Drug Monitor

Beta-blockers and Diabetes

Beta-blocker therapy is one of the most common treatments for hypertension. But how does it affect the development of new-onset diabetes, which puts hypertensive patients at particularly high cardiovascular risk?

To find out, researchers from St. Luke's-Roosevelt Hospital and Columbia University College of Physicians and Surgeons, both in New York, NY, and Chaim Sheba Medical Center and Sackler School of Medicine, Tel-Hashomer, Israel performed a meta-analysis of 12 randomized, controlled trials involving 94,492 patients. All of the trials compared beta-blocker therapy for hypertension with other antihypertensive therapies and evaluated the occurrence of new-onset diabetes.

The analysis showed that beta-blocker therapy increased diabetes risk by 33% compared with placebo and 22% compared with nondiuretic antihypertensive agents. Compared with thiazide diuretics, though, it decreased diabetes risk by 26%. In looking at specific beta-blockers, the researchers found that atenolol and metoprolol increased diabetes risk by 30% and 34%, respectively, compared with other antihypertensives. Although the pooled results of four propranolol trials indicated that this beta-blocker decreased diabetes risk by 23% compared with other antihypertensives, the comparison drugs in three of these trials were thiazide diuretics. The one trial that compared propranolol to placebo showed no risk reduction.

The researchers found that patients aged 60 years or older and those who had higher fasting blood glucose levels or body mass indexes at baseline were most vulnerable to the heightened diabetes risk. In addition, they found that this risk increased "exponentially" with longer duration of beta-blocker therapy and that beta-blockers raised the risk of stroke by 15%.

Given that 65 million Americans have hypertension, the researchers estimate that exclusive reliance on beta-blockers could lead to 910,000 cases of diabetes, 195,000 deaths, and 305,500 strokes every 4.4 years. They describe this possibility as "hardly an acceptable risk/benefit ratio."

Source: *Am J Cardiol.* 2007;100(8):1254–1262. doi:10.1016/j.amjcard.2007.05.057.

Topiramate for Alcoholism?

Patients who are trying to lessen their dependence on alcohol may have a valuable tool in topiramate, a sulfamate-substituted fructopyranose derivative. That was the finding of the Topiramate for Alcoholism Advisory Board and the Topiramate for Alcoholism Study Group, which conducted a 14-week trial of 371 patients diagnosed with alcohol dependence.

The researchers randomly assigned 183 patients to receive topiramate and 188 to receive placebo. The starting topiramate dosage of 25 mg/day was titrated up to a maximum of 300 mg/day during the first five weeks and then maintained for the remaining nine weeks. A minimum maintenance dosage of 50 mg/day was necessary for patients to continue in the trial.

All patients recorded their alcohol consumption on dietary cards, which they used to give self-reports at weekly assessment meetings. Through these reports, the researchers determined the percentage of study days during which patients engaged in heavy drinking (defined as five or more drinks for men or four or more drinks for women), which served as the study's primary outcome measure. Secondary outcome measures included patients' self-reported days without drinking and average number of drinks per drinking day. The researchers also measured patients' plasma γ-glutamyltransferase (GGT) levels at weeks zero, four, eight, 12, and 14 to monitor alcohol consumption.

Results indicated that topiramate was significantly more effective than placebo in helping patients to drink less, with the drug's beneficial effects occurring no later than week four and continuing throughout the trial. When patients who dropped out of the study were considered as having relapsed to baseline consumption levels, the reduction in heavy drinking days among patients taking topiramate was 8% greater than those taking placebo. Specifically, topiramate patients went from an average of 82% heavy drinking days at baseline to 44% at week 14, whereas placebo patients went from 82% to 52%. When study dropouts were left out of the calculations, the difference between the two groups doubled to 16%. The topiramate advantage over placebo was reflected by significant improvement in the other self-reported drinking outcomes and in plasma GGT measurements.

Among the adverse events reported by at least 10% of study participants, the following were significantly more frequent with topiramate than with placebo: paresthesia, taste perversion, anorexia, difficulty with concentration or attention, nervousness, dizziness, and pruritis. Given the trend toward increased adverse events with higher topiramate dosages, the researchers say, it would be of clinical interest to determine the effectiveness of lower topiramate dosages. ●

Source: *JAMA.* 2007;298(14):1641–1651.