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**JAMA**

## Metabolic effects of carvedilol vs metoprolol in patients with type 2 diabetes mellitus and hypertension: a randomized controlled trial.

**Bakris GL, Fonseca V, Katholi RE, McGill JB, Messerli FH, Phillips RA, Raskin P, Wright JT Jr, Oakes R, Lukas MA, Anderson KM, Bell DS; GEMINI Investigators.**

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**CONTEXT:** Beta-blockers have been shown to decrease cardiovascular risk in patients with hypertension and type 2 diabetes mellitus (DM); however, some components of the metabolic syndrome are worsened by some beta-blockers. **OBJECTIVE:** To compare the effects of beta-blockers with different pharmacological profiles on glycemic and metabolic control in participants with DM and hypertension receiving renin-angiotensin system (RAS) blockade, in the context of cardiovascular risk factors. **DESIGN, SETTING, AND PARTICIPANTS:** A randomized, double-blind, parallel-group trial (The Glycemic Effects in Diabetes Mellitus: Carvedilol-Metoprolol Comparison in Hypertensives [GEMINI]) conducted between June 1, 2001, and April 6, 2002 at 205 US sites that compared the effects of carvedilol and metoprolol tartrate on glycemic control. The 1235 participants were aged 36 to 85 years with hypertension (>130/80 mm Hg) and type 2 DM (glycosylated hemoglobin [HbA1c], 6.5%-8.5%) and were receiving RAS blockers. Participants were followed up for 35 weeks. **INTERVENTIONS:** Participants were randomized to receive a 6.25- to 25-mg dose of carvedilol (n = 498) or 50- to 200-mg dose of metoprolol tartrate (n = 737), each twice daily. Open-label hydrochlorothiazide and a dihydropyridine calcium antagonist were added, if needed, to achieve blood pressure target. **MAIN OUTCOME MEASURES:** Difference between groups in mean change from baseline HbA1c following 12 months of maintenance therapy. Additional prespecified comparisons include change from baseline HbA1c in individual treatment groups, treatment effect on insulin sensitivity, and microalbuminuria. **RESULTS:** The 2 groups differ in mean change in HbA1c from baseline (0.13%; 95% confidence interval [CI] -0.22% to -0.04%; P = .004; modified intention-to-treat analysis). The mean (SD) HbA1c increased with metoprolol (0.15% [0.04%]; P < .001) but not carvedilol (0.02% [0.04%]; P = .65). Insulin sensitivity improved with

carvedilol (-9.1%; P = .004) but not metoprolol (-2.0%; P = .48); the between group difference was -7.2% (95% CI, -13.8% to -0.2%; P = .004). Blood pressure was similar between groups. Progression to microalbuminuria was less frequent with carvedilol than with metoprolol (6.4% vs 10.3%; odds ratio 0.60; 95% CI, 0.36-0.97; P = .04). **CONCLUSIONS:** Both beta-blockers were well tolerated; use of carvedilol in the presence of RAS blockade did not affect glycemic control and improved some components of the metabolic syndrome relative to metoprolol in participants with DM and hypertension. The effects of the 2 beta-blockers on clinical outcomes need to be compared in long-term clinical trials.

Publication Types:

- Clinical Trial
- Multicenter Study
- Randomized Controlled Trial

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