

Concerns About Beta-blockers

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There is still a gap between proven benefits of beta-blockers and their utilization. The concern that beta-blockers are associated with substantial risks of depressive symptoms, fatigue, and sexual dysfunction may in part be responsible for the under-use of these agents in cardiac cases.

This Heartbeat will cover the many benefits of beta-blocker therapy—new and old—in the vast majority of patients with high-risk cardiovascular disease (CVD). It will also present the results of a recent meta-analysis, which has shown that most concerns about side effects of beta-blockers are unfounded and should not deter physicians from initiating treatment early and long-term when indicated. *Given the survival benefits associated with beta-blocker therapy, the real concern is under-usage—not side effects. The goal is to come up with a plan to get physicians to use the drugs that they should be using in more patients.*

Beta-Blockade Before Intervention

Numerous secondary prevention trials have shown that beta-blockers prevent death and reduce risk of re-infarction after MI. However, most of these studies were carried out before the role of revascularization procedures became so prominent. In the past, medical therapy and revascularization procedures were considered competitive strategies. Two recent studies have shown the complementary benefits of either percutaneous coronary intervention (PCI) or coronary artery bypass grafting (CABG) and concordant treatment with beta-blockers.

In the first study, which evaluated mortality benefit of beta-blocker after successful elective PCI, the authors concluded, “ Within this large prospective registry (4,553 patients), beta-blocker use was associated with a marked long-term survival benefit across the majority of patient sub-groups.”¹

In addition to the patients who had a history of MI, a striking survival benefit was found in patients with renal insufficiency and those who underwent multi-vessel PCI. Given the results of this large observational study, the researchers conclude, “*Medical therapy with beta-blockade and PCI should be considered complementary strategies.*”

Beta-blocker therapy has also been demonstrated to reduce cardiac events among high-risk patients undergoing major non-cardiac and vascular surgery. Updated guidelines from the American College of Cardiology and the American Heart Association were released this past spring and were covered in the March 2002 *Heartbeat*.²

Although extrapolation of these cardio-protective benefits of beta-blockers to cardiac surgery is plausible, usage has been limited (only around 60%) by concerns of depression of myocardial contractility and/or exacerbation of underlying reactive airways disease. Since CABG is one of the most commonly performed procedures in North America and the last major group of CV patients in whom this has not been tried, a review to determine whether use of beta-blockers is associated with lower operative mortality, and morbidity was performed.³ Reduction in adjusted mortality risk, as well as risk of major procedural complications were demonstrated. This benefit was shown among a variety of high-risk patient subgroups, including women, diabetics, elderly patients and those with chronic obstructive lung disease. Patients with moderate LV dysfunction appeared to benefit from beta-blockers, but those with severely depressed LV function (LVEF < 30%) were associated with a trend towards increased mortality. Major procedural complications were also reduced in patients receiving beta-blockade. Given the relatively low utilization of beta-blockers for an increasingly common procedure, the authors suggest that *boosting the number of patients receiving*

preoperative beta-blockade could translate into saving 500 lives per year.

Surgeons are now using beta-blockers to slow the heart rate during off-pump CABG surgery because it makes the operation easier, and now it's also beneficial for the patient to do that.

Prevention of Postoperative AF

In a recent meta-analysis of 52 randomized trials, Crystal et al conclude that beta-blockers, sotalol and amiodarone are all effective for the prevention of postoperative atrial fibrillation (AF), which occurs in 25-40 % of heart surgery patients.⁴ This treatment results in a reduction in hospital stay of about half a day. It should be noted that none of these strategies eliminate postoperative AF. The authors feel that *beta-blockers should be the mainstay of the strategy for reducing the incidence of postoperative AF.* Therapy with beta-blockers is inexpensive, well tolerated, and easy to initiate.

Sotalol, amiodarone or pacing strategies would be considered in conjunction with, or appropriate alternatives, if beta-blockers have failed or there is a very high preoperative probability for developing AF (patients with prior AF or mitral valve disease).

Unfounded Concerns

A quantitative review of randomized trials (15 trials involving more than 35,000 participants) was performed that tested beta-blockers in MI, heart failure and hypertension to determine the association between this class of drugs and adverse events.⁵

The conclusion was that there is no significant increase of depressive symptoms and only small absolute increased risks of fatigue and sexual dysfunction. Most of the studies that suggested associations were anecdotal. These conditions are also quite common in the placebo groups making it difficult to work out what is and what is not attributable to the medication.

Reported sexual dysfunction was evaluated in 6 studies involving 14,897 patients, with an increased risk of borderline significance—one additional report for every 199 patients treated in one year. There was

one withdrawal of study medication due to sexual dysfunction for every 438 patients treated in a year.

The authors conclude, *“Given the survival benefits associated with beta-blocker therapy, concerns about the development of these adverse effects should not deter physicians from initiating long-term treatment when indicated, although surveillance for adverse effects remains prudent.”*

Conclusion/Recommendations

The evidence supporting the use of beta-blockers in many clinical situations (post MI, LV dysfunction, hypertension, and preoperatively in high-risk patients for non-cardiac surgery) is clear. Concerns about side effects are unfounded. Expanding beta-blocker use to the pre-intervention group of coronary artery disease patients as complementary therapy to improve outcomes is warranted. Additionally it is the strategy of choice to prevent AF in cardiac surgery patients.

Twenty plus years ago, patients on beta-blockers were sent home for two weeks to let it wash out of their system. By contrast today, now that we know beta-blockers improve survival, the challenge for the interventionists, surgeons, or anesthesiologists will be to identify those patients who are candidates—not on beta-blockers—and initiate therapy, immediately before the procedure.

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Heartbeats can be found at www.sjhg.salu.net under Patient Education—From Your Physician.

¹ Chan AW, et al. Mortality benefit of beta-blockade after successful elective percutaneous coronary intervention. *J Am Coll Cardiol* August 25 2002; 40: 669-75.

² Maiese ML, et al. Reducing CV risk in non-cardiac surgery. *Heartbeat* 66 March 2002; www.sjhg.salu.net Patient education—from your physician

³ Ferguson TB, et al. Preoperative B-Blocker use and mortality and morbidity following CABG surgery in North America. *JAMA* May 1 2002; 287: 2221-27.

⁴ Crystal E, et al. Prevention of postoperative atrial fibrillation. *Circulation* June 2002; 106: 75-80.

⁵ Ko DT, et al. Beta-blocker therapy and symptoms of depression, fatigue, and sexual dysfunction. *JAMA* Jul 17 2002; 208: 351-57.