survival, palliation of symptoms, minimization of toxicity, and rarely, in a small fraction of patients, the potential for cure [2].

Combination of doxorubcin and paclitaxel results in superior overall response rates and median time to treatment failure, but did not improve either survival or quality of life compared to sequential single-agent therapy [3].

AIM

The aim of this study was to compare the efficacy and toxicity of weekly paclitaxel, and 3-weekly paclitaxel in combination with doxorubicin in metastatic carcinoma breast.

METHODS AND MATERIAL

This study was prospective randomised study with two arm were 30 patients were randomised to each arm after fulfilling inclusion and exclusion criteria.

Inclusion criteria

Age 18 to 60 years , performance status 0 – 2, stage IV carcinoma breast confirmed after histological proof and staging work up and measurable disease by RECIST criteria, normal blood chemistry, renal parameter sand liver function tests, echocardiogram with normal left ventricle function and ejection fraction > 50%. ,ECOG PS ≤ 2

Exclusion criteria

No willing to give consent, hypersensitivity to drugs, uncontrolled diabetes, uncontrolled hypertension, patients with any neuropathy and participation in other trials.

Combination chemotherapy in carcinoma breast

Arm A - Paclitaxel 75mg/m^2 hourly infusion (Day 1, 8 , 15) after doxorubicin 50mg/m^2 bolus (Day 1) every 21 days.

Arm B – Paclitaxel 175mg/m^2 3- hourly infusion (Day1) after doxorubicin 50mg/m^2 bolus (Day 1) every 21 days.

This study was done at Government Stanley Medical College during December 2016 to July 2018.The treatment was planned for 2 cycles only. Appropriate premedication and supportive therapy was given as needed. The response to chemotherapy will be assessed at end of 3 weeks after 2nd cycle. Further treatment in non-responders was individualised as per standard guidelines. Statistical data were analysed using SPSS.

RESULTS

The overall response rate of combination chemotherapy in this study was 40%. Arm A (43.3%) had better response rate than Arm B (36.7%) (Table 1).

The quality of life was poor in 18.3% of the total study population. In Arm A 33.3% had good quality of life, which was better than Arm B (23.3%). Quality of life was moderate in 50%

in Arm A and 56.7% in Arm B. In Arm A and Arm B, 16.7% and 20% had poor quality of life respectively (Table2).

TABLE 1 - EFFICACY OF CHEMOTHERAPY

RESPONSE	ARM A	ARM B	TOTAL
PRESENT	13(43.3%)	11(36.7%)	24(40%)
ABSENT	17(56.7%)	19(63.3%)	36(60%)
TOTAL	30	30	60

TABLE 2 - DISTRIBUTION OF QUALITY OF LIFE

QUALITY OF LIFE	ARM A	ARM B	TOTAL
GOOD	10(33.3%)	7(23.3%)	17(28.3%)
MODERATE	15(50%)	17(56.7%)	32(53.4%)
POOR	5(16.7%)	6(20%)	11(18.3%)
TOTAL	30	30	60

The most common toxicity was neuropathy in 70%, followed by neutropenia in 65%, anorexia in 63.3%, and fatigue in 55%, alopecia in 43.3%, and nausea in 30% of the total study population. The overall incidence of vomiting and nail changes was 21.7%, and incidence of anemia and thrombocytopenia was 18.3% and 6.7% respectively.

The incidence of neuropathy, neutropenia, anorexia, fatigue, alopecia ,nausea, vomiting ,nail changes, anemia and thrombocytopenia was 63.3%, 56.7%, 60%, 63.3%, 50%,33.3%, 20%, 23.3%, 16.7%, and 3.3% respectively in Arm A.

The incidence of neuropathy, neutropenia, anorexia, fatigue, alopecia ,nausea, vomiting ,nail changes, anemia and thrombocytopenia was 76.7%, 73.3%, 66.7%, 46,7%, 36.7%, 26.7%, 23.3%, 20%, 20%, and 10% respectively in Arm A.

The incidence of toxicity such as neuropathy, neutropenia, vomiting, anorexia, anemia and thrombocytopenia was found to less in Arm A than Arm B. The incidence of fatigue, alopecia, nausea and nail changes was found to be less in Arm B than Arm A.

TABLE 3 - DISTRIBUTION OF TOXICITY

TOXICITY	ARM A(n=30)	ARM B(n=30)	TOTAL(n=60)
NEUTROPENIA	17 (56.7%)	22 (73.3%)	39 (65%)
ANEMIA	5 (16.7%)	6 (20%)	11 (18.3%)
THROMBOCYTOPENIA	1 (3.3%)	3 (10%)	4 (6.7%)
NEUROPATHY	19 (63.3%)	23 (76.7%)	42(70%)
FATIGUE	19(63.3%)	14 (46.7%)	33 (55%)
NAUSEA	10 (33.3%)	8 (26.7%)	18 (30%)
VOMITING	6 (20%)	7 (23.3%)	13 (21.7%)
ALOPECIA	15 (50%)	11 (36.7%)	26 (43.3%)
NAIL CHANGES	7 (23.3%)	6 (20%)	13 (21.7%)
ANOREXIA	18 (60%)	20 (66.7%)	38 (63.3%)

DISCUSSION

Combination chemotherapy theoretically predicted that the use of non-cross-resistant agents with non-overlapping toxicities would result in therapeutic synergy, overcoming drug resistance [4]. Practical experience, beginning with the pioneering work of Greenspan, indicated that combination regimens are associated with higher response rates than single-agent regimens [5].

Combination therapy resulted both in a superior overall response rate and a superior time to treatment failure, two frequent measures of efficacy in metastatic chemotherapy trials [3]. Despite this superiority, combination therapy failed to improve overall survival. Perhaps more importantly, given the usually fatal nature of the disease, combination therapy did not improve quality of life [3]. Response rate and time to treatment failure may represent poor surrogates for overall survival, which in turn, may be more strongly related to the underlying biology of the disease like horomonal status, number of disease sites, and disease-free interval [3].

CONCULSION

Weekly paclitaxel had better response rate than 3-weekly paclitaxel in combination with doxorubicin in metastatic carcinoma breast. The quality of life was better in weekly paclitaxel than 3-weekly paclitaxel.

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