Preop Glycemic Control Decreases Infection Risk

BY KATE JOHNSON
Montreal Bureau

Diabetic patients with good preoperative glycemic control had significantly fewer postoperative infections in a retrospective analysis of data from the Veterans Affairs National Surgical Quality Improvement Program.

"If the association is confirmed in other studies, strategies to improve glycemic control prior to elective surgery can be employed to decrease infections and improve overall outcomes for diabetic surgical patients," wrote Dr. Annika S. Dronge of Yale University, New Haven, Conn., and her colleagues.

The study included 490 diabetic surgery patients from the National Surgical Quality Improvement Program database, which prospectively collects preoperative, intraoperative, and 30-day outcomes on major noncardiac operations. All patients had a hemoglobin A_{1c} (HbA_{1c}) level recorded within 180 days prior to the surgery, with good glucose control defined as a level of less than 7%. The primary outcome of the study was postoperative infectious complications, including pneumonia, wound infection, urinary tract infection, and sepsis (Arch. Surg. 2006;141:375-80).

After adjusting for several factors known to be associated with postoperative infections, the researchers found that good long-term glycemic control was strongly associated with significantly fewer postoperative infections (odds ratio 2.13). Age, American Society of Anesthesiologists score, operation length, and wound class were also significantly associated with the risk of postoperative infection.

The authors noted that while long-term glycemic control in diabetic patients is widely recognized as decreasing both the incidence and severity of many chronic complications, only three studies have investigated its effect on postoperative infections. Two of these studies had opposite findings, but both used an HbA_{1c} level of 11.5% as the point between what they defined as good and poor glycemic control, a definition not consistent with current recommendations (J. Urol. 1992;147:386-8; J. Urol. 1998;159:1537-9). The third study used an HbA_{1c} level of 8% and showed twice as many postoperative infections in patients with high levels, compared with those with low levels (8% vs. 4%), although this did not reach statistical significance (Infect. Control Hosp. Epidemiol. 2001;22:607-12). However, a highly significant finding of this study was the increased incidence of postoperative hyperglycemia in the poorly controlled group, compared with the well-controlled group (78% vs. 43%).

The reason for the current study's finding of decreased postsurgical infection in association with good preoperative glycemic control could be linked simply to the better likelihood of postoperative glycemic control, as demonstrated by the third study, noted the authors. "Acute hyperglycemia has clearly been shown to be associated with poor outcome in a variety of clinical settings. …Tight control of glucose in the postoperative period results in fewer complications, including infections, and decreased mortality in both diabetic and nondiabetic patients," they wrote.

Another possible explanation for their findings is simply "the overall improvement in general health and metabolic milieu of the well-controlled diabetic patient."

They noted limitations of their study, including the fact that all subjects came from a single Veterans Affairs hospital and were predominantly male, making generalizability to a larger diabetic population more difficult. Additionally, the database they used did not control for factors such as smoking, nutritional status, and perioperative antibiotic use. ■

Simvastatin Raises Blood Flow, Intraocular Pressure

BY MARY ANN MOON
Contributing Writer

Simvastatin increases retinal blood flow and decreases intraocular pressure in healthy subjects, making it a potential treatment for diabetic retinopathy and glaucoma, according to Dr. Taiji Nagaoka of Asahikawa (Japan) Medical College and associates.

Noting that long-term statin use has been reported to reduce the risk of retinal ischemic diseases, the researchers assessed the effect of simvastatin on the retinal circulation and on intraocular pressure in 12 healthy volunteers.

Retinal blood flow increased significantly, by 20% in the retinal arteries and by 23% in the retinal veins, after 1 week of simvastatin therapy.

The subjects were nonsmoking Japanese men aged 19-23 years. They were examined 90 minutes after a single 20-mg dose of the drug on one occasion and after taking a placebo on a separate occasion. They also underwent similar assessments after taking daily doses of either simvastatin or placebo for 1 week.

Retinal blood flow increased significantly, by 20% in the retinal arteries and by 23% in the retinal veins, after 1 week of simvastatin therapy. Intraocular pressure decreased significantly, from 14.3 mm Hg at baseline to 12.6 mm Hg after a single dose of the drug and to 12.4 mm Hg after 1 week of therapy. Plasma nitrite/nitrate levels also rose by 60% after 1 week on simvastatin.

In contrast, all retinal measurements remained unchanged after administration of the placebo.

This is the first study to show that simvastatin increases retinal blood flow, "probably via the increase in nitric oxide," the investigators said (Arch. Ophthalmol. 2006;124:665-70).

The increase appears to be exerted mainly on the more downstream vessels in the retinal microvascular network, notably the capillaries, they added.

A previous study involving six subjects suggested that statins might improve hard exudates and microaneurysms in diabetic retinopathy. "Although the findings in the present study are obtained from healthy men whose physiological response to simvastatin may be different from that of patients with diabetes, the increased retinal blood flow associated with treatment with simvastatin may be a potential therapy for diabetic retinopathy," Dr. Nagaoka and associates said.

Similarly, another study recently reported that statin use appears to reduce the risk for glaucoma but did not measure intraocular pressure. "In the present study, we document for the first time … that the intraocular pressure was slightly but significantly decreased by simvastatin," they added.

"Further study among more subjects is needed to examine the effects of age, sex, and systemic disorders such as hyperlipidemia, hypertension, and diabetes mellitus, on the retinal circulation that are associated with systemic administration of simvastatin," they said. ■

Comparable Efficacy With Once-Daily, Extended-Release Metformin

BY SHERRY BOSCHERT
San Francisco Bureau

Three different regimens of a new extended-release version of metformin, including two once-a-day regimens, were as effective as immediate-release metformin in reducing hemoglobin A_{1c} levels in adults with type 2 diabetes, Dr. Sherwyn Schwartz reported.

A double-blind, phase III trial randomized 750 patients to 24 weeks of treatment, and 706 patients with efficacy data were included in an intent-to-treat analysis. Patients on antihyperglycemic agents stopped the medications for 6 weeks before all patients began metformin at 1,000 mg once daily. Treatment was titrated over 2-3 weeks to assigned regimens of immediate-release metformin (Glucophage) at 1,500 mg/day b.i.d., or extended-release metformin (Glumetza) in dosages of once-daily 1,500 mg/day, the same dose but b.i.d., or once-daily 2,000 mg/day.

All groups showed significant reductions in hemoglobin A_{1c} (HbA_{1c}) levels by week 12. Levels continued declining until week 20, and were maintained until the end of the study at week 24, said Dr. Schwartz, an endocrinologist in a group practice in San Antonio, and his associates (Diabetes Care 2006;29:759-64). The study was funded by Depomed Inc., which makes Glumetza.

The reductions in mean HbA_{1c} levels were similar to results from clinical trials of Glucophage and of another extended-release metformin product (Glucophage XR, by Bristol-Myers Squibb). Glumetza is the first extended-release metformin formulation, however, to show equal efficacy in daily or twice-daily dosing, Dr. Schwartz said.

Among secondary end points in the current study, all treatment groups significantly reduced fasting plasma glucose concentrations to a comparable extent. Mean fructosamine levels declined in all groups, with a significantly greater drop in the 2,000-mg group.

In the trial, 529 patients who completed the protocol switched to the once-daily 2,000-mg dose of Glumetza in an open-label extension study. The decreases in HbA_{1c} from the randomized trial were maintained in the 24-week extension study.

Each of the Glumetza regimens in the randomized trial produced greater decreases in HbA_{1c} than did Glucophage in several subgroups: in women, in patients 65 years or older, in non-Caucasians, and in patients with a body mass index (kg/m^2) of 30 or greater. The daily 2,000-mg dose provided the greatest efficacy, with some subgroups achieving HbA_{1c} levels of less than 7% (in previously untreated patients and in those aged 65 years or older).

Other studies have reported that the effects of metformin monotherapy are independent of age, ethnicity, and body weight. "Our results indicate that the 2,000-mg/day dose may be more effective in some patient populations," Dr. Schwartz said.

There was a trend for triglyceride levels to increase slightly in patients on Glumetza (similar to trends in previous trials of extended-release metformin formulations), an effect not seen with Glucophage. The reason for this and its clinical significance are unclear.

Metformin is known to cause gastrointestinal side effects, including abdominal discomfort, nausea, and diarrhea. The overall incidence of adverse events was similar between groups. Patients in the Glumetza groups were less likely to report nausea during the first week of treatment. There was no increase in adverse events seen in the 2,000-mg/day Glumetza group.

Patients in the twice-daily drug regimen groups took 500 mg in the morning and 1,000 mg in the evening. All study drugs and placebo pills were taken after a meal.

Reasons for those who stopped treatment were similar between groups, except that fewer patients in the Glumetza 2,000-mg group stopped because of lack of efficacy compared with the Glucophage group (2% vs. 8%). Reasons included withdrawal of consent, lack of efficacy, and loss to follow-up. ■