

Calcium antagonists did not increase mortality in patients with coronary artery disease

Braun S, Boyko V, Behar S, et al., on behalf of the Bezafibrate Infarction Prevention Study Participants. **Calcium antagonists and mortality in patients with coronary artery disease: a cohort study of 11,575 patients.** *J Am Coll Cardiol.* 1996 Jul;28:7-11.

Objective

To determine the risk for death associated with the use of calcium antagonists (nifedipine, verapamil, or diltiazem) in patients with chronic coronary artery disease.

Design

Cohort study derived from the Bezafibrate Infarction Prevention (BIP) study.

Setting

18 cardiology departments in Israel.

Patients

15 502 patients with chronic coronary artery disease who were screened but not included in the BIP study. After a mean follow-up period of 3.2 years, mortality data were available for 11 575 patients (mean age 60 y, 79% men).

Commentary

A recent case-control study (1) and a meta-analysis (2) that link short-acting calcium channel blockers to an increase in the cardiovascular mortality rate have generated an inordinate amount of media coverage and concern. These preliminary reports, however, were not designed to establish a causal relation. The current observational study by Braun and colleagues reviews a large cohort of patients who were treated for known coronary artery disease. No increase in mortality rate was noted after careful adjustment for differences between patients who were receiving the calcium antagonists and those who were not. In addition, subgroup analysis failed to identify any group with an increase in risk for death.

This study should help quiet fears that were stimulated by the controversy over calcium channel blockers. Many patients

Assessment of risk factors

5843 patients who were receiving calcium antagonists (diltiazem, $n = 3320$ [57%]; nifedipine, $n = 1999$ [34%]; verapamil, $n = 350$ [6%]; and a combination of 2 calcium antagonists, $n = 174$ [3%]) were compared with 5732 patients who were not receiving calcium antagonists (control group).

Main outcome measures

Total mortality rate taken from national databases.

Main results

495 deaths (8.5%) occurred among the patients receiving calcium antagonists and 410 deaths (7.2%) occurred in the control group. The age-adjusted relative risk (RR) for death associated with calcium antagonists was 1.08 (95% CI 0.95 to 1.24). Multivariate analysis was done with further adjustment for differences between the groups in age, sex, previous myocardial infarction, angina, New York Heart Association (NYHA) functional class, hypertension, peripheral vascular disease, chronic obstructive pulmonary disease, diabetes, and smoking. The analysis showed that

in this trial who were treated for known coronary artery disease did not have adverse effects from receiving short-acting calcium antagonists. If small differences in risk for death do indeed exist among classes of antihypertensive medications, this conclusion will have to wait until well-designed randomized trials are completed.

Until then, what is the clinician to do? These studies point out that medications must be appropriately used. Short-acting calcium channel blockers should not be prescribed for chronic hypertension, and nifedipine (a short-acting dihydropyridine) is not indicated after a myocardial infarction (1, 2). Long-acting calcium antagonists have not been linked with any risk for death and should be preferentially prescribed instead of short-acting preparations. For patients with hypertension and angina, β -blockers are first-choice

the overall RR for death associated with calcium antagonist use was 0.97 (CI 0.84 to 1.11). After further adjustment for concomitant use of other medications (β -blockers, aspirin, nitrates, and diuretics), the overall RR for death did not substantially change (RR 0.94, CI 0.82 to 1.08). Subgroup analysis showed a decreased risk for death in patients who received calcium antagonists and who were in NYHA functional class II (RR 0.68, CI 0.53 to 0.86).

Conclusion

The use of calcium antagonists was not associated with an increased risk for death in patients with chronic coronary artery disease.

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For article reprint: Dr. S. Braun, Department of Cardiology, Tel Aviv Medical Center, 6 Weizman Street, Tel Aviv 64239, Israel. FAX 972-3-69-73-704.

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drugs; calcium antagonists and nitrates are considered as adjuvant therapy if symptoms persist. Also, patients should be warned not to suddenly stop taking their medications. Complications that arise from the progression of underlying diseases will far exceed the small hypothetical risk for death suggested by the calcium blocker studies.

*Matthew J. Sorrentino, MD
University of Chicago
Chicago, Illinois, USA*

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