Glycaemic variability is associated with microvascular complications in Emiratis with type 2, but not type 1 diabetes

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Background

Microvascular complications of diabetes mellitus are a major source of morbidity. Evidence exists that variability in blood glucose may contribute to microvascular complications of type 1 and type 2 diabetes mellitus.

Aims

To determine whether variability of HbA1c or early morning serum glucose contribute to the risk of microvascular complications of diabetes, controlling for established risk factors.

Method

We examined records from people of Emirati origin diagnosed with type 1 (n=994) or type 2 (n=18,904) diabetes mellitus, who underwent retinal screening between 01/01/2015 and 01/04/2017, with at least five available measurements of HbA1c and plasma glucose. “Average” and “variability” of HbA1c and glucose were expressed as the mean and standard deviation (SD) of measurements. Retinal disease in the more severely affected eye was classified as “none” (R0M0), “background” (R1M0) or “significant” (any higher grade). Microalbuminuria defined as urinary albumin:creatinine ratio ≥2.5 mg/mmol in females or ≥3.5 mg/mmol in males in both of the two most recent measurements. Microalbuminuria was considered diabetic in origin in all type 1 diabetes cases and in all individuals with type 2 diabetes with coexisting retinopathy. Smoking was graded in ordered fashion as "never smoked”, “passive smoking”, “ex-smoker” and “current smoker”. Logistic regression models were used to examine the contribution of average and variability of HbA1c and glucose to the likelihood of retinal or renal endpoints, controlling for diabetes duration, smoking, and most recently measured systolic blood pressure (sBP). Interaction terms were included for means and SDs of both HbA1c and glucose.

Results

Patients with type 1 diabetes had higher mean HbA1c (8.8% cf 7.4%, p<0.0001), mean glucose (11.7 mmol/L cf 9.1 mmol/L, p<0.0001), SD HbA1c (1.18% cf 0.88%, p<0.0001), and SD glucose (5.12 mmol/L cf 2.25 mmol/L, p<0.0001) compared to those with type 2 diabetes.

SD HbA1c was an independent predictor of both background (OR 2.093 (1.103-3.973), p=0.024) and significant (OR 11.367 (6.156-20.988), p<0.0001) retinopathy endpoints, and of the nephropathy endpoint (OR 2.400 (1.212-4.768), p=0.012), in people with type 2 diabetes. The interaction between SD and mean HbA1c was significant, indicting that the effect of HbA1c variability was greatest at lower values of mean HbA1c.

SD Glucose was an independent predictor of both background (OR 1.266 (1.095-1.464), p = 0.001) and significant (OR 1.264 (1.107-1.443), p =0.001) retinal disease endpoints, and of the nephropathy endpoint (OR 1.536 (1.323-1.787), p<0.0001) in people with type 2 diabetes. The interaction between SD and mean glucose was significant for the nephropathy and background retinopathy endpoints.

Neither SD HbA1c nor SD glucose were independent predictors of either of the diabetic retinopathy endpoints or the nephropathy endpoint in people with type 1 diabetes.

Average HbA1c, diabetes duration, smoking and systolic blood pressure significantly and independently predicted the nephropathy endpoint in both type 1 and type 2 diabetes; average glucose was also a significant nephropathy predictor in people with type 2 diabetes. Average HbA1c and diabetes duration were significant predictors of both background and clinically significant retinopathy in both type 1 and type 2 diabetes patients. Smoking was a significant predictor for both retinal endpoints in type 1 diabetes and for background disease in people with type 2 diabetes. sBP was a significant predictor for both retinal endpoints in type 2 diabetes and for significant retinal disease in type 1 diabetes.

Discussion

Glycaemic variability is an independent predictor of microvascular complications in type 2 diabetes, but its predictive power diminishes with increasing average HbA1c and glucose. Neither variability of glucose nor HbA1c significantly predicted microvascular outcomes in Emirati people with type 1 diabetes, despite higher variability of both than found in people with type 2 diabetes.