

Starting on three drugs at time of diagnosis benefits Type 2 diabetics

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Patients with type 2 diabetes fare significantly better if they are started on three medications at the time of diagnosis than if they are prescribed a single drug and have other therapies added later, a San Antonio researcher said June 22 at the 73rd Scientific Sessions of the American Diabetes Association in Chicago. The findings, from a study funded by the association, could revise the way physicians manage the endocrine disease.

UT Medicine San Antonio physician Ralph DeFronzo, M.D., chief of the [Diabetes](#) Division in the School of Medicine at The University of Texas Health Science Center at San Antonio, presented two-year results from 134 participants studied at University Health System's Texas Diabetes Institute. Half of the subjects received the [triple-therapy](#) regimen while the other half received the conventional regimen recommended by the ADA. The standard regimen begins with a single agent (metformin), adds another (sulfonylurea) when the first agent fails, and then adds [insulin injections](#) as needed to control blood glucose after the second agent fails.

Dr. DeFronzo reported that:

- Mean [hemoglobin A1c](#), a test that strongly predicts the risk of diabetic blood vessel complications such as blindness, [kidney failure](#), heart attacks, stroke and neuropathy, was 6.0 percent after 24 months in the triple-therapy group, compared to 6.6 percent in the conventional therapy group. (The [American](#)

[Diabetes Association](#) and the European Association for Study of Diabetes recommend a maximum hemoglobin A1c level of 6.5 percent.)

- While 42 percent of conventional-therapy participants failed to reach the 6.5 percent goal, only 17 percent of the triple-therapy recipients failed to reach it.
- In home blood glucose monitoring, triple-therapy patients showed consistent results within the normal range, whereas patients on conventional therapy registered up and down spikes, many of which were out of the normal range.
- Patients on triple therapy lost 2-3 pounds on average after two years while patients on conventional therapy gained 9-10 pounds.
- Fifteen percent of patients on triple therapy experienced one episode of hypoglycemia (low blood glucose), while 46 percent of those on conventional therapy had at least one hypoglycemic event.

Core deficits corrected

The triple therapy combines agents that correct two core defects in [type 2 diabetes](#)—the inability to respond to insulin normally (insulin resistance), and failure of insulin-secreting beta cells to produce enough insulin. Insulin is the hormone that lowers blood glucose levels. Before the study, Dr. DeFronzo and his colleagues, including co-investigator, Muhammad Abdul-Ghani, M.D., Ph.D., of UT Medicine, hypothesized that the triple therapy would produce a greater, more durable reduction in hemoglobin A1c, reduce the fluctuation in plasma glucose by decreasing both fasting and between-meal glucose levels, and prevent weight gain, which is a side effect of traditional therapy.

Two years of normalcy

Two years into the three-year study, it is clear that the triple therapy is accomplishing these therapeutic goals, and that beta cells are being preserved and the body is being sensitized to insulin. "These drugs are not cures, but patients are basically normal while taking them," Dr. DeFronzo said. "They are not going to develop the microvascular (blood vessel) complications as long as their [blood glucose](#) level remains within the normal range."

3 drugs, 3 mechanisms

The triple therapy consists of metformin, a drug that Dr. DeFronzo helped develop in the 1990s; pioglitazone, a newer class of medication for type 2 diabetes; and exenatide, another newer class of drug. Each drug works by a different mechanism, Dr. DeFronzo said. Conventional therapy is to start the patient on metformin and when the response stops, add a class of medication called a sulfonylurea. When those no longer work, the patient is placed on insulin.

Factors for patients, doctors to weigh

Problems with the conventional approach include weight gain, episodes of hypoglycemia and failure to prevent beta cell failure. The conventional approach is less expensive, however.

"We should tell people which drugs work better," Dr. DeFronzo said. "The individuals and doctors need to decide whether they can afford the treatment."

Failure at 10 years out

According to the United Kingdom Prospective Diabetes Study, patients on [conventional therapy](#) had an average hemoglobin A1c level of 8.6

percent after a mean of 10 years of follow-up, and nearly two-thirds (65 percent) were on insulin for glucose control.

The Texas Diabetes Institute, a program of University Health System, is the nation's largest and most comprehensive center, entirely devoted to diabetes prevention, treatment, education, professional training and the relentless search for a cure. Texas Diabetes Institute is located where it is most needed, on San Antonio's West Side, where the incidence of diabetes is the highest in the nation.

Provided by University of Texas Health Science Center at San Antonio

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