Anti-diabetic drugs could lower risk of primary and secondary brain cancer

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Diabetic patients who take anti-diabetic drugs—known as glitazones—long term had a lower risk of primary and secondary brain cancer compared with diabetic patients on other medications, new research led by the University of Bristol has found.

The study, published in *BMJ Open*, suggests these drugs could be repurposed to prevent brain metastasis in cancer patients who are at high risk of secondary cancers, if the current research is supported by future studies.

PPAR- α agonists (fibrates) and PPAR γ agonists (glitazones) drugs are clinically important due to their widespread safe use to treat high cholesterol (hyperlipidemia) and diabetes. Previous studies have suggested that fibrates and glitazones may have a role in brain tumor prevention. Given the safety and cost of the drugs, they have the potential to be repurposed to prevent brain cancers and reduce the risk of secondary tumors by stopping tumor growth.

Using primary care records from the UK GP database Clinical Practice Research Datalink (CPRD), which contains data from a network of over 2,000 GPs from more than 670 practices across the UK, the researchers examined if this theory could be supported.

The research team carried out two case-controlled studies using primary and secondary brain tumors identified within CPRD between 2000 and 2016. Cases and controls were selected from people who had been treated with any anti-diabetic or anti-hyperlipidemic drug.

The study identified 7,496 individuals with any brain tumor (4,471 primary; 3,025 secondary) in total. There were 1,950 cases and 7,791 controls in the fibrate and 480 cases with 1,920 controls in the glitazone analyses.

The researchers found long-term glitazone drug use by diabetic patients was associated with reduced primary and secondary brain tumor risk compared with diabetic patients on other medications. No association was found between fibrate use for hyperlipidemic patients and any type of brain tumor.

Kathreena Kurian, Professor of Neuropathology and Head of the Brain Tumor Research Centre at the University of Bristol and Honorary Consultant at North Bristol NHS Trust, and one of the study's authors, said, "The anti-diabetic drugs glitazones could potentially be involved in a pathway which prevents primary brain tumors and brain metastasis in diabetic and other patients.

"Our research could also be used to understand better pathways which prevent the development of primary brain tumors, such as glioma."

Yoav Ben-Shlomo, Professor of Clinical Epidemiology at the Bristol Medical School: Population Health Sciences (PHS) and corresponding author, added, "This is the largest study in diabetic patients showing a link between long-term glitazone use and decreased primary brain tumor and brain metastasis.

"If our research is validated in larger studies and trials, these drugs could be repurposed to prevent brain metastasis in cancer patients who are at high risk of secondary cancers, such as breast and lung cancer."

Further research is required to investigate whether these findings are replicated using independent datasets that are larger in size and/or with better data on blood sugar control and other potential causes and effects.

If the glitazone association is biologically causal, this could lead to a better understanding of pathophysiological mechanisms and potential therapies for the prevention of brain cancers. The researchers suggest this hypothesis could be tested in a future double-blind clinical trial if stronger evidence emerges from other studies, given the safety and current use of glitazones for managing diabetes.

More information: Jamie W Robinson et al, Use of drugs for hyperlipidaemia and diabetes and risk of primary and secondary brain

tumours: nested case–control studies using the UK Clinical Practice Research Datalink (CPRD), *BMJ Open* (2024). DOI: 10.1136/bmjopen-2023-072026