CONCOMITANT USE OF SULFONYLUREAS AND BETA-BLOCKERS AND THE RISK OF SEVERE HYPOGLYCEMIA: POPULATION-BASED COHORT STUDY

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Objective: Evidence suggests that beta-blockers increase the risk of hypoglycemia. However, their effects among users of sulfonylureas, drugs that also cause hypoglycemia, are not well understood. Thus, our study assessed the potential association between concomitant use of sulfonylureas and beta-blockers and the risk of severe hypoglycemia.

Design and method: This retrospective cohort study used the United Kingdom Clinical Practice Research Datalink linked to hospitalization and vital statistics data. It included patients with type 2 diabetes initiating sulfonylurea treatment between 1998 and 2020. Patients with use of beta-blockers in the 6 months prior to cohort entry were excluded. Time-dependent Cox proportional hazards models estimated confounder-adjusted hazard ratios (HRs) with 95% confidence intervals (CIs) of severe hypoglycemia associated with concomitant use of sulfonylureas and beta-blockers compared to sulfonylurea use alone. To account for residual confounding, we also performed an analysis using an active comparator, where the reference category was current concomitant use of sulfonylureas and thiazide diuretics. To explore the role of cardioselectivity in the hypoglycemic risk of beta-blockers, we further compared head-to-head current concomitant use of sulfonylureas and non-cardioselective beta-blockers (i.e., propranolol, carvedilol, sotalol, labetalol) versus current concomitant use of sulfonylureas and cardioselective beta-blockers (i.e., acebutolol, atenolol, bisoprolol, metoprolol, nebivolol, esmolol).

Results: Our cohort included 252,869 patients initiating sulfonylureas. During a mean (standard deviation) follow-up of 8.6 (5.7) years, there were 16,857 events of severe hypoglycemia (crude incidence rate, 7.8 [95% CI, 7.6–7.9] per 1000 person-years). Compared to sulfonylurea use alone, concomitant use of sulfonylureas and beta-blockers was associated with a 53% increased risk of severe hypoglycemia (adjusted HR, 1.53; 95% CI, 1.42–1.65). The use of an active comparator led to consistent findings (adjusted HR, 1.69; 95% CI, 1.42–2.01). When comparing concomitant use of sulfonylureas and non-cardioselective beta-blockers to concomitant use of sulfonylureas and cardioselective beta-blockers, we were not able to detect an increased risk of severe hypoglycemia (adjusted HR, 0.95; 95% CI, 0.74–1.24).

Conclusions: Our population-based study showed an increased risk of severe hypoglycemia associated with concomitant use of sulfonylureas and beta-blockers. Cardioselectivity of beta-blockers did not seem to play a major role in this regard.

BLOOD PRESSURE-INDEPENDENT RENOPROTECTION IN DIABETIC RATS TREATED WITH SMALL INTERFERING RNA TARGETING LIVER ANGIOTENSINOGEN

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Objective: Small interfering RNA (siRNA) targeting liver angiotensinogen (AGT) exerts beneficial effects on blood pressure and kidney function, but its effects in diabetes are still unknown.

Design and method: To address this, TGR(mREN2)27 rats (a model of angiotensin II-dependent hypertension) were made diabetic with streptozotocin for 18 weeks and treated with vehicle, AGT siRNA, the angiotensin receptor blocker valsartan, the ACE inhibitor captopril, valsartan + siRNA, or valsartan + captopril for the final 3 weeks. Arterial pressure was measured via radiotelemetry.

Results: Baseline mean arterial pressure (MAP) was 164 ± 1 mm Hg. Diabetes resulted in albuminuria, accompanied by glomerulosclerosis and podocyte effacement, without a further rise in MAP or a change in glomerular filtration rate. All treatments lowered MAP (by ~50 mm Hg) and cardiac hypertrophy identically. Treatment with siRNA resulted in the largest reduction in AGT, while in combination with valsartan AGT virtually disappeared. Only the dual treatment groups and captopril lowered circulating angiotensin II and aldosterone. No treatment affected renal AGT mRNA expression, confirming the liver-specificity of the siRNA. Yet, siRNA with or without valsartan, and valsartan + captopril, but not valsartan alone, or captopril alone, reduced renal angiotensin I and II. All treatments lowered albuminuria and proteinuria, while only siRNA with or without valsartan improved glomerulosclerosis and podocyte dysfunction. Multiple linear regression confirmed both mean arterial pressure and renal angiotensin II as independent determinants of albuminuria.

Conclusions: In conclusion, AGT siRNA exerts renoprotection in diabetic TGR(mREN2)27 rats, and this relies, at least in part, on the suppression of renal angiotensin II formation from liver-derived AGT. Consequently, AGT siRNA may prove beneficial in human diabetic kidney disease.

PROGNOSTIC VALUE OF THE GLYCOSYLATED HEMOGLOBIN TO THE MACE IN HYPERTENSIVE NON DIABETIC PATIENTS

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Objective: Of the study was the investigation of the association and the prognostic value of the level of serum glycosylated hemoglobin (HbA1c), with the MACE in hypertensive non diabetic patients

Design and method: This is a prospective analysis including 174 hypertensive treated or newly diagnosed untreated, non diabetic patients (57,3% female) of mean age at the entry of the study: 59,4 ± 13,3 years, mean office systolic/diastolic blood pressure (S/DBPo): 147,9 ± 18,2/91,8 ± 11,0 mmHg, mean office heart rate (HRo): 75,0 ± 12,4 beats/min, MBMI: 28,5 ± 4,7 kg/m2 The median follow-up period was 7,5 years.
The MHbA1c (5,7 ± 0,92 %) was measured at the entry of the study. Major cardiovascular events (MACE) (myocardial infarction, unstable angina, transient ischemic attack or stroke, peripheral vascular intervention, heart failure events, cardiovascular death) were registered. We estimated the prognostic value of the HbA1c to the MACE.
Cox proportional hazard model were employed to determine the prognostic value of HbA1c.

Results: The median follow-up period was 7,5 years.
There were 70 (40,2%) MACE at the end of the study and the cox regression analysis revealed that HbA1c was strong predictor factor for the MACE (HR: 1,32 95%cl: 1,093–1,599 p value 0.004)

Table

Prognostic value for the HbA1c to the MACE	Hazard ratio	95% Confidence Intervals	P value
HbA1C (mg/dl)	1,32	1,093–1,599	0,004

HbA1c = glycosylated hemoglobin

Conclusions: HbA1c levels have significant predictive value for MACE, in hypertensive non diabetic patients in a follow up of 7.5 years

LEVEL OF ADHERENCE TO THE PHARMACOLOGICAL AND NON-PHARMACOLOGICAL TREATMENT OF PATIENTS WITH DIABETES MELLITUS

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Objective: To identify the level of adherence to pharmacological and non-pharmacological treatments according to age, sex and time of evolution in patients with diabetes mellitu

Design and method: Cross-sectional observational analytical descriptive study, population 739 patients, with a sample of 272, which were randomly selected. Bonilla questionnaire validated with a Crombach alpha of 0.86 was applied. Tests