Kardiotoksičnost uzrokovana trastuzumabom Cardiotoxicity caused by trastuzumab therapy

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UVOD: Trastuzumab je humanizirano monoklonsko protutijelo na HER2 protein koje se koristi za imunoterapiju raka dojke. Njegova najvažnija nuspojava je kardiotoksičnost koja se najčešće manifestira kao reverzibilno smanjenje kontraktilnosti lijeve klijetke. Međutim, ponekad bolest može napredovati do ireverzibilne dilatacijske kardiomiopatije. Do sada, se još uvijek ne može jasno procijeniti individualni rizik kardiotoksičnosti kao i predvidjeti ireverzibilnost bolesti.

METODE: U ovoj studiji provedenoj u kliničkom centru pratili smo bolesnice s ne-metastatskim karcinomom dojke, liječenih standardnim adjuvantnim protokolom trastuzumabom kroz godinu dana. Kardiotoksičnost je definirana smanjenjem istisne frakcije lijeve klijetke (EFLV) za 15% od početne vrijednosti ili 10% od normalnih vrijednosti. Ehokardiografija je učinjena prije početka terapije i u tromjesečnim razmacima tijekom terapije.

REZULTATI: Određeni stupanj kardiotoksičnosti ustanovljena je u 13,2% bolesnica. Povećani rizik razvoja kardiotoksičnosti utvrđen je kod bolesnica s tumorom lijeve dojke, mutiranim D/D genotipom gena za angiotenzin konvertirajući enzim (ACE) i s pozitivnom obiteljskom anamnezom kardiovaskularnih bolesti. Smanjen rizik utvrđen je u bolesnica prethodno liječenih po FEC protokolu. Ireverzibilni oblik kardiotoksičnosti češće je nađen u bolesnica s većim smanjenjem EFLV i u bolesnica kojima je imunoterapija trastuzumabom započeta ranije nakon prethodne kemoterapije.

ZAKLJUČAK: Bolesnice s tumorom lijeve dojke, D/D genotipom za ACE i pozitivnom obiteljskom anamnezom za kardiovaskularne bolesti imaju veći rizik razvoja kardiotoksičnosti na imunoterapiju trastuzumabom stoga je kod takvih bolesnica potreban poseban oprez prilikom praćenja i liječenja. Trastuzumabom izazvana kardiotoksičnost će vjerojatnije biti ireverzibilna u bolesnica s izraženijim padom EFLV i ako je vrijeme između prethodne kemoterapije i primjene trastuzumabom bilo kraće od 30 dana.

INTRODUCTION: Trastuzumab is humanized monoclonal antibody to the HER2 protein, in use for immunotherapy of breast cancer. It's most important side effect is cardiotoxicity, mainly manifested as a reversible reduction in left ventricular contractility. However, sometimes the disease can progress to irreversible dilated cardiomyopathy. So far, it is still unclear how to assess individual risk for cardiotoxicity and how to predict irreversibility of the disease.

METHODS: In this single center study we followed patients (pts) with non-metastatic breast cancer, treated with trastuzumab for one year with the standard adjuvant therapy protocol. Cardiotoxicity was defined with the reduction of left ventricular ejection fraction (LVEF) by 15% from the baseline or by 10% of normal values. Echocardiography was performed before the beginning and in three months period during therapy.

RESULTS: Cardiotoxicity was established in 13.2%. We found that pts with left side tumor, D/D ACE genotype and with a positive family history of cardiovascular disease had an increased risk of cardiotoxicity. A decreased risk of cardiotoxicity was found in patients previously treated with FEC protocol. Pts with irreversible cardiotoxicity had significantly greater reduction of LVEF and in those pts trastuzumab was started earlier after prior chemotherapy.

CONCLUSION: Pts with tumor of the left breast, D/D ACE genotype and positive family history of cardiovascular disease have higher risk of developing cardiotoxicity with trastuzumab therapy and should be treated as high risk pts. Trastuzumab induced cardiotoxicity is more likely to be irreversible in pts with more extensive fall of the EFLV and with the time between prior chemotherapy and administration of trastuzumab shorter than 30 days.

LITERATURE

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