diagnosis, in patients under steroid therapy, who do not wean from mechanical ventilation after 48-72 hours of the resolution of the underlying disease process.

Received 15th February 2005. Accepted for publication in final form 18th May 2005.

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Paclitaxel in relapsed high risk anthracycline treated breast cancer patients

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Breast cancer is the most common malignancy afflicting women, and second most common cause of cancer death in women. Considerable progress has been made in the treatment of breast cancer, and mortality is decreasing in developed countries. Despite this, the majority of breast cancer patients will develop metastases and eventually die of the disease. Response to chemotherapy, while frequent, is usually short-lived and the median survival for patients treated with chemotherapy for metastatic disease ranges between 18-24 months.[1] The introduction of new agents has improved prognosis in chemotherapy, pretreated patients.[1] In 1994, paclitaxel was approved for the treatment of metastatic (or advanced) breast cancer (MBC) following failure with standard anthracycline -based on chemotherapy, or in patients who had relapsed after initial chemotherapy.

In this study, we report our experience with paclitaxel in our patients who relapsed following anthracycline chemotherapy, and who are mostly premenopausal women, as opposed to other studies that included mostly postmenopausal women. The aim of this study is to assess response rate, mean duration of response, median time to progression, and survival rate in MBC patients who received paclitaxel. This retrospective study was performed at Tripoli Medical Center, Tripoli, Libya. Women with a histologically confirmed diagnosis of breast carcinoma and evidence of metastatic disease who were on regular follow up and relapsed after adjuvant treatment, were included in our study. All patients included have an Eastern Cooperative Oncology Group (ECOG) performance status of 0-2. All patients received paclitaxel as single agent in a dose of 175 mg/m^2 IV infusion over 3 hours every 3 weeks. Premedication with dexamethasone and antihistamine was given prior to the paclitaxel dose. Median of 6 cycles was administered per patients (1-9 cycles). Imaging procedures included chest, abdomen, CT scan and bone isotope scans. These were repeated to assess objective response every 3 treatment cycles. Forty-two patients were included in this study in the period between June 1997-June 2004. The age of the patients ranged from 28-67 years with a median age of 45 years at diagnosis. Premenopausal women represented 61.9% and postmenopausal women represented 38.1%, 58.14% had stage II disease, 25.6% had stage III, 14% had stage IV, and 2.3% were unknown, 86% were node positive, 11.6% were negative and unknown in 2.4%. Histological diagnosis was as follows: invasive duct carcinoma in 81.4%, 11.6% lobular carcinoma, 4.7% medullary carcinoma and inflammatory type in 2.3%. Estrogen and progesterone receptors were studied in 43% of patients where their receptors were positive in 44.4% and 55.6% were negative. Regarding type of surgery, modified radical mastectomy was carried out in 81.4% and lumpectomy and axillary clearance was carried out in 11.6%, and only biopsy was done in 9.3%. In those who had positive lymph nodes, the median number of involved node >4 (5-8 lymph node). Radiotherapy as loco regional treatment as 50 gray over 25 fraction was given to 73%, in those who have more than 3 positive lymph node, locally advanced disease or those who had breast conserving surgery. Tamoxifen tab. 20 mg/day was given to all patients who have estrogen positive or where the receptor status was unknown. Chemotherapy as CAF Cyclophosphamide,

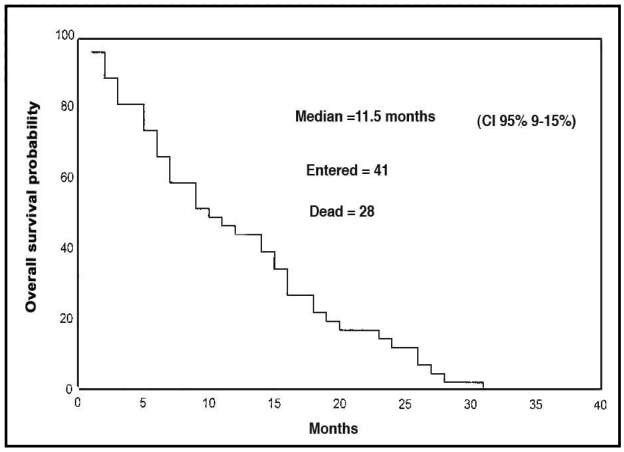

Figure 1 - Overall survival time (months).

adriamycin, and 5-flourouricil were given to 85.7% every 3 weeks from 6-9 cycles, and 14.3% received CMF Cyclophosphamide, methotrexate, and flourouricil, as they have contraindication to adriamycin with cardiac function impairment. The median time to relapse was 19.5 months (95% confidence interval [CI], 14.5-27%). The most common sites of relapse were in bone 66%, and visceral metastases in 63.4% (lung 22%, liver 27% and brain 14.6%), pleura in 5%, lymph node in 12.2%, and local recurrence in 39%. Overall response rate after paclitaxel was 22/42 (54%) (95% CI, 43-69%), wherein 13/42 (32%) (95% CI, 18-46%) had complete response, and 9/42 (22%) (95% CI, 9%-35%), had partial response or stable disease. Nineteen out of 42 (46%) (95% CI, 31%-61%) had no response or progressive disease. The response rate of our study was consistent with other studies such as Sato et al[2] study (weekly paclitaxel was administered) with 40.5% (95% CI, 29, 4%-51.7%) and Acuna et al[3] study (both paclitaxel and vinorelbine used as first line chemotherapy) with 60% (95% CI, 46%-74%). The response rate was also significantly better than that reported by Bishop et al[4] with 29% (95% CI, 21%-39%), O'Shaughnessy et al[5] with 25.6% (95% CI, 20%-30.9%), and Albain et al[6] with 22% (95% CI, 17%-27.2%), possibly as these studies include older women (median age was 53 years). The median age of our patients was 45 years, 28/42 (66.7%) of patients relapsed and median time to progression after paclitaxel was 6 months (95% CI, 3.5%-10%), which is similar to the study of Bishop et al,[4] 5.3 months (95% CI, 4.1%-5.6%), O'Shaughnessy et al[5] 3.5 months (95% CI, 2.9%-4.0%), Albain et al[6] 2.9 months (95% CI, 2.6%-3.7%), Sato et al[2] 4.8 months and Acuna et al[3] 7 months. The median duration of response (from detection of response until relapse or death) was 9 months (95% CI, 6.5%-12%), which is similar to O'Shaughnessy et al[5] study 7.2 months (95% CI, 6.8%-8.6%). The median survival after paclitaxel was 11.5 months (95% CI, 9%-15%). **Figure 1**, which is consistent with Bishop et al[4] study 17.3 months (95% CI, 12.6%-21.4%). Over all median survival (from diagnosis to death) was 34.5 months (95% CI, 28%-41 %). In terms of therapy-related toxicities of paclitaxel administration, 12% had grade 3 febrile neutropenia and anemia, and 4.7% developed grade 3 peripheral neuropathy. Bishop et al[4] reported febrile neutropenia and infection or both in 10% of paclitaxel patients and grade 3 peripheral neuropathy in 9% of patients. O'Shaughnessy et al[5] reported grade 4 neutropenia in 6.6% of patients and grade 4 anemia in 0.4% of patients. This study confirm the tolerability of paclitaxel therapy in Libyan women with advanced or metastatic breast cancer. Given the above information, it appears that a dose and schedule of 175 mg/m^2 by 3 hours infusion every 21 days is both effective and well tolerable, and a reasonable therapeutic choice. In our study, we used paclitaxel as a single agent. This is because there is no good evidence, that combination chemotherapy is more effective, especially as our women were in a stable condition and did not present with life threatening emergencies. Paclitaxel has significant activity against metastatic breast cancer that extends to patients who received prior chemotherapy.

We conclude that single agent paclitaxel offers a very good option in the management of metastatic breast cancer in women who have been heavily treated with anthracycline and that toxicity is acceptable and manageable.

Received 1st March 2005. Accepted for publication in final form 29th May 2005.

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Effect of antioxidant serum levels of myocardial ischemia markers in patients with ischemic heart disease after treadmill exercise testing

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Heavy physical exercise increases oxygen consumption, and potentially initiates formation of reactive oxygen species (ROS), which leads to oxidative stress and cellular damage if not properly counteracted. The increase in malondialdehyde (MDA), released after intracoronary platelet aggregation might be a biochemical marker of coronary artery disease (CAD). Meanwhile, oxygen-derived free radicals after temporary coronary occlusion causes myocardial stunning.[1] Exercise leads to an increase in metabolic rate, production of ROS, and compromised antioxidant defense systems. The development of treadmill exercise testing, has allowed early and better evaluation of electrocardiogram (ECG) results, during and after exercise testing for the detection of ischemic changes. We undertook the present study to determine whether the plasma antioxidant status could help in confirming the diagnosis of CADs in borderline cases of treadmill exercise testing results. Also, whether changes in the parameters involved could help in the early detection and possible prevention of CADs especially in people with a family history.

We selected 62 subjects (42 patients and 20 control). We positively diagnosed all patients with CAD. We instructed all not to take any cholesterol lowering drugs and stop taking β-blockers or calcium channel blockers 3 days before doing the exercise test. We applied the Bruce protocol, starting with an initial work rate low enough for the least able subject. Progression continued until we reached the rate suitable for the most vigorous subject. We used stages of 3 minutes duration, permitting 5 different exercise intensity levels, which may be spaced more closely in terms of work rate and thus, may be more precise in measuring maximal functional capacity.[2] We terminated the test on any evidence that further exercise might be harmful to the subject. The exercise endurance in males was approximately 11.5 minutes and in females 7.6 minutes. We only included patients with true positive exercise results in this study. After the return of all parameters to recovery, we asked the patient to hyperventilate for 2 minutes, and we took a 12 lead ECG, which may reproduce the ST-depression in suspicious positive cases.

We took blood samples immediately before, and half an hour after finishing the exercise test. The biochemical tests included: lipid profile total cholesterol (TC), triglycerides (TG), high density lipoproteins (HDL), low density lipoproteins (LDL) and very low density lipoproteins (VLDL), serum very low density lipoproteins cholesterol (VLDL-C), and low density lipoproteins cholesterol (LDL-C) was calculated by Friedewald formula. The formula is only valid at serum triglyceride concentration of less than 400 mg/100 ml.

We measured lipid peroxidation in the form of MDA, a secondary product of lipid peroxidation. Its measurement is based on the colorimetric reaction with thiobarbituric acid. We measured uric acid, and albumin as antioxidants and the last parameter was creatine kinase. The heart rate progressively increases with every stage as maximal aerobic exercise capacity is reached, then it reaches a plateau like the oxygen consumption curve. There was a progressive increase in systolic blood pressure with increasing exercise intensity and very little change in diastolic pressure. At peak exercise it ranged from 162-216 mm Hg, while the diastolic may fall slightly in younger age groups, however, in middle-aged people this may rise not to exceed 10 mm Hg. A pathological fall in systolic blood pressure is highly specific for severe CAD. Failure of systolic blood pressure to rise reflects an inadequate elevation of cardiac output especially in left main stem disease, or equivalent coronary disease, and in 3 vessels disease.

The results of the positive exercise test revealed that the ECG changes of ST-depression will be found mainly in the bipolar leads. Only 2 cases out of 55 positive cases showed changes in the standard leads (3.6%). There was a significant rise of mean albumin level in the post-exercise samples of the control and patient groups **(Table 1).**

The pre-exercise samples of the patients group showed lower levels of albumin than the control group. The percentage rise in the control group more than the patient group. Albumin is considered a sacrificial antioxidant,[3] and the hypervolemia resulted after exercise account for the increased