A Systematic Literature Review:
The role of guideline directed medical therapy in trastuzumab induced heart failure and cardiotoxicity

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ABSTRACT

PURPOSE

When chemotherapy medications that can cause cardiotoxicity or heart failure are administered, such as trastuzumab, the administration of guideline-directed medical therapy (GDMT) for heart failure is necessary. Administration of heart failure medications is especially important to prevent the exacerbation of heart failure, and further, the need for transplant. Current AHA guidelines suggest that the use of beta-blockers and ACEi in patients with trastuzumab-induced cardiomyopathy are effective in improving LV dysfunction. ARNI, ARBs, SGLT2s, and ivabridine may also be effective in treating trastuzumab-induced cardiomyopathy. The purpose of this study was to evaluate the usage and effectiveness of ARNI, ARBs, SGLT2s, and ivabradine in addition to ACEi and/or beta-blockers in adult patients for the prevention and treatment of trastuzumab-induced cardiomyopathy.

METHODS

A systematic literature search was done using the Medline databases to identify relevant articles. The terms “trastuzumab”, “ARNI”, “SGLT2”, and “ARB” were used as search criteria in the database. Inclusion criteria included studies with adult women greater than or equal to 18 years of age receiving trastuzumab and administration of GDMTs for the prevention and/or treatment of heart failure. The primary objective was to identify if the administration of GDMTs improved either the clinical manifestations or morbidity and mortality of heart failure. Improvement of clinical manifestations of heart failure was defined as the reduction in shortness of breath, edema, and fatigue. Improvement of morbidity and mortality was assessed by a reduction in heart failure exacerbation hospitalizations and death.

RESULTS

Three articles were identified to meet the above inclusion criteria. 92 patients were analyzed. Two of the articles compared the use of ARBs in conjunction with beta blockers. One article evaluated the use of Ivabradine

CONCLUSIONS

Use of ARBs and/or Ivabradine in addition to ACEi and/or beta blockers to treat trastuzumab-induced cardiomyopathy may be effective in some patients. Further investigation needs to be done to determine if effectiveness depends on treatment length, initiation of additional agents, and/or heart failure severity, as determined by morbidity, mortality and clinical manifestations. Also, more studies need to be done to determine whether SGLT2s and ARNIs are effective in the prevention and/or treatment of trastuzumab-induced cardiomyopathy.

RESEARCH

BACKGROUND

Trastuzumab is associated with symptomatic and asymptomatic left ventricular dysfunction. Often leading to discontinuation of trastuzumab and cardiac morbidity.

Trastuzumab induced cardiotoxicity is reversible and dosage dependent .

The receptor targeted by trastuzumab erbB2,is a receptor tyrosine kinase essential for cardiac development, and can result in dilated cardiomyopathy. When used in combination with anthracyclines it worsens cardiac damage by preventing the protective effects of neuregulin-1.

ARNI, ARBs, ACE-I, and beta blockers are mainstays in heart failure to reduce morbidity and mortality.

OBJECTIVE

The primary objective of this study is to identify if use of guideline directed medical therapy (GDMT) such as ARB, ARNI, SGLT2, and Ivabradine can improve morbidity or mortality in trastuzumab induced heart failure and cardiotoxicity

METHODS

A systematic literature search was done using the Medline databases.

The search terms “trastuzumab”, “ARNI”, “SGLT2”, and “ARB” were used as search criteria in the database.

Case reports and studies containing patients 18 years or older receiving ARBS, SGLT2, ARNI, or Ivabradine for the prevention and/or treatment of heart failure were included in analysis.

RESULTS

Article	Patients	Treatment	Reduction in Morbidity or Mortality	Notes
Blanter, Julia B	N	ARB	Y	Patients in this study were treated with both beta blockers and ARBs. This study demonstrated early intervention can preserve LVEF and prevent cardiotoxicity.
Heck, Siri	62	ARB	Y	Patients were treated with candesartan o r metoprolol or both in this study. Patients treated with candesartan demonstrated beneficial effect on cardiac remodeling but did not prevent myocardial injury except when used in conjunction with metoprolol.
Sarrochi, Mateo	30	Ivabradine	Y	After 6.5 months treatment with ivabradine resulted in an increase in LVE, improved fatigue and NYHA class

CONCLUSIONS

Ivabradine use resulted in increased LVEF, reduction in fatigue, and NYHA class improvement.
ARBs did not prevent myocardial injury but did result in an overall preservation of systolic function and improved cardiac remodeling
ARBs used with beta blockers can result in improved outcomes.
More trials need to be completed but both ivabradine and ARBs could play a key role in prevention and treatment of trastuzumab induced heart failure.

REFERENCES

- Circulation: Heart Failure. 2013;6:358–361

DISCLOSURES

Authors of this presentation have nothing to disclose concerning possible financial or personal relationships with commercial entities that may have a direct or indirect interest in the subject matter of this presentation