Incidence and progression of diabetic retinopathy within a private diabetes mellitus clinic in South Africa

Objective:
The study objective was to examine the influence of glycaemic control and ethnic variations on the incidence and progression of diabetic retinopathy (DR).

Design, subjects and setting:
Eight hundred and ninety-two persons with type 1 diabetes mellitus, and 1 998 persons with type 2 diabetes mellitus, who were enrolled in a private diabetes mellitus management programme in South Africa, participated in the study. Survival analyses were conducted to assess the relationship between the risk factors and the incidence of DR and referable DR, and the progression of DR.

Outcome measures:
Cumulative incidence of diabetic retinopathy and referable diabetic retinopathy.

Results:
The seven-year cumulative incidence of DR and referable DR was 536 and 50 cases per 1 000 persons with type 1 diabetes mellitus without DR at baseline, and 351 and 47 cases per 1 000 persons with type 2 diabetes mellitus. The seven-year cumulative incidence of referable DR was 332 cases per 1 000 persons with type 1 diabetes mellitus with background DR at baseline, and 360 cases with type 2 diabetes mellitus. This represented a seven- and eightfold increase compared to no DR at baseline. After controlling for known risk factors for DR, a high baseline haemoglobin A1C (HbA1c) and non-Caucasian ethnicity were associated with the incidence of referable DR in patients with type 1 and type 2 diabetes mellitus.

Conclusion:
It was revealed in the first study to report on the incidence and progression of DR in South Africa that a high baseline HbA1c, ethnicity, and the presence of background DR increased the risk of the development of referable DR.

SOURCE:
Should butter intake be reduced to a minimum in cases of hypercholesterolemia?

Butter is rich in saturated fats, particularly palmitic and myristic acids which are known for their hypercholesterolaemic effects. This is the main reason behind the recommendation to limit butter intake with cardiovascular risk factors. Several clinical trials have shown that high butter intake increases LDL-C but does not affect HDL-C levels. The effect of moderate butter intake had not been rigorously examined until the study by Sara Engel and Tine Tholstrup sponsored by the Danish Dairy Research Foundation.

**Butter or olive oil**

This double-blinded crossover dietary intervention study was conducted in 47 volunteers (33 women and 14 men, mean age 40 years, mean BMI 23.5 kg/m², LDL cholesterol 2.88 mmol/L). The subjects’ habitual diet was modified during two 5-week periods (“butter intake” and “olive oil intake”). During the “butter” period, subjects ate buttered bread (15 g of butter, the amount being calculated so that 4.5 % of total energy came from butter). During the “olive oil” period, subjects ate bread spread with olive oil (containing an identical amount of fats). Each period was preceded by a 14-day run-in during which subjects consumed their habitual diets. Subjects were weighed weekly and it was checked that there was no change in the level of physical activity or dietary habits outside of what was prescribed.

A marked effect of butter on LDL cholesterol

Compared with the “olive oil” period, the “butter” period increased LDL-C by 5.6 % (from a mean of 2.88 mmol/L to 3.04 mmol/L). While butter intake also led to an increase in HDL-C, olive oil had no effect on this parameter. Neither butter nor olive oil had any effect on plasma triglycerides, HOMA-estimated insulin resistance, or high sensitivity CRP, a marker of underlying inflammation. The authors noted a larger than expected effect of butter on LDL-C levels and pointed out that the potential cardiovascular consequences are significant because a 1 mmol/L decrease in LDL-C over the long term is associated with a 20 % reduction in cardiovascular mortality. Furthermore, while observational epidemiological data indicate that raising HDL-C could theoretically counteract the increase in LDL-C, this hypothesis has been widely questioned by recent data showing that increasing HDL-C is not systematically beneficial. In fact, it is the quality of HDL particles, i.e. their anti-atherogenic function, rather than their quantity in plasma that should be improved in order to lower cardiovascular risk, and the effect of butter on this function of HDL-C is not known.

This study shows that moderate daily intake of butter for several weeks has a cholesterol-raising effect. This confirms the recommendation that consumption of butter should be kept to a minimum in people with hypercholesterolaemia and/or at high cardiovascular risk.

Why do statins increase the risk of type 2 diabetes mellitus?

Background
Statins increase the risk of new-onset type 2 diabetes mellitus. We aimed to assess whether this increase in risk is a consequence of inhibition of 3-hydroxy-3-methylglutaryl-CoA reductase (HMGCR), the intended drug target.

Methods
We used single nucleotide polymorphisms in the HMGCR gene, rs17238484 (for the main analysis) and rs12916 (for a subsidiary analysis) as proxies for HMGCR inhibition by statins. We examined associations of these variants with plasma lipid, glucose, and insulin concentrations; bodyweight; waist circumference; and prevalent and incident type 2 diabetes. Study-specific effect estimates per copy of each LDL-lowering allele were pooled by meta-analysis. These findings were compared with a meta-analysis of new-onset type 2 diabetes and bodyweight change data from randomised trials of statin drugs. The effects of statins in each randomised trial were assessed using meta-analysis.

Findings
Data were available for up to 223 463 individuals from 43 genetic studies. Each additional rs17238484-G allele was associated with a mean 0.06 mmol/L (95 % CI 0.05-0.07) lower LDL cholesterol and higher body weight (0.30 kg, 0.18-0.43), waist circumference (0.32 cm, 0.16-0.47), plasma insulin concentration (1.62 %, 0.53-2.72), and plasma glucose concentration (0.23 %, 0.02-0.44). The rs12916 SNP had similar effects on LDL cholesterol, bodyweight, and waist circumference. The rs17238484-G allele seemed to be associated with higher risk of type 2 diabetes (odds ratio [OR] per allele 1.02, 95 % CI 1.00-1.05); the rs12916-T allele association was consistent (1.06, 1.03-1.09). In 129 170 individuals in randomised trials, statins lowered LDL cholesterol by 0.92 mmol/L (95 % CI 0.18-1.67) at 1-year of follow-up, increased bodyweight by 0.24 kg (95 % CI 0.10-0.38 in all trials; 0.33 kg, 95 % CI 0.24-0.42 in placebo or standard care controlled trials and −0.15 kg, 95 % CI −0.39 to 0.08 in intensive-dose vs moderate-dose trials) at a mean of 4.2 years (range 1.9-6.7) of follow-up, and increased the odds of new-onset type 2 diabetes (OR 1.12, 95 % CI 1.06-1.18 in all trials; 1.11, 95 % CI 1.03-1.20 in placebo or standard care controlled trials and 1.12, 95 % CI 1.04-1.22 in intensive-dose vs moderate dose trials).

Interpretation
The increased risk of type 2 diabetes noted with statins is at least partially explained by HMGCR inhibition.

Source: The Lancet: 30 September 2014

According to the epidemiological analysis of patients included in the United Kingdom Prospective Diabetes Study (UKPDS), coronary risk in patients with type 2 diabetes (T2D) depends on five independent factors, including high HbA1c levels, increased LDL cholesterol and systolic blood pressure, low HDL cholesterol, and tobacco smoking. When all patients from both the intensive and conventional groups were included in a post-hoc analysis, a strong linear correlation was found between mean HbA1c during follow-up and cardiovascular events. Each 1% reduction in mean HbA1c levels was associated with a decrease of 14% in risk for myocardial infarction, 12% for stroke, 43% for lower-limb amputation, and of 16% for heart failure.

These results have been confirmed by two recent studies. In the first, performed in 2137 Chinese aged ≥65 attending a geriatric health service in Hong Kong, correlations between HbA1c levels and coronary events, strokes, cardiovascular events, and coronary and all-cause mortality were examined over a mean 7.9 year follow-up. After adjustment for confounders, patients with high HbA1c levels (>8.5%) compared with those in the 7.5% to 8.4% range, presented with an increased risk of cardiovascular events (HR 2.11) and of stroke mortality (HR 2.43). Compared with those with HbA1c 6.5% or less, they presented with an increased risk of all-cause mortality (HR 1.41) and of coronary mortality (HR 2.44). In addition, the relationship between HbA1c levels and stroke mortality presented as a U-shaped curve, similar to what was observed when examining the relationship between HbA1c and cardiovascular events and deaths in ADVANCE, or in population studies.

The second study was a post-hoc analysis of 7479 T2D patients (44% women), enrolled in the Sibutramine Cardiovascular OUTcomes (SCOUT) trial. The goal was to establish the optimal HbA1c levels for preventing cardiovascular events and deaths in overweight and obese T2D patients. At baseline, mean age was 62 years, HbA1c 7.2%, diabetes duration 7 years, and BMI 34 kg/m². For each 1% percentage point increase in HbA1c, the multi-adjusted HR for the primary composite end point (myocardial infarction, stroke, cardiac arrest, or cardiovascular mortality) was 1.17. The influence of the increase in HbA1c levels was greater in women than in men, with HR 1.22 vs 1.12 for each 1% percentage point increase in HbA1c. These results were not modified when adjusted for glucose-lowering treatments, diabetes duration, or history of cardiovascular disease. In addition, in this population of overweight and obese T2D patients, there was no evidence of an increased risk in patients with HbA1c ≤6.4% as seen in the ACCORD population. Similar results have reported in a UK study performed in the general practice. This may be explained by the protection against severe hypoglycaemia related to decreased insulin sensitivity in overweight and obese patients with T2D. Some data from ACCORD seem to indicate that T2D patients with markers of auto-immunity against β-cells were at increased risk for severe hypoglycaemia.

While some controversies have been raised concerning the impact of decreasing HbA1c in patients with T2D for reducing cardiovascular events and premature mortality, these results are in favour of better glycaemic control in the long term in such patients, especially when overweight or obese.

**SOURCE:** Prof P-J. Guillausseau