

Letter to the Editor

The interplay between antidiabetic medications and cancer risk

Sir,

Diabetes mellitus (DM) refers to a group of metabolic disorders marked by chronic hyperglycemia. Its primary cause usually involves impaired insulin secretion or impaired insulin action.¹ Its prevalence is escalating globally. Type II DM (T2DM) is becoming more common, and it is expected to afflict 7.7% (439 million) of persons aged 20 to 79 by 2030.² Diabetes appears to be linked to an increased risk of a variety of cancers, ranging from a 20 to 30% greater risk of breast or colorectal cancer to a 97% increased chance of intrahepatic cholangiocarcinoma or endometrial cancer. Shared risk factors and potential biochemical pathways have prompted investigations into the effect of antidiabetic medications (ADMs) on cancer risk. We intend to investigate the link between diabetes drugs and cancer development.

Diabetes and cancer share common risk factors such as tobacco use, physical inactivity, obesity, and poor diet.³ These factors intertwine to heighten the risk of various cancers. A higher prevalence of type II diabetes coupled with its shared etiology with cancer underlines the importance of understanding the impact of ADMs on cancer risk. Recent studies have yielded intriguing results regarding the relationship between ADMs and cancer incidence. While metformin and thiazolidinediones were linked to a lower risk of cancer incidence, insulin, sulfonylureas, and alpha-glucosidase inhibitors appear to elevate cancer risk.⁴ The implications of these divergent outcomes are vital for diabetic patients. Thus, all the patients taking ADMs should undergo age and sex appropriate cancer screenings for primary prevention and early detection of cancer in routine diabetes assessment.⁵

Insulin and insulin-like growth factor (IGF) not only regulate metabolic processes but also influence cell growth and proliferation. Disturbances in these pathways, particularly the phosphoinositide 3-kinases (PI3Ks) and mitogen-activated protein kinases (MAPK) pathways, contribute to cancer progression. The role of Fox proteins in linking insulin and androgen pathways further exacerbates the progression of cancer.⁶ Sulfonylureas and alpha-glucosidase inhibitors, both used in T2DM impact cancer risk through distinct mechanisms. Sulfonylureas stimulate insulin production, potentially increasing the risk of cancers associated with elevated insulin levels. In contrast, alpha-glucosidase inhibitors lower insulin levels

and may decrease the risk of specific cancers, such as pancreatic ductal adenocarcinoma (PDAC).⁷

The interplay between ADMs and cancer risk warrants consideration in diabetic care. While certain drugs appear to reduce cancer risk, others may contribute to its development. The disparities in outcomes associated with various diabetes drugs highlight the importance of individualized treatment approaches. To ensure early detection and prevention, it is prudent to add age and gender-appropriate cancer testing into routine diabetes evaluations. This letter sheds light on the complex relationship between diabetic medicines and cancer risk, emphasizing the importance of careful consideration in diabetic care for successful treatment and optimal patient outcomes as diabetes prevalence rises.

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