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Research Journal of Congenital Diseases

2021

Vol.4 No.1

5 year experience of Transthoracic Echocardiographic assessment of left ventricular systolic dysfunction in Hormone receptor positive Breast cancer patients on Trastuzumab therapy

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Received date: November 25, 2021; Accepted date: December 01, 2021; Published date: December 10, 2021

Introduction

Trastuzumab has been used as an adjunct to chemotherapy in receptor positive breast cancer patients. However it is known to cause cardiomyopathy with left ventricular systolic dysfunction in about 27%, with NYHA class ¾ symptoms in 16% of cases. Consequently, guidelines suggest screening and regular follow up transthoracic echocardiograms at 3 monthly intervals, to assess left ventricular systolic dysfunction (LVSD).

Purpose

The aim of this 5 year study was to compare mortality, morbidity, predisposing factors and regional wall motion abnormalities (RWMA) on Echocardiogram influencing prognosis in Hormone receptor positive Breast cancer patients treated with Trastuzumab.

Methods

This is a retrospective cohort study obtained from the echocardiography registry and patient electronic case records at Heart of England NHS trust, from January 2010 to December 2015. We analyzed 134 female patients referred for Echocardiographic assessment who had received adjunctive Trastuzumab therapy, following usual standard treatment with (5- Fluorouracil, Epirubicin, Cyclophosphamide and Docataxel). All patients had screening and 3 monthly follow up echocardiograms to assess left ventricular systolic function(LVSF), (Ejection fraction calculated by Simpson's Biplane method) along with regional wall motion abnormality assessment (RWMA) and independently verified (blinded) by a senior clinical scientist. Patients with ejection fraction(EF) of <50% or a drop of 10 points in EF, were promptly intimated to the referring oncologist and started on standard heart failure treatment, Trastuzumab therapy was discontinued until reversal of systolic function was achieved.

Results

134 Female patients underwent screening echocardiogram. 12 of these had RWMA on screening (with normal LVSF). 115 patients had stable left ventricular systolic function (Group 1) and 19 patients developed left ventricular systolic dysfunction (LVSD) during treatment, necessitating discontinuation of Trastuzumab therapy (Group2).Patients in group 1 were 2 years older (59.9 group 1 vs 57.8 years group 2). In Group 1, 4 of 115 patients had RWMA as compared to 8 of 19 in Group 2 (P=0.0001). In group 2 with RWMA, 5 had complete reversibility of left ventricular systolic function (LVSF) 1 had partial reversibility (<50%) and 2 had mild reversibility (< 10%). Further, in Group 2, 11 patients with no RWMA, 9 had complete reversibility and 2 had mild reversibility. None of the patients in both groups had documented ventricular arrhythmias. 1 patient in group 1 died of Metastases to Liver, whereas there were no deaths in Group 2. 1 patient in Group 1 had Metastasis to bone and liver, but had stable LVSF with Trastuzumab therapy. The mean period to development of LVSD in patients with RWMA was 139 days as compared to 192 days in patients with no RWMA.

Conclusion

Simpson's biplane method for calculation of LVSF proved to be a cost effective tool in calculating ejection fraction, for monitoring LVSF in patients with Breast cancer on Trastuzumab therapy. Patients with screening echocardiographic evidence of RWMA appear to have higher incidence of LVSD following adjuvant chemotherapy with Trastuzumab, as compared to patients with no RWMA. Patients with pre-existing RWMA seem to develop LVSD quicker than in patients without RWMA on screening echocardiograms. However, this does not appear to be a predictor of complete reversibility of LVSF. Closer follow-up of these patients may be necessary. Future authentic, randomized control trials would be invaluable in predicting outcomes in certain patient groups, thus facilitating early cessation of therapy and prevention of heart failure.

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