

Lifestyle Intervention Worked Well in Diabetes

BY MARY ANN MOON

FROM THE ARCHIVES OF
INTERNAL MEDICINE

An intensive lifestyle intervention produced significant improvements in weight, cardiovascular fitness, blood pressure, hemoglobin A_{1c}, triglycerides, and HDL-cholesterol, which were largely maintained throughout 4 years of follow-up.

The study, involving 5,145 overweight or obese patients with type 2 diabetes, compared the intensive intervention against usual patient care, which included standard diabetes education.

"Effects of the magnitude that we observed for fitness, HDL-C and HbA_{1c} levels, and blood pressure have been associated with decreased cardiovascular events and mortality in previous medication trials and observational studies," said Rena R. Wing, Ph.D., of the department of psychiatry at Miriam Hospital/ Brown University, Providence, R.I., and her associates in the LookAHEAD (Action for Health in Diabetes) trial. "The critical question is whether the differences between groups in risk factors will translate into differences in the development of CVD [cardiovascular disease]. These results will not be available for several additional years."

The researchers previously reported on the 1-year benefits of the intensive lifestyle intervention, compared with usual care. They now report that patients who received the intervention maintained the positive changes they made for 3 more years, albeit with some regression to baseline levels of all measures.

The trial enrolled subjects aged 45-76 years at 16 U.S. medical centers. About 60% of the subjects were women, and 37% were from racial or ethnic minorities. The average body mass index was 36 kg/m², and the average duration of diabetes was more than 6 years.

In all, 2,570 subjects were randomly assigned to intensive intervention and 2,575 to usual care with diabetes education.

The intervention included dietary

modification with a calorie goal of 1,200-1,800 kcal a day, less than 30% of calories from fat, and at least 15% of calories from protein. A portion-controlled diet was provided. The exercise goal was at least 175 minutes of physical activity a week at an intensity level comparable with that of brisk walking. Behavioral strategies included self-monitoring, goal setting, and problem solving.

Subjects in the intervention group met individually and in groups every week for the first 6 months and three times a month for the next 6 months. During years 2 through 4, they were seen individually at least once a month, contacted by phone or e-mail once a month, and attended three group sessions and assorted group classes throughout the year.

These sessions were led by registered dietitians, behavioral counselors, or exercise specialists trained in lifestyle counseling. At each session, subjects were weighed, their self-monitoring records were reviewed, and a new lesson was presented. Complete physical assessments were performed annually, and subjects were given a \$100 honorarium to encourage participation.

"Averaged across the 4 years, participants in the [intervention] group experienced greater improvements in weight, fitness, glycemic control, blood pressure, and levels of HDL-C and triglycerides than those in the [usual care] group," the researchers said, noting that "the mean maximal weight loss (8.6%) in the [intervention] group occurred at 1 year, but participants ... maintained a mean weight loss of 4.7% at year 4, compared with 1.1% in the [usual-care] group" (Arch. Intern. Med. 2010;170:1566-75).

At 1-year follow-up, cardiovascular fitness rose by 20% in the intervention group and 5% in the usual-care group. It regressed over time, but at year 4 the fitness level of the intervention group was still 5% over baseline, whereas that of the usual-care group was 1% below baseline.

The intervention group maintained greater improvements than did the usual-care group in systolic blood pressure,

HbA_{1c} levels, and HDL-C levels, but initial improvements in diastolic blood pressure and triglycerides disappeared by year 4. There were no differences between the groups in improvement in LDL-C levels.

"This study shows that lifestyle interventions can produce long-term weight loss and improvement in fitness and sustained beneficial effects on CVD risk factors," the investigators said.

"Although the differences between the two groups were greatest initially and decreased over time for several measures, the differences between the groups averaged across the 4 years were substantial and indicate that the [intervention] group spent a considerable time at lower CVD risk," they added. "Longer follow-up will [help] determine whether the differences between groups in CVD risk factors can be maintained and whether the [intensive intervention] has positive effects on cardiovascular morbidity and mortality."

The LookAHEAD study was support-

ed by the National Institute of Diabetes and Digestive and Kidney Diseases; National Heart, Lung, and Blood Institute; National Institute of Nursing Research; National Center on Minority Health and Health Disparities; Office of Research on Women's Health; Centers for Disease Control and Prevention; U.S. Department of Veterans Affairs; Indian Health Service; and research centers at Johns Hopkins Medical Institutions, Massachusetts General Hospital, Massachusetts Institute of Technology, Colorado Health Sciences Center, University of Tennessee at Memphis, and the University of Pittsburgh. FedEx Corp., Health Management Resources, LifeScan Inc., OPTIFAST, Hoffmann-La Roche, Abbott Nutrition, and Slim-Fast have committed to make major contributions to the ongoing trial. Dr. Wing's associates reported financial ties to BodyMedia Inc., University of Pittsburgh Medical Center Health Plan, Proctor & Gamble, and Free & Clear. ■

Solid Evidence of Sustained Benefit

VIEW ON THE NEWS

For patients with type 2 diabetes, these exciting findings provide solid evidence of the sustained benefit of simple interventions on numerous important cardiovascular risk factors. The results are particularly encouraging because, unlike drug therapy for the disorder, lifestyle interventions carry little risk of inducing hypoglycemia, said Dr. Prakash C. Deedwania.

However, it is unlikely that the frequent and regular instruction, visits with registered dietitians and exercise specialists, special diets given free of charge, and monetary incentives used in this intervention can be translated on a broad scale to clinical practice. And the recidivism that occurred over time toward baseline

levels raises questions about the long-term sustainability of such an intensive intervention in everyday clinical practice.

Overall, however, the LookAHEAD findings show that "simple, established approaches based on conventional wisdom work well, and there is no need to rush to newer or novel approaches unless convincing evidence supports such a move," he said.



DR. DEEDWANIA is chief of cardiology at Veterans Affairs Central California Health Care System, Fresno. He reported no relevant financial disclosures. These comments are taken from his editorial accompanying the LookAHEAD report (Arch. Intern. Med. 2010;170:1575-7).

Metformin's Anticancer Potential Is Generating a Buzz

BY MIRIAM E. TUCKER

FROM THE ANNUAL MEETING OF THE EUROPEAN
ASSOCIATION FOR THE STUDY OF DIABETES

STOCKHOLM – Excitement is rising in the diabetes and oncology worlds regarding the potential anticancer effects of metformin.

"An off-patent, old drug, famous for its role in type 2 diabetes, is now a hot topic in cancer research," Dr. Michael Pollak said at a press briefing at the meeting.

Epidemiologic data have shown that rates of colon, lung, breast, and prostate cancer among diabetes patients treated with metformin are lower than those of the general population (BMJ 2005;330:1304-5 and Diabetes Care 2010;33:1304-8).

"We don't mean 2% lower or 10% lower: It was roughly half the expected cancer rate. Cancer epidemiologists pay a lot of attention when we see that kind of a finding to try and prove that it's an artifact or some kind of mis-

take, because a reduction of cancer mortality of 50% is something we've never seen before as a consequence of any prevention strategy," said Dr. Pollak, professor of medicine and oncology at McGill University, Montreal.

Since all the epidemiologic data are retrospective, researchers initially were skeptical. But laboratory studies supported the epidemiology, showing that metformin appears to reduce tumor aggressiveness in a variety of cancer models (Cancer Res. 2007;67:10804-12 and 2006;66:10269-73).

There are several theories about the mechanism. Metformin acts primarily in the liver, where it reduces glucose secretion. The drug also reduces insulin levels, which could inhibit tumors whose growth is stimulated by insulin.

Research is aimed at determining precisely which molecular subtypes are likely to respond. "We don't believe it will work uniformly in all tumors in all people," said Dr. Pollak, who is also director of the Cancer Prevention

Centre at SMBD-Jewish General Hospital, Montreal.

Research is "administratively unusual," because the drug is off patent, so there is limited private sector interest. But academic research is taking off in many countries, with many proposed and some initiated epidemiologic studies, laboratory investigations, and even clinical trials of nondiabetic patients with cancer.

"We're not here to announce the final conclusions. We're here to share the excitement that something unexpected and interesting has happened, and it's now under investigation," Dr. Pollak said.

It's too early to suggest that cancer patients begin taking metformin. Even so, "If you have cancer and diabetes that can be controlled by metformin, metformin becomes a pretty rational choice at this point. Not because we're sure it will help, but because there's a chance."

Dr. Pollak has ties to or has consulted for Novo-Nordisk, Eli Lilly & Co., Pfizer Inc., Sanofi-Aventis, and Boehringer Ingelheim GmbH. ■