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A₂ phospholipase and oligoelements Zn, Se and Mn in breast cancer treatment; 1086 cases, 7 years follow-up

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SUMMARY

One thousand eighty six patients were treated during at least six months through different periods of time with oligoelements Zinc, Selenium and Manganese combined to phospholipase A₂ (O-PLA₂). Follow up was performed during seven years or until the moment of death. The patients were divided in groups according stage and associated treatments. Global survival, seven years survival rates and mean survival were stated. Survival rates were over the usually observed by other authors in similar stages with similar treatments. Ninety one point two (91.2) % of patients in stage 1, 89.7 % of patients in stage 2 and 3 and 43.2 % of patients in stage 4, were alive 7 years after. Mean survival could only be stated in stage 4 and was 3.5 years. The effects were attributed to the antioxidant action of trace elements and the immunostimulant properties of O-PLA₂.

INTRODUCTION

The objective of this work is to evaluate the improvement in survival observed in O-PLA₂ treated breast cancer patients. Based on ours¹ and other authors^{2,3} experiments with trace elements on tissue cultures and tumor bearing Sprague-Dawley rats we developed a combined therapy with A₂ phospholipase. Other authors have demonstrated the effect of Se and Zn protecting normal cells but not atypical ones from massive doses of chemotherapeutical agents in tissue cultures⁴. Experiments in this sense were concluded in normal rats treated with CMF, the most common association for breast cancer chemotherapy⁵. It was also demonstrated the inhibitor effect of O-PLA₂ on cultured cells derived from mammary carcinomas with concomitant stimulatory effect on normal cells⁶.

More than 57400 patients required O-PLA₂ treatment in the last seven years for different malignancies, of them 6459 for breast cancer. Many patients considered the O-PLA₂ treatment their main therapy; others consider it an adjuvant treatment meanwhile they continue with traditional oncological therapies. None of our staff members tried to discourage patients from continuing traditional treatments. In some cases our staff surgeons performed surgical ablations and diagnostic biopsies.

MATERIAL AND METHODS

Between 1991 and 1996 patients of breast cancer were selected from our 6459 cases according to the following eligibility criteria: 1) Six months of continuous O-PLA₂ treatment. 2) Mammary carcinoma biopsy confirmed in any stage, with adequate follow up of clinical status. 3) Patients whose actual state was known trough concurrence to our center or inquires. 4) Patients with confirmed death.

Patients were treated with daily parenteral intramuscular applications of A₂ phospholipase 0.1 µg/kg body weight/day; combined with 1.5 µg/kg body weight/day of each, Selenium, Manganese and Zinc in 2ml saline buffered solution. The doses were adjusted after the analysis of previous experiences in animal trials and tissue cultures. Rats received 500 times the extrapolated human doses without complications. Treatment was applied through long periods of time, in some cases more than 60 months, without signs of toxicity or undesired effects. Similar treatment was applied in a previously presented 291 patients series with hepatic metastases of colon adenocarcinoma without side effects and improvement in survival⁷.

RESULTS AND DISCUSSION

Seven years survival rate (7YSR) for patients in stage 1 was 91.2 %; mean survival was impossible to state due to the scarce death events occurred. This value is comparable with NCI rates⁸ for early stages diagnosed cases 93 % 5YSR considering that 55 % of our patients received only the O-PLA₂ treatment after surgery (Fig 1). Patients of stages 2 and 3 had a 7YSR of 89.7 % (Fig 2), better than some comparative trials for CMF (>than 85 % optimal dose) that result in 80 % 7YSR⁸ (Fig 3) and NCI values (72 %) for 5YSR regional disease⁸. Are specially encouraging the results observed in stage 4 patients when compared with NCI values⁸ distant disease 43.2% against 18 %. For all stages 7YSR was 76 % (Fig 5) and could be compared to the 5YSR from NCI⁸ (79 %), and to the 7YSR in public hospitals in USA (50 %)⁹ and the Netherlands (62 %)¹⁰.

These are very positive results considering the condition of our patients, mainly with low socioeconomic status. The most common annuals incomes are between 6000\$ and 13000\$ and for a great quantity of retired elderly women are even worst. It has been demonstrated that eliminating the gradient in survival by deprivation

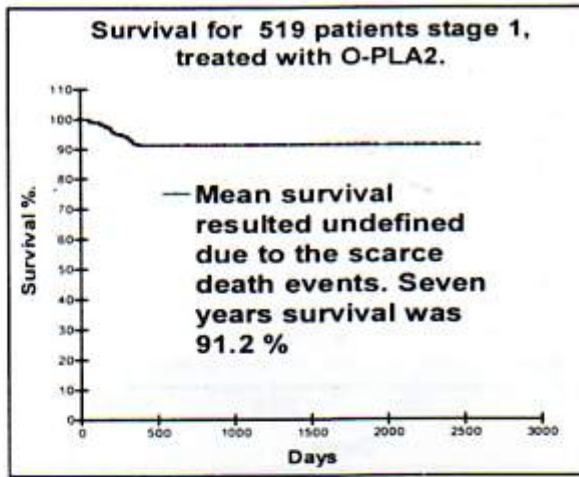


Figure 1: Survival seven years curve of patients in stage 1 post surgery.

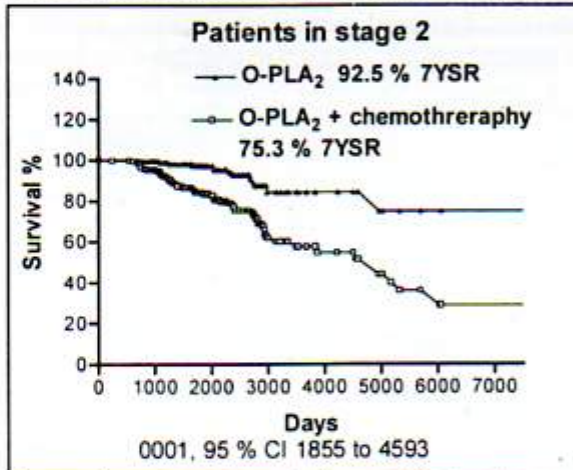


Figure 2: Comparative seven years survival curve of patients in stage 2 according to associated treatment.

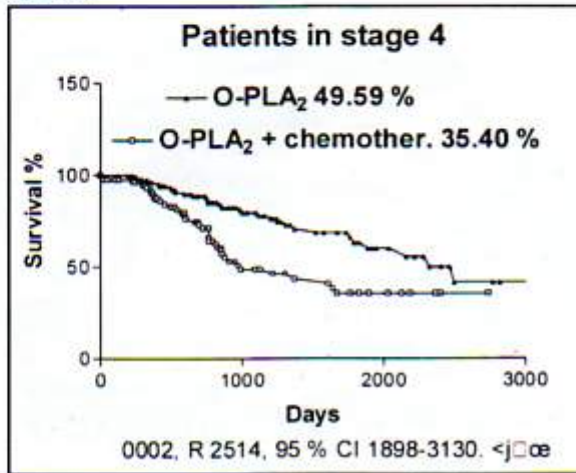


Figure 3: Comparative seven years survival curve of patients in stage 4 according to associated treatment.

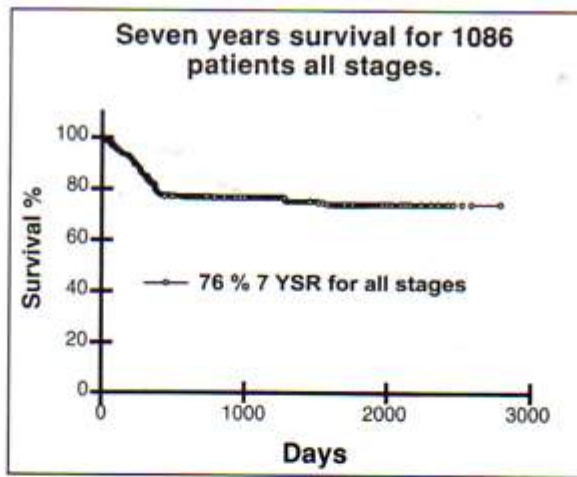


Figure 4: Survival curve of patients in all stages post surgery.

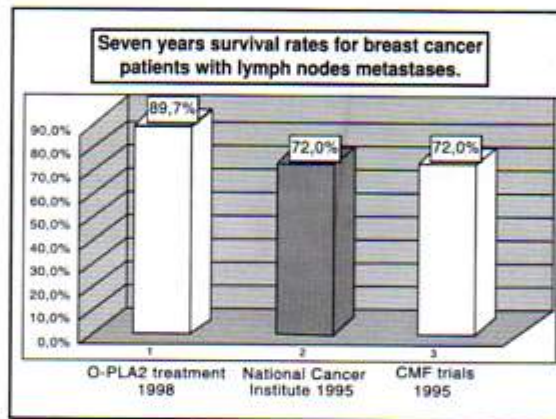


Figure 5: Survival values in comparison with other groups.

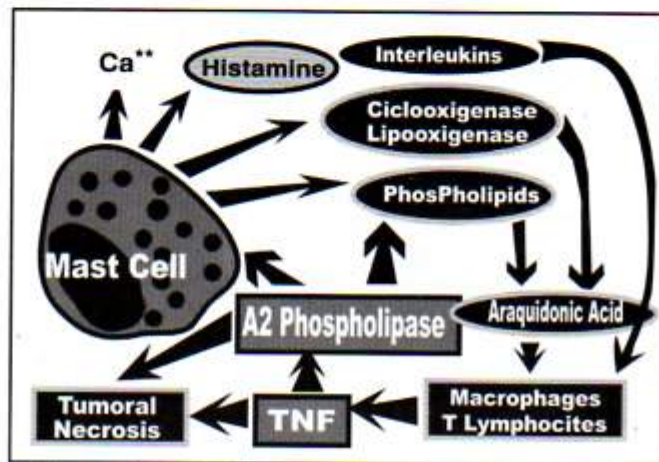


Figure 6: Proposed mechanism of PLA₂ action, through mast cell degranulation, interleukine liberation, induction of TNF production and activation.

category can change survival in about 10 % for breast cancer patients (50% versus 60 % 5YSR)^{9, 10}. If we consider the time spent without symptoms and toxicity (TWiST) the comparisons are largely favorable to our method; all our patients were absolutely free of side effects or complications. The relapse free time in our patients is totally free of toxicity interval¹¹. Even dose included in chemotherapeutic treatment improved faster their blood counts post chemotherapy and referred less vomiting and nausea. This effect is surely related with the proven antioxidant effects of the oligoelements used^{4,13} (Fig 6).

We are convinced that the prolongation in survival rates even when some patients received only the O-PLA₂ treatment, depends on the immunostimulant properties of PLA₂ associated to the oligoelements. In this sense was proven in 1966 the PLA₂ ability to release histamine from mast cells and other tissues¹⁴. Histamine is well known as early messenger in immune reaction, causing enhancement in NK cell activity and other interleukine mediated cellular response¹⁵ (Fig 7).

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