Common diabetic therapy reduces risk of pancreatic cancer, study finds

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Donghui Li, Ph.D., is a professor in University of Texas M. D. Anderson Cancer Center's Department of Gastrointestinal Medical Oncology. Credit: M. D. Anderson

Taking the most commonly-prescribed anti-diabetic drug, metformin, reduces an individual's risk of developing pancreatic cancer by 62 percent, according to research from The University of Texas M. D. Anderson Cancer Center, published in the Aug. 1 issue of *Gastroenterology*.

"This is the first epidemiological study of metformin in the cancer population, and it offers an exciting direction for future

chemoprevention research for a disease greatly in need of both treatment and prevention strategies," said Donghui Li, Ph.D., professor in M. D. Anderson's Department of Gastrointestinal Medical Oncology.

An oral medication, metformin is the most commonly prescribed drug for type 2 diabetes. According to Li, more than 35 million prescriptions for the drug are filled annually, and it's most often given to type 2 diabetic patients who are obese and/or have insulin resistance.

"Metformin works by increasing the cellular sensitivity to insulin and decreasing its level circulating in diabetics. Insulin also seems to have a growth-promoting effect in cancer," said Li, the study's senior author. "Metformin activates the AMP kinase, which is a cellular engery sensor. Recent publications have described that AMP kinase also plays an important role in the development of cancer by controlling cell division and growth."

Li also cited a previous animal study showing that metformin prevented pancreatic tumor development, as well as numerous epidemiologic studies in the diabetic population that showed taking the drug reduced the risk for cancer overall.

"Given these earlier findings, and knowing that diabetes is a risk factor for the development of pancreatic cancer and that 10 percent of such cancers are associated with diabetes, we wanted to better understand the specific association between different anti-diabetic therapies and this lethal disease," explained Li.

For the case control study, the researchers enrolled 1,838 participants - 973 patients with pancreatic adenocarcinoma treated at M. D. Anderson between 2004 and 2008 to compare 863 cancer-free individuals, all companions of M. D. Anderson patients. Of all participants, 259 patients and 109 controls were diabetics. The groups were matched by age, race

and sex. Using a detailed questionnaire, personal interviews were conducted to collect such information as their smoking history, family history of cancer, alcohol use and body mass index throughout their lives. Diabetics were also asked about their anti-diabetic medication history, both the names and the duration.

Diabetics were categorized by their use of four common classes of anti-diabetic therapies - insulin or insulin secretagogues, metformin, thaizolidinediones (TZDs), and/or other common anti-diabetic therapies and the duration of use.

The researchers found that diabetics who took metformin alone or in any combination with other diabetic therapies had a 62 percent reduction of risk of developing pancreatic cancer, compared to those who never used the drug. When the analysis was restricted to those who never used insulin or those who had diabetes more than two years, the protective effect of metformin remained significant. Other diabetesassociated risk factors, such as history of smoking, overweight or obesity, and glycemic control, did not have a significant effect on the relationship between metformin use and pancreatic cancer risk.

In contrast, diabetics who had taken insulin or insulin secretagogues had a 4.99- and 2.52-fold increased risk for the disease, respectively, compared with never users.

Findings regarding TZDs and the other drug classes and the risk of pancreatic cancer were inconclusive because of the small sample size; a larger cohort is needed to understand the association between their use and pancreatic cancer.

Li noted the study is not without limitations, including the relatively small size of the study's diabetic population; she hopes the research will be replicated in a larger sample size. Still, the findings present the

immediate opportunity to explore metformin as a chemopreventive agent.

Pancreatic cancer is the fourth leading cause of cancer death in men and women in this country. According to the American Cancer Society, more than 42,470 persons will be diagnosed and 35,240 will likely die from the disease in 2009. The median survival for patients with the disease is less than 10 months and the five-year survival rate is less than five percent.

"While further validation is needed, our findings show metformin's potential as a chemopreventive agent," said Li. "Currently, once pancreatic cancer is diagnosed, we have few successful therapeutic agents to offer our patients, so obviously, for those at greatest risk, a preventive mechanism such as metformin would be a welcome option."

According to the American Diabetes Association, in 2007, 1.6 million new cases of type 2 diabetes were diagnosed in people 20 years old or older. It's estimated that 23.5 million people older than the age of 20 have the disease.

In a corresponding editorial, Yu-Xiao Yang, M.D. of the University of Pennsylvania School of Medicine noted that the American Diabetes Association, as well as the European Association for the Study of Diabetes, have both recommended the inclusion of metformin for all type 2 diabetes patients without contraindications and notes that the possible chemopreventive properties of the drug "may provide an additional incentive for patients and physicians to follow this recommendation."

Source: University of Texas M. D. Anderson Cancer Center (news : web)