

EP-2303 should radiotherapy be avoided after neoadjuvant chemotherapy in complete response breast cancer?

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Purpose or Objective

The increasing use of neoadjuvant chemotherapy (NACT) raises doubts about the utility of radiotherapy (RT) and/or surgery in early stage breast cancer (BC) patients who present a pathologic complete response (pCR) after NACT.

The aim of the present study was to investigate whether the alterations in the serum levels of energy balance-associated metabolites after RT are related to obtaining a pCR in patients treated with NACT.

Material and Methods

We included 37 women with BC, all were treated with NACT. RT schedule was normofractionated or hypofractionated. Prior to irradiation, and one month after RT, serum samples were obtained and stored at -80°C until batched-processed for targeted quantitative metabolomics analyses. The control group was composed of 44 healthy women participating in a population-based study conducted in our geographical area. We analyzed the concentrations of metabolites involved in glycolysis, citric acid cycle and amino acid metabolism using gas chromatography coupled to quadrupole time-of-flight mass spectrometry with an electron impact source (GC-El-QTOF-MS). Statistical calculations were performed with SPSS 22.0. Differences between two groups were assessed with Student's t-test. The diagnostic accuracy of the measured metabolites was assessed by receiver operating characteristic (ROC) curves.

Results

Patients receiving NACT had significant alterations pre-RT in the serum levels of energy balance-related metabolites. They had increased concentrations of pyruvate, aspartate, aconitate, and citrate, and decreased concentrations of lactate, alanine, valine, leucine, isoleucine, proline, malonyl coenzyme A, glycine, succinate, serine, ketoglutarate, and glutamate. RT largely corrected these alterations and interestingly, this improvement was significantly superior in patients with a pCR than in those with a partial response. Metabolites that presented the greatest differences between the pCR patients and those that had a partial response were glycine and malonyl coenzyme A. Serum glycine measurement had a sensitivity of 0.889 and a specificity of 0.700 at 107 mM. Serum malonyl coenzyme A had a sensitivity of 1.000 and a specificity of 0.636 at 1.30 mM.

Conclusion

The present study showed that RT after NACT corrected most of the alterations in energy metabolism in BC patients. Our results support, then, that RT should not be avoided after NACT in any case. The present study

suggests that the measurement of serum glycine and/or malonyl coenzyme A post-RT have a high sensitivity and specificity to discriminate between pCR and partial response. Therefore, these analyses may have prognostic value. Studies in wider series of patients would be necessary to ascertain this hypothesis.

EP-2304 Selenium does not affect radiosensitivity of human breast cancer cell lines

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Purpose or Objective

Breast cancer is the leading cause of cancer death in women worldwide. The standard treatment is a multimodal approach combining surgery, chemotherapy, hormone therapy, immunotherapy and radiotherapy. Despite improvement of radiotherapy techniques, side effects in the surrounding normal tissue due to radiation-induced reactive oxygen species (ROS) remain a problem. Supplementation with the antioxidant selenium is frequently used in breast cancer patients in order to protect the normal tissue from radiation-induced side effects. However, there is still concern, whether selenium may also protect tumor cells from radiation-induced cell kill and thereby reduces efficacy of radiotherapy. The aim of the present study was to evaluate the effect of selenium administration on the radiosensitivity of human breast cancer cell lines.

Material and Methods

Breast cancer cell lines MDA-MB-231 and MCF7 were used in all experiments. Cells were treated for 24h with sodium selenite (0, 70 and 140 µg/l) and then irradiated with x-rays (200 kV, RS225A irradiation device; Gulmay Medical Ltd). Apoptosis was analysed 24h after irradiation by Caspase 3/7 staining with subsequent flow cytometry. DNA double strand breaks were detected by microscopical analysis of γH2AX foci 24h after irradiation. The radiosensitivity was measured by colony forming assay.

Results

Physiological relevant selenium concentrations (70 and 140 µg/l) did not affect radiation-induced DNA double strand breaks (γH2AX foci) and apoptosis (Caspase-3/7) in both cell lines. Most importantly, clonogenic survival data revealed that selenium supplementation does not impair the radiosensitivity of the investigated breast cancer cell lines.

Conclusion

Our data demonstrate that administration of selenium in physiological relevant concentrations does not affect radiosensitivity of breast cancer cells in vitro. However, preclinical as well as clinical studies comparing the effectiveness of radiotherapy and the associated side effects in breast cancer patients with and without selenium supplementation are required.

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EP-2305 Selective ATP hydrolysis inhibition in F1Fo ATP synthase enhances radiosensitivity in A549 cells

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