Evaluation Approach can Significantly Influence Oral Glucose-Lowering Drugs Total Mortality Risks in Retrospective Cohorts of Type 2 Diabetes Mellitus Patients

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Abstract:

Background: Retrospective evaluations of mortality risks in cohorts of patients with type 2 diabetes (T2D), receiving oral glucose-lowering drugs (OGLDs) gave conclusions about association between certain OGLDs and mortality that do not exactly agree with each other. Different approaches were used: recording the outcomes depending on the first prescription, later changes were ignored or receiving one of OGLDs according to data of last documented visit before the end of observation period; without change of OGLD during the whole observation; treatment intervals - period from onset of treatment to onset of the next drug treatment, or until outcome. Impact of each study approach was not evaluated yet. We conducted such comparative analysis using the database of Ukrainian Diabetes Register.

Methods: All-cause mortality in retrospective cohorts of 36 449 type 2 diabetes patients treated with glibenclamide, gliclazide or metformin monotherapy all of which were included at least in one of evaluation models: “first prescription” - 2 862/257, “last prescription” - 34 818/4 224; “unchanged” - 8 786/680 and “treatment intervals” - 13 546/3 142 T2D patients / death cases respectively, were evaluated using Cox regression with gender, age, and diabetes duration adjusting. We compared the mortality risk (Hazard ratios -HRs) associated with Gliclazide or Metformin versus Glibenclamide monotherapy.

Results: Gliclazide or metformin-treated patients demonstrated lesser mortality risk than glibenclamide-treated ones in all four evaluation models, but age and duration stratification can influence this phenomenon in case of “first prescription model”. In case of “without change OGLD” model the increase of mortality risk in glibenclamide-treated group is the most evident when comparing to gliclazide-treated, rather than to metformin-treated one. When comparing gliclazide vs metformin mortality risk for this model, gliclazide-treated patients demonstrated lesser mortality risk than metformin-treated ones: gender, age and diabetes duration adjusting HR = 0.51 (0.35-0.72), p<0.001.

Conclusion: Different approaches used for mortality analysis in observation studies of T2D patients can present discrepant results.

Keywords: Total mortality risks, type 2 diabetes, evaluation models, gliclazide, metformin, glibenclamide.