Phase I randomized, placebo-controlled, cross-over dose-finding pharmacokinetic study of Coenzyme Q10 during one cycle of doxorubicin treatment for breast cancer.

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Abstract

Aim: To determine the safety of Coenzyme Q10 (CoQ10) in breast cancer patients receiving doxorubicin treatment. Methods: Phase I randomized, placebo-controlled, cross-over, dose-finding pharmacokinetic study among women with stage I-III breast cancer receiving 4 cycles of doxorubicin plus cyclophosphamide. The study was designed to test the maximum tolerated dose of CoQ10 using up to 1200 mg/day. Eligible patients were randomized to Arm A (CoQ10 after Cycle 3, followed by placebo after Cycle 4) or Arm B (placebo after cycle 3, followed by CoQ10 after cycle 4). CoQ10 concentrations and total antioxidant capacity (TAC) were measured before and after chemotherapy cycles. Non-compartmental pharmacokinetic parameters of doxorubicin and its active metabolites were measured with and without CoQ10. Paired t-tests assessed intra-patient differences in pharmacokinetic parameters, serum CoQ10 concentrations, TAC and adverse events. Results: Six patients received 300 mg/day of CoQ10 [Arm A (n=3), Arm B (n=3)]. One patient received 600 mg/day of CoQ10 but was discontinued due to non-adherence. Serum CoQ10 concentrations were increased in patients receiving 300 mg/day (mean±SD change: CoQ10, 1.6±0.9 ug/mL; placebo, -0.01±0.3 ug/mL; P=0.01). There were no clinically significant pharmacokinetic interactions between 300 mg/day CoQ10 and doxorubicin and no differences in TAC or adverse events during treatment and nontreatment periods. The trial was closed early due to slow accrual. Conclusions: 300 mg/day of CoQ10 with doxorubicin did not change doxorubicin pharmacokinetics and was not associated with treatment-related adverse events. Future studies should evaluate the long-term effects of CoQ10 at 300 mg/day and safety studies should examine higher doses.

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The authors confirm that the Principal Investigator for this paper is Heather Greenlee, ND, PhD, MPH, and that as Director of the Breast Medical Oncology Program at Columbia University Irving Medical Center, Dawn Hershman, MD, MS had direct clinical responsibility for patients.

Running Head: CoQ10 and doxorubicin pharmacokinetics in breast cancer patients

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What is known about this subject

- Doxorubicin is a life-saving chemotherapy regimen for breast cancer, but it is associated with cardiomyopathy and congestive heart failure.
- In breast cancer patients, there are no routinely used, effective interventions to prevent doxorubicin-induced cardiotoxicity.
- Coenzyme Q10 (CoQ10) is a fat-soluble antioxidant dietary supplement which has been hypothesized to prevent cardiotoxicity from doxorubicin and/or its metabolites.

What this study adds

- CoQ10 at 300 mg/day over one cycle of treatment did not change doxorubicin pharmacokinetics for breast cancer patients.
- Co-administration of doxorubicin and CoQ10 at 300 mg/day did not increase treatment-related serious adverse events for breast cancer patients.
- Poor accrual to this trial demonstrates the challenge of testing CoQ10 with concurrent chemotherapy and warrants future studies to replicate and extend study results.

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