Carvedilol reduced mortality and hospital admission in severe chronic heart failure, regardless of pretreatment systolic BP


Clinical impact ratings IM/Ambulatory care ★★★★★ Internal medicine ★★★★★ Cardiology ★★★★★★☆

How does pretreatment systolic blood pressure (SBP) affect the efficacy and safety of carvedilol in patients with severe chronic heart failure (HF)?

More patients in the carvedilol group than in the placebo group reported dizziness (24% vs 17%, {p < 0.001}), hypotension (15% vs 9%, {p < 0.001}), syncope (8% vs 5%, {p = 0.0045}), and bradycardia (12% vs 5%, {p < 0.001}), whereas fewer patients reported HF (28% vs 34%, {p = 0.002}), to a similar extent in each BP subgroup. The risk of a serious adverse event increased as pretreatment BP decreased (p < 0.001). However, patients in the carvedilol group were less likely to have a serious adverse event than those who received placebo (39% vs 46%, {p = 0.002}). This benefit increased as pretreatment SBP decreased (interaction p = 0.03).

CONCLUSION

In patients with severe chronic heart failure, carvedilol reduced the risk of all cause mortality and combined mortality and general and cause specific hospital admission regardless of pretreatment systolic blood pressure.

*R*Calculated from data in article.

Commentary

The COPERNICUS study was designed to examine the effect of carvedilol on mortality in patients with severe HF and a left ventricular ejection fraction <25%. Clearly, with a 35% reduction in mortality, COPERNICUS proved the benefits of carvedilol in patients with severe HF having symptoms at rest or with minimal exertion. However, some clinicians may be reluctant to initiate carvedilol in patients with advanced HF with relative hypotension below a SBP of 110 mm Hg. Rouleau et al help to alleviate concerns regarding use of β-blockers, specifically carvedilol, in patients with severe HF and low BP. In their retrospective subgroup analysis of COPERNICUS, the authors showed that patients who had the lowest BP, and thus the highest risk of death or morbidities, derived the greatest absolute benefit from treatment with carvedilol. Interestingly, these patients also have other characteristics supporting their advanced stage of disease, with a lower ejection fraction, higher creatinine concentrations, lower sodium concentrations, and a higher rate of spironolactone use. Since this publication, others have addressed similar concerns of the adverse effects of β-blockers by performing a meta-analysis of 9 trials (14 000 patients) to reach the same conclusion that adverse effects, including hypotension, are low, whereas the overall benefits are quite large. However, it is important to remember that patients with the most advanced HF (eg, those with ongoing decompensated HF or those requiring inotropic support) were not included in these studies. Furthermore, patients with SBP < 85 mm Hg were excluded from COPERNICUS. Thus, initiation of β-blockers is supported once acute issues have resolved, even in patients with relative hypotension. For most patients, it is safe to initiate β-blockers before discharge, and evidence suggests that outpatient use of β-blockers is higher if started before discharge.

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