Cancer diagnosis makes diabetes patients less adherent to their prescribed diabetes drugs

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Diabetes patients become less adherent to their diabetes medications following a diagnosis of cancer, concludes a new study published in *Diabetologia*. The research is led by Marjolein Zanders, Netherlands Comprehensive Cancer Organisation, Eindhoven, the Netherlands, Jeffrey Johnson, School of Public Health, University of Alberta, Edmonton, Canada and colleagues.

Cancer patients with diabetes have a significantly higher overall mortality risk compared with patients without diabetes. Most research on diabetes and cancer has focussed on the influence of diabetes and glucose lowering drugs (GLDs) on outcomes after cancer diagnosis; yet cancer itself might affect outcomes associated with diabetes, in part by affecting adherence to their prescribed GLDs. Although one previous study has found that breast cancer patients were less likely to take their diabetes drugs as directed after being diagnosed with cancer, this study lacked a control group without cancer. In this new study, the authors aimed to evaluate changes in adherence to GLDs following a cancer diagnosis, taking into account changes in adherence to GLDs among similar diabetic patients without cancer.

All new users of GLDs (1998-2011) who lived in the Eindhoven Cancer Registry-PHARMO Database Network (which includes out-patient pharmacy data) catchment area were selected. From the 52,228 GLDs users selected, 3,281 cases with cancer and 12,891 controls without cancer during follow-up were included in the study, with a mean age of 68 years in each group. The Medication Possession Ratio (MPR) was

used as an indicator for medication adherence. The MPR represents the amount of medication patients had in possession over a certain time period. Thus, a 10% decline in MPR translates to a difference of 3 days in a 30-day month that are not covered by the use of GLDs (that is, 3 days in that month where the patients did not take their diabetes medications). For every month the MPR for cases was compared with the MPR for matched controls, which represented the overall trend among individuals with diabetes but without cancer.

The data showed that before cancer diagnosis the MPR increased by 0.10% per month. Besides a significant drop in MPR at the time of cancer diagnosis of -6.3%, there was an ongoing, yet lower, monthly decline in MPR (-0.20%) after cancer diagnosis. The largest drops in MPR at the time of cancer diagnosis, in the range of 11-15%, were seen among patients with stage IV cancer disease and gastrointestinal or pulmonary cancers.

Different effects were seen for the various tumour types studied: while no important decline in MPR was seen at the time of diagnosis for prostate (+2.1%) and breast cancer (-0.5%), large drops were seen among patients with oesophageal, stomach, pancreas or liver cancer (-12.5%;) and pulmonary cancers (-15.2%). Among those patients with large adherence drops, the MPR after cancer diagnosis decreased approximately 0.5% monthly, indicating ongoing declining medication adherence in such cases (oesophageal, stomach, pancreas or liver cancer -0.45%; pulmonary cancers -0.54%).

Within cancer subgroups, the largest declines in MPR at the time of cancer diagnosis were seen for liver and oesophageal cancer (-35% and -19% respectively), while for each extra month after cancer diagnosis, the largest decline in MPR of almost 1% each month was seen among patients with pancreatic cancer (-0.97%). Moreover, the higher (more serious) the stage of cancer, the greater the observed decline in

medication adherence at cancer diagnosis. Among patients with stage IV cancer disease, the drop in MPR was -10.7%, while each extra month after cancer diagnosis the MPR declined an additional -0.64%.

This population-based study revealed that among new GLDs users, the diagnosis of cancer negatively influenced medication adherence, with a decrease in MPR of 6% at the time of cancer diagnosis. This translates to a difference of 2 days in a month that are not covered by the use of GLDs following a diagnosis of any cancer. Importantly, the influence of cancer on GLDs adherence seemed to be influenced by the type of cancer, with more pronounced effects among patients with oesophageal, stomach, pancreas or liver cancer and pulmonary cancers. Also, more advanced cancer stages at diagnosis resulted in substantially lower MPRs at the time of cancer diagnosis.

The authors suggest that the devastating effects of a serious cancer diagnosis could relegate the importance of taking medication for diabetes or other conditions. "Users of GLDs with more lethal cancers might prioritise the fight against cancer over the effort required to have a good metabolic control for their diabetes," they explain. "The MPR might be a good indicator for medication adherence, although the physician could have advised the patient to stop the treatment with GLDs, which could not be investigated within the study. Reasons for stopping their treatment for diabetes are unknown - is it because of frequent hypoglycaemic events due to cancer or intolerable oral intake of drugs, for example among oesophageal or stomach cancer patients?"

The authors conclude: "This study revealed that the medication adherence among users of GLDs was influenced by cancer diagnosis. Although the impact of cancer was more pronounced among cancers with a worse prognosis and among those with more advanced cancer stages, the difference in prognosis associated with these cancers seemed to only partly explain the impact of cancer on medication adherence.

The decline in adherence seen among users of GLDs with cancer might negatively impact survival and (partly) explain the established association between diabetes, cancer and mortality. In future studies, the reason for the decline in MPR needs to be further elucidated among the different cancer types - is it the patient who prioritises the fight against cancer or the advice of the physician to stop the treatment?"

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