Review: β blockers reduce mortality and therapy withdrawal in heart failure but increase dizziness and bradycardia


Clinical impact ratings GP/FP/Primary care ★★★★★☆☆ IM/Ambulatory care ★★★★★☆☆ Internal medicine ★★★★★☆☆

Q In patients with heart failure (HF) with systolic dysfunction, what are the risks associated with β blocker therapy?

METHODS

Data sources: studies were identified by searching Medline (1966–2002) and bibliographies of relevant articles.

Study selection and assessment: studies were selected if they were randomised controlled trials (RCTs) that used non-crossover designs, compared β-blocker therapy with placebo in patients with HF with left ventricular systolic dysfunction, enrolled >100 patients in each treatment group, had ≥6 months of follow up, and reported adverse effects.

Outcomes: all cause therapy withdrawal, all cause mortality, HF hospital admission, worsening HF, hypotension, dizziness, bradycardia, and fatigue.

MAIN RESULTS

9 RCTs (14 594 patients, mean age range 49–67 y) with mean follow up 6–24 months were included. Interventions included carvedilol (3 RCTs), metoprolol (3 RCTs), bisoprolol (2 RCTs), and bucindolol (1 RCT). Compared with placebo, β-blockers reduced the risks of all cause mortality, HF hospital admission, worsening HF, and all cause withdrawal of treatment but increased the risks of dizziness and bradycardia; groups did not differ for hypotension or fatigue (table).

CONCLUSION

In patients with heart failure (HF) with systolic dysfunction, β blockers reduce the risks of all cause mortality, HF hospital admission, worsening HF, and all cause withdrawal of treatment, but are associated with increased risks of dizziness and bradycardia.

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Commentary

The review by Ko et al of placebo controlled trials of β blockers for HF discusses the overall benefits of these agents, which are substantial, in the context of adverse effects, which are minimal and do not seem to affect therapy withdrawal (except to actually prevent therapy withdrawal). The only criticism of this review is that no quality rating was used for the individual studies. The most relevant quality component would be the use of a systematic method for assessing side effects within each study and whether this affected the differential discovery of adverse events. Without a systematic method, one could imagine potential bias against finding adverse events or side effects, making it possible to underestimate the incidence of side effects. Nevertheless, the fact that patients were less likely to withdraw from other lifesaving therapies when they were receiving a β blocker shows that this may not be a substantial issue.

Other side effects that might have been attributable to β blockers not reported in this synthesis include depression and sexual dysfunction. In a previous meta analysis by these authors, no increased risk of depressive symptoms was associated with β blockers, and only a small increased risk of sexual dysfunction or fatigue was seen. Thus, it seems quite clear that, in patients with HF with systolic dysfunction, one should not be deterred against finding adverse events or side effects, making it possible to underestimate the incidence of side effects. Nevertheless, the fact that patients were less likely to withdraw from other lifesaving therapies when they were receiving a β blocker shows that this may not be a substantial issue.

Some lingering questions remain, however. Because the upper age limit was 67 years, how generalisable are these results to older patients who have the largest illness burden from HF and who take more medications with which β blockers could interact? Are there differential effects of different types of β blockers? Are all β blockers equally effective?

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<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Number of trials (n)</th>
<th>Weighted event rates</th>
<th>RRR (95% CI)</th>
<th>NNT (CI)</th>
<th>NNT/year</th>
</tr>
</thead>
<tbody>
<tr>
<td>All cause mortality</td>
<td>9 (14 594)</td>
<td>β blocker 13%</td>
<td>Placebo 17%</td>
<td>27% (15 to 38)</td>
<td>22 (16 to 39)</td>
</tr>
<tr>
<td>HF hospital admission</td>
<td>8 (13 478)</td>
<td>β blocker 17%</td>
<td>Placebo 23%</td>
<td>26% (17 to 34)</td>
<td>17 (13 to 26)</td>
</tr>
<tr>
<td>Worsening HF</td>
<td>4 (4 439)</td>
<td>β blocker 26%</td>
<td>Placebo 34%</td>
<td>17% (2 to 29)</td>
<td>18 (11 to 150)</td>
</tr>
<tr>
<td>All cause withdrawal of treatment</td>
<td>9 (14 594)</td>
<td>β blocker 16%</td>
<td>Placebo 18%</td>
<td>11% (2 to 19)</td>
<td>51 (30 to 278)</td>
</tr>
<tr>
<td>Dizziness</td>
<td>4 (10 082)</td>
<td>β blocker 22%</td>
<td>Placebo 17%</td>
<td>37% (9 to 71)</td>
<td>17 (9 to 67)</td>
</tr>
<tr>
<td>Bradycardia</td>
<td>7 (13 796)</td>
<td>β blocker 6%</td>
<td>Placebo 2%</td>
<td>262% (148 to 428)</td>
<td>22 (14 to 39)</td>
</tr>
<tr>
<td>Hypotension</td>
<td>7 (13 796)</td>
<td>β blocker 8%</td>
<td>Placebo 6%</td>
<td>41% (4–106)</td>
<td>Not significant</td>
</tr>
<tr>
<td>Fatigue</td>
<td>3 (7 993)</td>
<td>β blocker 24%</td>
<td>Placebo 22%</td>
<td>4% (3 to 11)</td>
<td>Not significant</td>
</tr>
</tbody>
</table>

*Abbreviations defined in glossary; RRR, RRI, NNT, NNH, and CI calculated from data in article using a random effects model.
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