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

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ABSTRACT

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-1, 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 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 ARNI are effective in the prevention and/or treatment of trastuzumab-induced cardiomyopathy.

BACKGROUND

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

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

RESULTS

<table>
<thead>
<tr>
<th>Article</th>
<th>Patients</th>
<th>Treatment</th>
<th>Reduction in Morbidity or Mortality</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blanter, Julio B</td>
<td>N ARB</td>
<td>Y</td>
<td>Patients in this study were treated with both beta blockers and ARBs. This study demonstrated early intervention can preserve LVEF and prevent cardiotoxicity.</td>
<td></td>
</tr>
<tr>
<td>Heck, Siri</td>
<td>62 ARB</td>
<td>Y</td>
<td>Patients were treated with candesartan or a 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.</td>
<td></td>
</tr>
<tr>
<td>Sarrochi, Mateo</td>
<td>30 Ivabradine</td>
<td>Y</td>
<td>After 6.5 months treatment with ivabradine resulted in an increase in LVEF, improved fatigue and NYHA class.</td>
<td></td>
</tr>
</tbody>
</table>

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


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.