COMMENT ON CHO ET AL.

Antidiabetic Medications and Mortality Risk in Individuals With Pancreatic Cancer–Related Diabetes and Postpancreatitis Diabetes: A Nationwide Cohort Study. Diabetes Care 2019;42:1675–1683

Anne-Claire Devouge, Ninon Foussard, Pauline Poupon, Marie Monlun, Laurence Blanco, Kamel Mohammedi, and Vincent Rigalleau

Diabetes Care 2019;42:e189–e190 | https://doi.org/10.2337/dc19-1504

We were interested by the recent article from Cho et al. (1), who reported that mortality was reduced by half in metformin-treated subjects with postpancreatitis diabetes mellitus (PPDM). This information is important: the proportion of type 3c diabetes has long been underestimated as a result of misdiagnosis as type 2 diabetes. PPDM can reach 1.8% of new adult-onset diabetes cases (2) and up to 9.2% among hospitalized patients (3), second in frequency after type 2 diabetes.

Cho et al. concluded that metformin monotherapy appeared to be the best front-line treatment in individuals with PPDM, which seems provocative at first sight. Chronic pancreatitis was previously considered the most important cause of type 3c diabetes, accounting for 78.5% of cases (3). Nausea, abdominal complaints, diarrhea, and weight reduction are clinical symptoms of chronic pancreatitis, and they are also usual side effects of metformin, which may not be tolerated by such patients. However, the majority (59.6%) of the subjects with PPDM in the registry used by Cho et al. could use metformin, but its low mean dose (1,000 mg/day) suggests that tolerance was not always good.

In fact, most of these patients probably did not have chronic pancreatitis. In a previous report, Cho et al. (4) distinguished their PPDM cases as resulting from chronic (261/959 [27.2%]) versus acute (698/959 [72.8%]) pancreatitis. Moreover, compared with subjects with type 2 diabetes, the all-cause mortality was significantly higher only for the subjects with diabetes due to chronic pancreatitis (4).

The characteristics of PPDM resulting from chronic versus acute pancreatitis have been compared by Woodmansey et al. (2): low BMI and high HbA_{1c} were more frequent among subjects with chronic pancreatitis, who were more often coded as having type 1 diabetes and were twice as likely to require insulin therapy (2). Two-third of subjects with PPDM resulting from acute pancreatitis had overweight or obesity. We hypothesize that such patients probably better tolerate metformin, with a potential benefit to their survival.

Cho et al. (1) did their best to exclude diabetes preceding pancreatic diseases, as they only included subjects whose diagnosis of diabetes was stated more than 3 months after their first episode of pancreatitis. But type 2 diabetes is insidious and often neglected, and it is associated with a doubled incidence of acute pancreatitis, even without being treated with glucagon-like peptide 1 analogs or dipeptidyl peptidase 4 inhibitors (5). Therefore, despite the authors' efforts, the subjects who were included in the New Zealand registry due to acute pancreatitis may not always have been screened for diabetes, and we suspect that some of them may, in fact, have ignored type 2 diabetes before.

Because most of their registered PPDM cases occurred after acute pancreatitis, the study from Cho et al. suggests that metformin can be tolerated and beneficial after acute pancreatitis, which is an important point. However, the tolerability and benefits of metformin in subjects with PPDM need to be more precisely analyzed according to the type of pancreatitis. Were the proportions of patients treated by metformin similar in patients with chronic and acute pancreatitis? Were mortality rates similarly reduced in both groups on metformin?

Duality of Interest. No potential conflicts of interest relevant to this article were reported.

References

1. Cho J, Scragg R, Pandol SJ, Goodarzi MO, Petrov MS. Antidiabetic medications and mortality risk in individuals with pancreatic cancer–related diabetes and postpancreatitis diabetes: a nationwide cohort study. Diabetes Care 2019; 42:1675–1683
2. Woodmansey C, McGovern AP, McCullough KA, et al. Incidence, demographics, and clinical characteristics of diabetes of the exocrine pancreas (type 3c): a retrospective cohort study. Diabetes Care 2017;40:1486–1493

Endocrinology-Nutrition Department, Centre Hospitalier Universitaire de Bordeaux, Pessac, France

Corresponding author: Anne-Claire Devouge, anne-claire.devouge@chu-bordeaux.fr

3. Ewald N, Kaufmann C, Raspe A, Kloer HU, Bretzel RG, Hardt PD. Prevalence of diabetes mellitus secondary to pancreatic diseases (type 3c). Diabetes Metab Res Rev 2012;28: 338–342

4. Cho J, Scragg R, Petrov MS. Risk of mortality and hospitalization after post-pancreatitis diabetes mellitus vs type 2 diabetes mellitus: a population-based matched cohort study. Am J Gastroenterol 2019;114:804–812

5. Garg R, Chen W, Pendergrass M. Acute pancreatitis in type 2 diabetes treated with exenatide or sitagliptin: a retrospective observational pharmacy claims analysis. Diabetes Care 2010; 33:2349–2354