



**ROBERTA H. MCDUFFIE, APRN,BC, MSN, CDE, CNS**

**DO YOU THINK PATIENTS WITH PREDIABETES SHOULD BE STARTED ON EITHER ORAL AGENTS OR INSULIN? WHAT ABOUT STATINS AND ANGIOTENSIN-CONVERTING ENZYME INHIBITORS?**

Currently, there are no medications approved to treat prediabetes. That said, at least 3 medications appear to slow the progression from prediabetes to type 2 diabetes (T2DM). The Diabetes Prevention Program (DPP) demonstrated that metformin decreases the risk of developing T2DM by 31% compared with placebo. The Troglitazone in Prevention of Diabetes (TRIPOD) study randomized Hispanic women with a history of gestational diabetes to troglitazone or placebo for 2.5 years. The progression to T2DM was reduced by 55% in the troglitazone group. In the Study to Prevent Non-Insulin-Dependent Diabetes Mellitus (STOP-NIDDM), patients were randomized to acarbose or placebo for 3.3 years. In the acarbose group, progression to T2DM was reduced by 25%, cardiovascular disease events were decreased by 49%, and new-onset hypertension incidence was decreased by 34%.

The benefit of statin treatment in prediabetes is unknown since no prospective studies have targeted this group and no prospective studies have been conducted to evaluate angiotensin-converting enzyme (ACE) inhibitors. However, the Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (ALLHAT) compared a thiazide diuretic, a calcium channel blocker, and an ACE inhibitor in hypertensive patients older than 55 years and with at least 1 additional coronary heart disease (CHD) risk factor. After 5 years, although there was no significant difference in primary outcome (CHD death or nonfatal myocardial infarction) or all-cause mortality, the thiazide group was more likely to develop T2DM while the ACE inhibitor group was 40% less likely to develop T2DM. This and other studies indicate that ACE inhibitors and angiotensin receptor blockers may slow or prevent progression to T2DM in hypertensive individuals. Research also exists to indicate that orlistat may help delay or prevent the development of T2DM.

**WOULD YOU PLEASE DISCUSS THE ROLES OF INSULIN DEFICIENCY AND INSULIN RESISTANCE IN THE METABOLIC ABNORMALITIES ASSOCIATED WITH DIABETES?**

There are 4 significant metabolic abnormalities that characterize T2DM: impaired insulin sensitivity, impaired insulin secretion, increased endogenous glucose secretion, and obesity. At present, the sequence of development of each abnormality and the contribution of each to the development of individual complications are largely unknown. While macrovascular complications are strongly associated with the hyperinsulinemia related to insulin resistance, many other mechanisms, as well as glucose metabolism, accelerate the progression of complications in T2DM.

## RECOMMENDED READING

The ALLHAT Officers and Coordinators for the ALLHAT Collaborative Research Group. Major outcomes in high-risk hypertensive patients randomized to angiotensin-converting enzyme inhibitor or calcium channel blocker vs. diuretic. The Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (ALLHAT). *JAMA*. 2002;288:2981-2997.

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