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THE POTENTIAL PROTECTIVE EFFECT OF METFORMIN AGAINST PANCREATIC CANCER: PRELIMINARY RESULTS FROM A CASE-CONTROL STUDY IN TWO UK CENTRES

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Introduction There are plausible biological mechanisms for how metformin, an oral hypoglycaemic agent, may have protective antitumour activity in adenocarcinoma of the pancreas. Metformin disrupts crosstalk between insulin/insulin-like growth factor-1 (IGF-1) receptor and G-coupled receptor signalling through its agonist effect on 5' AMP-activated protein

kinase (AMPK). This inhibits cell proliferation, promotes apoptosis, and reduces tumorigenic factors such as VEGF. The aim of this study was to conduct an epidemiologic aetiological investigation of metformin and pancreatic cancer in two large UK populations.

Methods All cases of pancreatic cancer diagnosed in Norfolk (2004–2006) and Leicestershire (2007) were identified, and the diagnosis and staging confirmed by reviewing the clinical notes. The use of metformin was recorded in both cancer patients and a group of dermatology controls of similar ages. The OR of developing pancreatic cancer was estimated using unconditional logistic regression adjusted for gender, age at diagnosis, cigarette smoking, and type II diabetes.

Results A total of 206 cases of adenocarcinoma of the pancreas were identified (median age 71 years, range 49–99 years, 52% women) and also 251 controls. The OR for cigarette smokers was 3.71 (95% CI 1.94 to 7.08) and for type II diabetes OR=3.47 (95% CI 1.72 to 7.02). In patients with type 2 diabetes metformin was prescribed less in cancer patients than controls (49% vs 73%, $p=0.11$). The use of metformin had a borderline statistically significant negative association with the development of pancreatic cancer, OR=0.28 (95% CI 0.06 to 1.22, $p=0.09$). No effect was found for the sulphonylurea hypoglycaemic drugs (OR= 0.38, 95% CI 0.08 to 1.70, $p=0.20$).

Conclusion These results may support the hypothesis that metformin has anticancer effects for pancreatic cancer, although further identification of cases and controls is continuing to more precisely define the association. Currently, the use of metformin should be measured in future aetiological studies of this aggressive tumour. If the results are consistent, then metformin may be assessed in clinical trials as a chemoprotective agent in those at high risk of the disease.

Competing interests None.

Keywords Aetiology, Metformin, Pancreatic cancer.