Drug Therapy for 'Prediabetes' Held Premature

BY MITCHEL L. ZOLER

NEW YORK — Drug treatment that is designed to prevent patients with "prediabetes" from progressing to outright, type 2 diabetes by controlling hyperglycemia is not ready for routine use, according to a Food and Drug Administration official.

Although lifestyle interventions have proved effective and make sense for this indication—as has aggressive control of cardiovascular risk factors—the routine administration of an agent that controls blood sugar levels "is not generally applicable to any prediabetes patient," Dr. Mary H. Parks said at a meeting sponsored by the American Diabetes Association.

"For drug intervention we need to look at efficacy and side effects. If there is a side effect profile of concern, is there a benefit that offsets that?" So far, the answer is no because the benefit derived from the use of drugs that control hyperglycemia in patients who have prediabetes has not been clearly shown, while these drugs might produce adverse effects such as liver toxicity or increased cardiovascular disease risks, said Dr. Parks, who is director of the division of metabolism and endocrinology products at the Center for Drug Evaluation and Research of the FDA.

Dr. Parks reviewed results from five separate, placebo-controlled assessments of the ability of oral hypoglycemic drugs to cut the progression from prediabetes to type 2 diabetes. Results from the five studies, published during the past 7 years, showed that treatment with a single drug such as metformin, acarbose (Precose), or a thiazolidinedione cut the rate of progression to diabetes by a relative rate of about 25%-60%, compared with placebo.

Despite this success, the data are not persuasive because "the risk reduction was modest, and less than with intensive lifestyle modification except when an insulin sensitizer [a thiazolidinedione] was used," Dr. Parks said. Perhaps more important, all of the results were flawed by uncertainty as to "whether diabetes was prevented or if there was masking of the disease by treatment."

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The studies also failed to address whether drug treatment did more than simply slow the appearance of hyperglycemia and actually reduced the rate of clinical complications.

Dr. Parks summarized the findings from three lifestyle-intervention studies, also placebo controlled, that were published between 1997 and 2002.

The studies involved three diverse populations, in China, Finland, and the United States. In all three groups a diet and exercise intervention program led to relative drops in the rate of diabetes onset of 31%-58%, compared with placebo. Lifestyle interventions are also safe, and so Dr. Parks endorsed them without reservation. The only problem, she acknowledged, is that they are not easy to implement or maintain.

Prediabetes is usually defined as a fasting blood glucose level of 100-125 mg/dL, or a 2-hour postchallenge level of 140-199 mg/dL. Over several years, the general trend for most people with blood glucose levels like these is for the level to rise and reach the threshold for a diagnosis of diabetes.

Study results have shown that about 5%-10% of people with prediabetes based on either their fasting glucose or postchallenge glucose level will progress to outright diabetes during the following year.

But as these numbers suggest, the short-term prognosis for any one individual is difficult to predict. Over the course of a few years, roughly a third progress to having outright diabetes, about a third will remain with prediabetes, and about a third will have their glycemia levels improve to the normal range, Dr. Parks said. ■