Addition of Biphasic, Prandial, or Basal Insulin to Oral Therapy in Type 2 Diabetes

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Background
Adding insulin to oral therapy in type 2 diabetes mellitus is customary when glycemic control is suboptimal, though evidence supporting specific insulin regimens is limited.

Methods
In an open-label, controlled, multicenter trial, we randomly assigned 708 patients with a suboptimal glycated hemoglobin level (7.0 to 10.0%) who were receiving maximally tolerated doses of metformin and sulfonylurea to receive biphasic insulin aspart twice daily, prandial insulin aspart three times daily, or basal insulin detemir once daily (twice if required). Outcome measures at 1 year were the mean glycated hemoglobin level, the proportion of patients with a glycated hemoglobin level of 6.5% or less, the rate of hypoglycemia, and weight gain.

Results
At 1 year, mean glycated hemoglobin levels were similar in the biphasic group (7.3%) and the prandial group (7.2%) ($P = 0.08$) but higher in the basal group (7.6%, $P<0.001$ for both comparisons). The respective proportions of patients with a glycated hemoglobin level of 6.5% or less were 17.0%, 23.9%, and 8.1%; respective mean numbers of hypoglycemic events per patient per year were 5.7, 12.0, and 2.3; and respective mean weight gains were 4.7 kg, 5.7 kg, and 1.9 kg. Rates of adverse events were similar among the three groups.

Conclusions
A single analogue-insulin formulation added to metformin and sulfonylurea resulted in a glycated hemoglobin level of 6.5% or less in a minority of patients at 1 year. The addition of biphasic or prandial insulin aspart reduced levels more than the addition of basal insulin detemir but were associated with greater risks of hypoglycemia and weight gain. (Current Controlled Trials number, 51125379.)