Metformin Adjuncts Studied

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Sulfonylureas, alpha-glucosidase inhibitors, and possibly glinides have similar efficacy when added on to failing metformin therapy in patients with type 2 diabetes, according to a new a meta-analysis.

Thiazolidinediones (TZDs) have less efficacy as an add-on to metformin—that is, less effect in lowering hemoglobin A_{1c}—in the first 6 months, but may become more efficacious over the long term. And insulin as an add-on to failing metformin therapy is not clearly superior to adding on a sulfonylurea, the meta-analysis indicated.

Those results aside, there are few studies on the subject, and the choice of which drug to add for a patient failing metformin cannot clearly be made based on evidence of differences in hypoglycemic efficacy, commented Dr. Matteo Monami and colleagues from the department of critical care medicine and surgery at the University of Florence (Italy). Differences are not definitively confirmed by the clinical trials, the researchers noted.

Adjusting for baseline HbA_{1c}, the investigators found that the reduction from adding a sulfonylurea was greater than the reduction from adding a TZD.

The researchers conducted their analysis by searching the U.S. National Library of Medicine's Medline database for randomized clinical trials investigating the efficacy of add-on therapy in patients failing either metformin or another oral antihypoglycemic agent. Limiting their selection to trials that lasted at least 16 weeks, they identified 27 studies that fit their criteria (Diab. Res. Clin. Pract. [2007], doi:10.1016/j.diabres.2007.08.024).

In all, 16 of those trials compared an add-on drug with placebo in patients on metformin; 5 of the trials added on a sulfonylurea; 5 trials, an alpha-glucosidase inhibitor; 3 trials, a thiazolidinedione; 2 trials, a glinide; and 1 trial, the glucagon-like peptide 1 agonist exenatide.

Combining data from those trials showed that adding on a sulfonylurea reduced the hemoglobin A_{1c} (HbA_{1c}) level by an average of 0.85%; adding on a thiazolidinedione reduced HbA_{1c} by 0.42%; and adding on an alpha-glucosidase inhibitor reduced HbA_{1c} by 0.61%.

Adjusting for baseline HbA_{1c} level, the investigators found that the reduction from adding a sulfonylurea was greater than the reduction obtained by adding a TZD. But they also found that the difference between a sulfonylurea and an alpha-glucosidase inhibitor was not statistically significant; neither was the difference between an alpha-glucosidase inhibitor and a TZD.

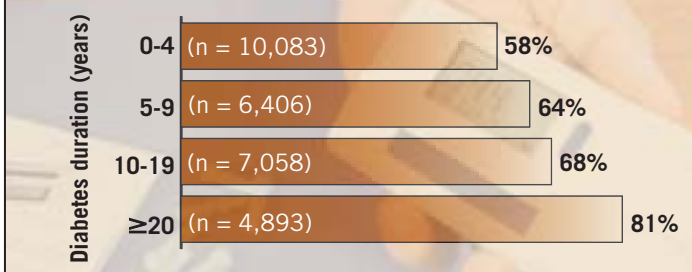
A total of 11 trials were found that compared different agents added on to existing therapy. Combining data from the trials that directly compared a sulfonylurea add-on with a TZD add-on, the sulfonylurea add-on was found to produce the greater reduction in HbA_{1c}, of 0.17%. In direct comparison of sulfonylurea with insulin, there was no significant difference in the reduction obtained.

Six of the trials were conducted in patients failing metformin therapy. In data from those trials, the sulfonylurea add-on had greater efficacy than the TZD add-on, with a difference in HbA_{1c} of 0.24%.

The data suggesting equivalence between a sulfonylurea and insulin should be viewed with caution, the authors said. The meta-analysis included only two studies addressing that issue; each was only 16 weeks long, they noted. ■

DATA WATCH

Adults With the Longest Diabetes Duration Most Likely to Self-Monitor Blood Glucose Daily



Note: Based on 2006 U.S. data.
Source: Centers for Disease Control and Prevention

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