

Global Cancer Conference & Medicare Summit

September 15-17, 2014 Hyderabad International Convention Centre, India

Fish oil prevents bone metastasis of breast cancer and off-target toxicity of chemotherapies

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Objective: Nearly 85% of breast cancer patients are dying due to bone metastasis of breast cancer. Beside this, off-target toxicity of chemotherapeutic drugs is a major constraint in treatment of cancer patients. Non-toxic omega-3 fatty acids DHA and EPA, active components of fish oil, shows several beneficiary effects to our health including anti-tumorigenic activity. This study has investigated to know whether fish oil prevents systemic toxicity of chemotherapeutic drugs, and breast cancer bone metastasis.

Methods: To test bone metastasis, human breast cancer MDA-MB-231 cells were administered to left cardiac ventricles of nude mice by intra cardiac injection and to test side effects of chemotherapeutic drugs, these drugs were orally fed to cat fishes, followed by fish oil and PBS treatment for experimental and control groups of animals. Western blotting and quantitative RT-PCR were performed for the detection of CD44 and miR-21. Biochemical assays were performed to test liver and kidney functions.

Results: Metastasis model experiments showed a significant inhibition of breast cancer osteolytic bone metastasis in hind limb of fish oil-treated mice as compared to control mice. DHA and EPA, active components of fish oil, inhibit breast cancer cells migration by blocking cancer stem cell marker CD44. Levels of osteoclastogenic colony stimulating factor-1 (CSF-1) and oncomiR miR-21 were found to be remarkably high in metastatic breast cancer cells as compared to non- metastatic breast cancer cells. Treatment of cat fishes with doxorubicin/cisplatin showed severe skin damages which were prevented by omega-3 fatty acids treatment, indicating a preventive role of omega-3 fatty acids in chemotherapeutic drug-induced toxicity. Chemotherapeutic drugs-elevated SGPT, ALP and MMPs activity were diminished by fish oil treatment. Moreover, fish oil treatment reverses chemotherapeutic drugs-mediated inhibition of SOD activity to shut down ROS level and MMPs activity.

Conclusions: The study for the first time unravels that fish oil inhibits breast cancer bone metastasis by targeting CD44, miR-21 and CSF-1 in nude mice model and omega-3 fatty acids prevent chemotherapeutic drug-driven systemic toxicity presumably by reducing ROS level.

Significance: This study recommends that omega-3 fatty acids may possibly be used in combination with chemotherapeutic drugs for treatment of different cancers to lessen chemotherapeutic drugs-associated systemic toxicity and to augment anti-metastasis activity of breast cancer.

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