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Metformin Protects Against Cancer in Type 2 Diabetes

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October 1, 2009 (Vienna, Austria) — Metformin was found to reduce risk in pancreatic and colon cancers in patients with type 2 diabetes in an epidemiologic study presented here at the European Association for the Study of Diabetes (EASD) 45th Annual Meeting.

"Our observational study shows the risk of developing cancer over 5 years with insulin and with metformin. We found that patients on insulin were twice as likely to develop colon carcinomas than those on metformin. With pancreatic cancer there is a major difference between the 2 — patients on insulin alone had 4.5 times the risk. These are remarkably big differences and it suggests that metformin could play a significant role in pancreatic cancer — a particularly lethal form of cancer," said study coauthor Dr. Edwin Gale, MD, from the Department of Diabetic Medicine and head of the Department of Clinical Science at the University of Bristol in the United Kingdom.

The retrospective cohort study drew information relating to the treatment of diabetic patients from 300 British general practice records. Patients were excluded if they had had previous cancer and data were only collected from patients treated after the year 2000. Insulin exposure was estimated by the number of prescriptions filled per year (categorized as <7, 7–10, 11–15, or >15). The researchers analyzed data from 4829 patients taking insulin alone (11,415 patient-years), 5035 taking insulin plus metformin (15,725 patient-years), and 30,421 taking metformin alone (71,261 patient-years). The primary outcome measure was the diagnosis of the first solid tumor.

Crude cancer rates showed a notable 60 cancer events per 1000 patient-years in the group exposed to the highest amount of insulin alone, compared with 34 cancer events per 1000 patient-years in the insulin plus metformin group. After adjustment for age, sex, and smoking status, the same ratio was true for insulin plus metformin vs insulin alone (5.73 vs 3.20).

Craig Currie, PhD, a medical epidemiologist from Cardiff University in Wales, who coauthored the study, said: "In the insulin-only group, there was a distinct dose-response relationship, with a 6-fold increase in all forms of cancer in the highest group, compared with metformin monotherapy. This dose-response relationship brings us 1 step closer to suggesting a causal relationship, although further work needs to be done for a definitive answer. Metformin, on the other hand, does have important properties that appear to reduce cancer risk and we need to analyze these risks further," he told *Medscape Diabetes & Endocrinology*.

Chairing the session, current EASD president Ulf Smith, MD, from Sahlgrenska University Hospital in Göteborg, Sweden, acknowledged that further research is needed to determine whether the relationship with cancer rates is due to high insulin dose or to the insulin resistance that is associated with type 2 diabetes. "There are reasons to involve insulin resistance per se. Findings at a cellular level and in animals suggest insulin resistance may be an important factor in this. This epidemiological study shows an association but we need further study to be conclusive," he said.

"A really important conclusion is that metformin reduces cancer risk," Dr. Smith said. "The story with metformin is very exciting because clinical studies show that patients treated with chemotherapy for breast cancer do considerably better when metformin is added. Another extremely exciting paper this week shows that metformin also targets cancer stem cells that remain after chemotherapy and can cause metastases. We are now starting clinical studies in nondiabetic patients."

Acknowledging the advent of an exciting research agenda over the coming years, Dr. Gale said that "in the future, we need to look at the possibility of links between cell metabolism, cell turnover, and cancer, and possibly the nondiabetic use of metformin. Understanding more about the link between insulin resistance and cancer and moving toward targeted screening of high-risk groups could save thousands of lives."

Dr. Gale, Dr. Currie, and Dr. Smith have disclosed no relevant financial relationships.

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