Metformin at Diagnosis

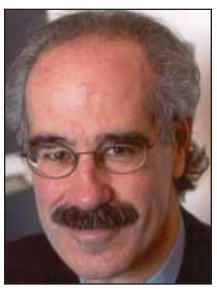
Type 2 Diabetes *from page 1*

terventions fail to achieve or maintain metabolic goals."

The algorithm also advocates adding basal insulin, a sulfonylurea, or a thiazolidinedione (glitazone) within 2-3 months of the initiation of therapy or "at any time" that A_{1c} levels are 7% or greater.

The strong recommendation to consider insulin as a second-line drug "was a little surprising, since few people do it," said one member of the panel, Dr. Mayer B. Davidson, of Charles R. Drew University of Medicine and Science, in Los Angeles.

However, such a change in clinical practice could be "very effective," he said in an interview.



The guidelines contain detailed advice for initiating and adjusting insulin regimens, the complexity of which may contribute to delays in aggressive therapy that could optimize patient outcomes.

If a combination of lifestyle changes, metformin and a second-line drug fail to achieve glycemic control, the algorithm endorses adding another of the second-line choices (basal insulin, a sulfonylurea, or glitazone) or intensifying insulin therapy.

"Although three oral agents can be used, initiation and intensification of insulin therapy is preferred based on effectiveness [and] expense," the authors noted in the algorithm approved by the Professional Practice Committee of the American Diabetes Association (ADA) and an ad hoc committee of the European Association for the Study of Diabetes.

Consensus panel members deplored the lack of "high-quality evidence" comparing diabetes drugs head to head, adding that "there are insufficient data at this time to support a recommendation of one class of glucose-lowering agents or one combination of medications over others with regard to effects on complications."

They therefore focused on the effectiveness of drug classes in lowering glycemic levels as the "overarching principle" guiding their choice of agents as first- and second-line therapy.

Pramlintide, exenatide, α-glucosidase inhibitors, and the glinides were not included in the algorithm "owing to their generally lower overall glucose-lowering effectiveness, limited clinical data, and/or relative expense," although the authors acknowledged that they might be "appropriate choices in selected patients."

Diabetes experts from within and outside the ADA applauded the guidelines committee led by Dr. David M. Nathan, director of the diabetes center at Massachusetts General Hospital and professor of medicine at Harvard Medical Center, both in Boston.

Nonaggressive approaches, plus reluctance to use insulin, contribute to failure to achieve treatment targets.

DR. NATHAN

Dr. Robert A. Rizza, president of the ADA and director of research at the Mayo Clinic, Rochester, Minn., called the algorithm choices "sensible. I think they strike a balance between what has been shown to be effective and what is economically sustainable over the long run."

Furthermore, the panel established criteria for advocating preferred diabetes drugs. This way, the algorithm can be adjusted to reflect advances in scientific knowledge about the effectiveness of various approaches, Dr. Rizza said in an interview.

Dr. Richard Hellman, president-elect of the American Association of Clinical Endocrinologists, commended A_{1c} targets in the algorithm that "move much closer" to 2002 recommendations made by AACE.

"From our point of view, aggressive control of glucose is incredibly important in the care of our patients," said Dr. Hellman, clinical professor of medicine at the University of Missouri-Kansas City.

He also agreed with the new algorithm's emphasis on aggressive treatment of type 2 diabetes in the first year following diagnosis, including the early integration of insulin into the treatment regimen.

"There is emerging evidence that insulin should be used early in the course of this disease," he said in an interview.

Dr. Hellman expressed hope that primary care physicians would use the algorithm and soon-to-be published updated AACE diabetes guidelines in directing their care of patients. "The people most expert in this disease are relatively few in number: a few thousand endocrinologists, when there are 18 million, soon to be 20 million people with diabetes in this country, the majority of them with type 2," he said.

The most important message to primary care physicians is to hit the disease hard, early on, he said. "Deterioration is more common when physicians wait a long time to gradually accelerate the treatment."

In an interview, Dr. Jaime A. Davidson, of University of Texas Southwestern Medical Center, Dallas, pointed out that "the closer we can get to normal, the better off the patients are, the better off the economy is, and the less suffering we will have. We have shown from recent clinical trials that we can get patients safely and effectively to an A_{1c} of 6.5% with simple algorithms like the AACE guidelines."

Dr. Rizza said he believes that the guidelines will be well received by clinicians besieged with an epidemic of disease and a host of new treatment options.

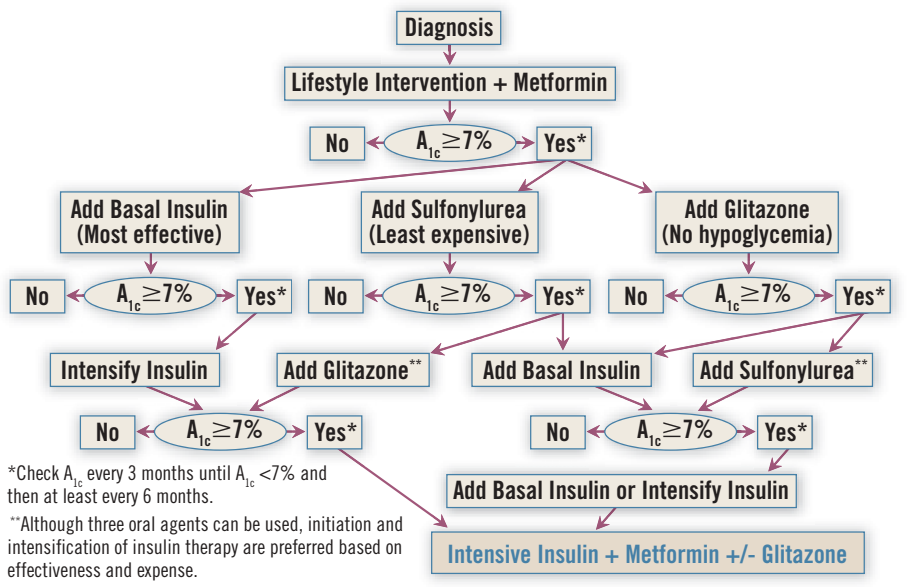
"All of a sudden we're dealing with numbers of patients and complexities of treatment that we have never seen before. These guidelines will help us all deliver the best possible care to our patients," Dr. Rizza said.

Indeed, "heightened uncertainty regarding the most appropriate means of treating this widespread disease," was one of the driving forces behind the development of the treatment algorithm, the authors noted. "Although numerous reviews on the management of type 2 diabetes have been published in recent years, practitioners are often left without a clear pathway of therapy to follow."

Barriers to glycemic control include the cost and complexity of medication regimens, Dr. Nathan noted. "In addition, slow and nonaggressive implementation of treatment regimens, including a reluctance to use insulin, contribute to the failure to achieve and maintain treatment targets."

"We hope that the recommendations, by setting specific goals and timelines for interventions, and providing a guide for the orderly implementation of treatments, will help improve patient care and outcomes." ■

Algorithm for Metabolic Management of Type 2 Diabetes



*Check A_{1c} every 3 months until A_{1c} <7% and then at least every 6 months.

**Although three oral agents can be used, initiation and intensification of insulin therapy are preferred based on effectiveness and expense.

Source: Diabetes Care 2006;29:1-10

Thiazolidinedione May Cut Incidence of Alzheimer's Disease

BY MICHELE G. SULLIVAN
Mid-Atlantic Bureau

MADRID — Thiazolidinediones may reduce the incidence of Alzheimer's disease or forestall its progression in both diabetic and nondiabetic patients, researchers reported at the 10th International Conference on Alzheimer's Disease and Related Disorders.

Diabetes is thought to increase the incidence of Alzheimer's disease through several pathways, including decreased cortical utilization of glucose, and increased oxidative stress, inflammation, and deposition of amyloid-β. Besides regulating insulin and improving glucose usage, the drugs have been shown in animal models to suppress microglial-mediated inflammation and reduce amyloid plaque formation, Donald Miller, Sc.D., and Dr. David Geldmacher said at a press conference during the meeting, which was sponsored by the Alzheimer's Association.

Dr. Miller examined the incidence of new Alzheimer's cases among a cohort of 142,328 veterans (mean age 66 years) with diabetes, who were followed for 6 years. The group included patients who received a new prescription for either a thiazolidinedione (74,525) or insulin (67,803).

After 6 years' follow-up, there were 3,191 new cases of Alzheimer's, a rate of 0.24% per year.

Patients who got a thiazolidinedione were 19% less likely to develop the disorder than were those treated with insulin, said Dr. Miller of the department of health services at Boston University School of Public Health. The results remained significant even after controlling for potential confounders including demographics, body mass index, and other medications.

Dr. Miller obtained similarly significant results favoring thiazolidinediones when he compared the drugs with metformin.

More research is necessary before any firm conclusions can be drawn, however. "It would be premature to say that these drugs prevent Alzheimer's in diabetes patients," he said. "These are preliminary results, although they are encouraging."

Dr. Geldmacher, director of the memory disorder program at the University of Virginia, Charlottesville, examined the effect of pioglitazone compared with placebo in nondiabetic patients with probable Alzheimer's disease. The randomized, controlled trial included 30 subjects (mean age 70 years) whose mean Mini-Mental State Examination score was 21.

All patients maintained their existing antidementia drugs during the trial; 15 also received pioglitazone (45 mg/day), while the remaining 15 received the placebo.

After 18 months, there was a nonsignificant trend toward better cognitive performance in the treated patients, Dr. Geldmacher said. "None of the measures reached statistical significance, but the effect size we saw was similar to that seen with existing antidementia drugs."

In fact, he said, pioglitazone appeared to have a synergistic effect with existing drug therapy, doubling its cognitive impact.

Just as importantly, the drug was safe and well tolerated, he added. "We were somewhat concerned that it could cause hypoglycemia in these patients, none of whom had diabetes, but that was not the case." The only significant adverse event observed was lower extremity edema, a side effect also seen in diabetic patients who take the drug. ■