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Cardioprotective Agents for the Primary Prevention of Trastuzumab-Associated Cardiotoxicity: A Systematic Review and Meta-Analysis

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In recent years, the incidence of breast cancer has been increasing on an annual basis. Human epidermal growth factor receptor-2 (HER2) is overexpressed in 15-25% human breast cancers, which is associated with poor prognosis and a high recurrence rate. Trastuzumab is the first humanized monoclonal antibody against HER2. Trastuzumab-induced cardiac dysfunction is one of the major side effects of trastuzumab therapy in breast cancer patients and the main reason for discontinuation, which significantly limits its safe use. Unfortunately, the mechanism causing this cancer therapy-related cardiac dysfunction (CTRCD) is still not completely understood and the use of preventive interventions remains controversial. There are significant considerations about the prevention of cardiotoxicity caused by trastuzumab therapy in patients with breast cancer, leading to discontinuation. The present meta-analysis aimed to address the question of whether there is a clinical benefit from the early administration of cardioprotective drugs in parallel to trastuzumab therapy in patients without any previous cardiac dysfunction. The primary objective of this systematic review and meta-analysis was to evaluate the primary prevention of cardiotoxicity, via cumulative cardioprotective effects of pharmaceutical agents (BBs, ACEIs or ARBs) versus placebo, in patients with HER-2 positive breast cancer undergoing trastuzumab chemotherapy without any index of HF at the beginning of the therapy. The secondary objective was the comparative evaluation of ACEIs, ARBs and BBs in cardiotoxicity prevention, by assessing: (1) the number of patients who discontinued trastuzumab therapy, (2) the changes in LVEF or global longitudinal strain (GLS) after 3 months of follow-up and (3) the change in cardiac serological biomarkers. The secondary objective was obtained by comparing patients receiving either a single drug or any combination of those cardioprotective drugs with patients receiving placebo. Recently, randomized controlled trials (RCTs) have evaluated the effects of early commitment of beta-blockers (BBs), angiotensin receptor blockers (ARBs) and angiotensin converting enzyme inhibitors (ACEIs) during trastuzumab chemotherapy in order to prevent the related cardiotoxicity. The present systematic review and meta-analysis of six RCTs included patients who have predominantly non-metastatic, HER2-positive, breast cancer and received trastuzumab as primary or adjuvant therapy. Those patients did not have any obvious cardiac dysfunction or any previous therapy with cardioprotective agent. We evaluated the efficacy of the aforementioned medications for primary prevention of cardiotoxicity, using random effects models. Any preventive treatment did not reduce cardiotoxicity occurrence compared to controls (Odds ratios (OR) = 0.92, 95% CI 0.54-1.56, $p = 0.75$). Results were similar for ACEIs/ARBs and beta-blockers. Treatment with ACEIs/ARBs led to a slight, but significant, increase in LVEF in patients compared to the placebo group. Only two studies reported less likelihood of discontinuation of trastuzumab treatment. More adequately powered RCTs are needed to determine the efficacy of routine prophylactic therapy.

Biography

Kyriakos Goulas, a dedicated medical researcher, lends his expertise to innovative healthcare solutions from Switzerland. With a strong background from the University of Cyprus Medical School and Aristotle University of Thessaloniki he seamlessly integrates medical expertise with cutting-edge advancements. Affiliated as resident with Inselspital, Universitätsspital Bern, he drives transformative changes in patient care. His commitment to evidence-based medicine is evident in prolific research, notably in preventing cardiotoxicity from trastuzumab therapy for breast cancer. Beyond cardio-oncology, Kyriakos extends his influence to AI in healthcare, leveraging its potential for early disease detection and personalized treatment. He serves as Assistant Researcher at Aristotle University's Laboratory of Hygiene, Social & Preventive Medicine, as well as the 3rd Department of Internal Medicine at General Hospital Papageorgiou. Kyriakos's journey underscores unwavering commitment to patient well-being, bridging medicine and technology. His diverse contributions establish him as a respected figure in medical and technological circles, leaving an indelible mark on modern medicine.