Best Add-On to Metformin in Type 2 Not Yet Clear

BY ROBERT FINN
San Francisco Bureau

A meta-analysis has failed to clarify whether one drug is better than another when added to metformin in patients with type 2 diabetes.

Sulfonylureas and α-glucosidase inhibitors—and possibly glinides as well—appear to have about equal efficacy when used as add-ons to failed metformin monotherapy, Dr. Matteo Monami and his colleagues from the University of Florence (Italy) determined in their analysis of 27 clinical trials (Diabetes Res. Clin. Pract. 2008;79:196-203).

On the other hand, thiazolidinediones appear to have a lesser effect on hemoglobin A_{1c} (HbA_{1c}) at 6 months, although in the long term they may actually work better than insulin secretagogues.

Sulfonylureas reduced hemoglobin A_{1c} by an average of 0.85%, thiazolidinediones by 0.42%, and α-glucosidase inhibitors by 0.61%.

"Despite the fact that many patients with type 2 diabetes receiving metformin need additional treatments in order to reach an adequate metabolic control, the number of clinical trials assessing the effects of combined therapy with metformin and other agents in type 2 diabetes is surprisingly small," the investigators wrote. "For this reason the result of the present meta-analysis should be considered with caution, as further evidence, if available, could affect the conclusions."

The investigators conducted their Medline search in January 2007, looking for randomized clinical trials in which metformin was associated with any one of a large number of add-on therapies. For their meta-analysis, they included only trials in which a hypoglycemic agent was compared either with placebo or with another active drug in combination with metformin for at least 16 weeks. They excluded trials of "triple therapy" that tested two or more drugs in combination with metformin.

The investigators identified 16 placebo-controlled trials and 11 trials in which two active treatments were compared. Among the placebo-controlled trials, five included sulfonylureas, five included α-glucosidase inhibitors, three included thiazolidinediones, two included glinides, and one included GLP-1 agonists. They were unable to identify trials involving pramlintide or DPP-IV inhibitors that met their inclusion criteria.

Combining trials for each class of drugs, sulfonylureas reduced HbA_{1c} by an average of 0.85%, thiazolidinediones by 0.42%, and α-glucosidase inhibitors by 0.61%. After the researchers corrected for baseline HbA_{1c}, the reduction obtained with sulfonylurea with respect to placebo was significantly greater than that of thiazolidinediones. On the other hand, there were no significant differences between sulfonylurea and α-glucosidase inhibitors or between α-glucosidase inhibitors and thiazolidinediones.

Among the trials in which two active agents were compared, sulfonylureas were significantly superior to thiazolidinediones, with an overall difference between the two treatments of 0.17% in reducing HbA_{1c}. There were no significant differences between sulfonylureas and insulin. Insulin regimens that were based on two administrations of biphasic insulin analogues were more effective than insulin glargine once a day.

The investigators disclosed receiving speaking fees, consultancy fees, and/or research grants from Abiogen Pharma, GlaxoSmithKline, Guidotti, Eli Lilly & Co., Menarini, Merck Sharp & Dome, Merck KgA, Novo Nordisk, Sanofi-Aventis, Takeda, and Novartis. ■

Diabetes Drug Guides Offered

Two new guides from the Agency for Healthcare Research and Quality offer information on oral medications for adults with type 2 diabetes. One is designed for consumers and includes information on the efficacy, side effects, and costs of the drugs; the other is for physicians and includes research findings on each drug. Online and audio versions are available at http://effectivehealthcare.ahrq.gov/index.cfm. For more information, call Ellen Crown at 301-427-1258. ■