

Screen Children Early and Often

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That's turning out to be a false assumption, since children with type 2 diabetes are demonstrating "all of the complications we see in adults," within 5-6 years of their diagnoses, Dr. Wyne said at the meeting, also sponsored by the American College of Cardiology.

Compared with adolescents who have type 1 diabetes, those with type 2 diabetes have more obesity, overweight, hypertension, high triglycerides, low HDL cholesterol, microalbuminuria, and retinopathy.

"Once you start seeing hypertension, high triglycerides, and low HDL, you know the process has already started. You need to look for other complications, because they're going to follow right behind," said Dr. Wyne.

By putting numbers on the problem, Dr. Wyne reported that in Dallas County alone, children seen in outpatient clinics for obesity, dietary surveillance, abnormal weight gain, or acanthosis nigricans soared from 665 in 2001 to 1,378 in 2005. Diagnoses of type 2 diabetes more than doubled, from 69 to 137.

Texas academic centers are currently seeing 250 children a year with type 2 diabetes, aged 4-16 years. "This is not a disease of kids postpubertal," she said. "This goes the full range of kids' [ages]."

If an estimated one-third of adults with diabetes are undiagnosed, the percentage could be much higher in children, according to Dr. Wyne.

Based on obesity rates among the 1 million children in Houston, for example, there could be 5,600 children with "silent" type 2 diabetes in that city alone, she said.

One practical suggestion to prevent cardiovascular catastrophes in young adults is to screen children early and screen them often, using two important risk factors: a family history of diabetes and obesity.

She asks patients to take a glucose meter to a family dinner or holiday celebration and check everyone's blood sugar 2 hours into the meal.

"Anyone who is above 200 mg/dL needs to come into the office the next day," she advises. "Anyone who is between 140 and 199 mg/dL has impaired glucose tolerance and needs to come in."

Lifestyle interventions are the first line of therapy of youth and adolescents, just as in adults. Almost always, the whole family is involved in dietary and exercise patterns that put them at risk for diabetes, so interventions must be family-wide.

If those steps fail to produce results, Dr. Wyne said she has "no problem" prescribing ACE inhibitors, statins, and angiotensin II receptor blockers (ARBs) to symptomatic teenagers and younger children.

"What I don't know [is how to treat] newly diagnosed youth and adolescents who have no complications yet," she said.

Often, Dr. Wyne makes emotional appeals to the par-

ents and grandparents of children who seem to be destined for the cardiac catheterization laboratory in young adulthood.

"If I've got grandparents in their 40s and 50s with diabetes and heart disease and they have a fat little [grand]kid, I know that kid is heading in that direction," she said.

County hospitals in Texas are currently seeing patients with congestive heart failure in their 30s, 40s, and 50s, said Dr. Wyne. She's been diagnosing elementary school children with type 2 diabetes for 10 years, and they have been developing complications in 5-6 years.

The math suggests that some of these children will develop heart failure in their 20s and 30s, she said. "A few years ago, it struck me, this is going to be a generation where parents are burying their children." ■

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Telmisartan Promising in Type 2 Diabetes Prevention

BY BRUCE JANCIN
Denver Bureau

SAN ANTONIO — The discovery that the angiotensin II receptor blocker telmisartan also acts as a partial agonist of peroxisome proliferator-activated receptor- γ makes it a uniquely promising candidate for the treatment of metabolic syndrome and prevention of type 2 diabetes and cardiovascular disease, Dr. Theodore W. Kurtz said at a meeting of the American Heart Association Council for High Blood Pressure Research.

Whether telmisartan fulfills this promise should be known sometime in 2008, when results are expected from two large ongoing clinical trials with a variety of cardiovascular and metabolic end points, added Dr. Kurtz, professor of laboratory medicine at the University of California, San Francisco.

The Ongoing Telmisartan Alone and in Combination With Ramipril Global Endpoint Trial (ONTARGET) has randomized more than 25,000 patients at high cardiovascular risk to telmisartan, ramipril, or both. A companion study, the Telmisartan Randomized Assessment Study in ACE-Intolerant Subjects With Cardiovascular Disease (TRANSCEND), is comparing telmisartan to placebo in nearly 6,000 high-risk patients.

"We're looking forward to the outcome of these trials with great anticipation," he said. "We predict telmisartan may reduce cardiovascular events and decrease the incidence of new-onset type 2 diabetes, [and] ramipril may protect against cardiovascular events as shown in the HOPE trial but may not prevent new-onset diabetes, and we think the combination of telmisartan and ramipril might be even better than either molecule alone because here you're getting more complete interruption of the renin-angiotensin system plus the added effect of PPAR- γ [peroxisome proliferator-activated receptor- γ] activation."

Dr. Kurtz was honored with the Novartis Award for Hypertension Research at the meeting, in part for groundbreaking work in which he identified several genes that play a key role in the development of components of the metabolic syndrome in rats. Subsequent work indicates these same genes figure importantly in human metabolic syndrome.

One of these genes is Cd36, also known as FAT (fatty acid translocase), an insulin-resistance gene causing defective fatty acid and glucose metabolism. Another is mitochondrial cytochrome C oxidase-1 (MTCO 1), a variant linked to increased plasma insulin and triglyceride levels, increased muscle triglyceride, and reduced muscle insulin sensitivity.

Metabolic syndrome is associated with a fivefold to ninefold increased risk of developing type 2 diabetes and twice to four times the risk of cardiovascular morbidity and mortality. The emerging consensus is that abnormal deposition of fat in tissues where it doesn't belong, such as visceral organs and muscle, lies at the syndrome's core.

Treatment of metabolic syndrome has been a thorny issue. β -Blockers and diuretics are time-proven antihypertensive drugs but their use can worsen dyslipidemia and reduce insulin sensitivity.

Dr. Kurtz noted that PPAR- γ activators such as pioglitazone and rosiglitazone modulate Cd36 and MTCO 1 activity, enhance fatty acid metabolism, and stimulate mitochondrial function. They are also known to be useful for treatment of the metabolic syndrome and type 2 diabetes.

Recently PPAR- γ activators have also been shown to be effective in preventing development of type 2 diabetes in high-risk individuals. However, they are not optimal agents for treatment of metabolic syndrome because they have only modest blood pressure-lowering effects and have the problematic side effects of fluid retention, weight gain, and increased risk of heart failure, he added.

When Dr. Kurtz and coworkers were enlisted in a program to search for PPAR- γ activators having stronger antihypertensive action without the side effects of conventional PPAR- γ agonists, they noted that telmisartan alone among the angiotensin II receptor blockers (ARBs) bore a structural similarity to the conventional PPAR- γ activators. In in vitro studies, telmisartan exhibited a PPAR- γ -activating effect at therapeutically relevant concentrations, while other ARBs did not, even at very high concentrations.

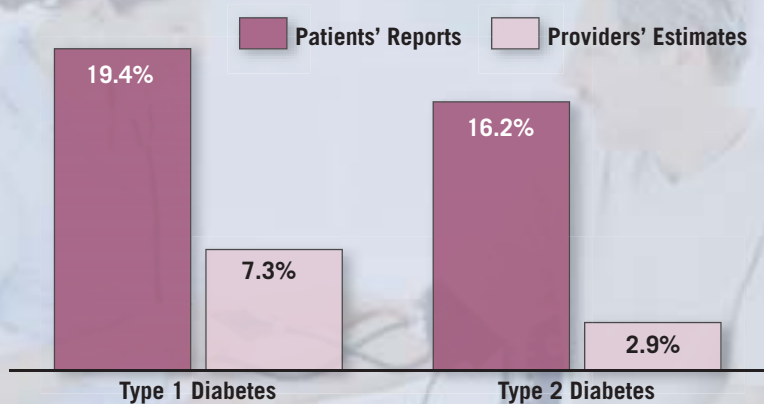
In his studies of animals with diet-induced insulin resistance, Dr. Kurtz showed that telmisartan modulated the expression of Cd36 and MTCO 1, protected against visceral fat deposition, and improved lipid and glucose metabolism.

A recent Japanese CT study showed that telmisartan also protected against visceral fat accumulation in humans, while European studies showed that telmisartan improves insulin sensitivity and lipid profiles in patients with metabolic syndrome. Moreover, telmisartan's selective effect on PPAR- γ activation genes means it doesn't have the side effects seen with full agonists of PPAR- γ .

Dr. Kurtz has been the recipient of research grants from Boehringer Ingelheim, which markets telmisartan, as well as numerous other pharmaceutical companies. ■

DATA WATCH

Providers Estimate Fewer Diabetes Patients Follow Recommendations Than Patients Report



Note: Based on data from Diabetes Attitudes, Wishes, and Needs study of 850 people.
Source: Clinical Diabetes 2006;24:154-5