Journal Watch

Changes in Diabetes-Related Complications in the United States, 1990–2010

EDITOR'S VIEW

It is a nice study showing improvement in the rate of diabetic complications likelower-extremity amputation, end-stage renal disease, acute myocardial infarction, stroke, and death from hyperglycemic crisis between 1990 and 2010. Improvement is much more with acute myocardial infarction probably because of more awareness about the cardiac care both of the patient and the clinicians. But till date we are far from our target.

Preventive care for adults with diabetes has improved substantially in recent decades. The authors examined trends in the incidence of diabetes-related complications in the United States from 1990 through 2010.They used data from the National Health Interview Survey, the National Hospital Discharge Survey, the U.S. Renal Data System, and the U.S. National Vital Statistics System to compare the incidences of lower-extremity amputation, end-stage renal disease, acute myocardial infarction, stroke, and death from hyperglycemic crisis between 1990 and 2010, with age standardized to the U.S. population in the year 2000.

Rates of all five complications declined between 1990 and 2010, with the largest relative declines in acute myocardial infarction (−67.8%; 95% confidence interval [CI], −76.2 to −59.3) and death from hyperglycemic crisis (−64.4%; 95% CI, −68.0 to −60.9), followed by stroke and amputations, which each declined by approximately half (−52.7% and −51.4%, respectively); the smallest decline was in end-stage renal disease (−28.3%; 95% CI, −34.6 to −21.6). The greatest absolute decline was in the number of cases of acute myocardial infarction (95.6 fewer cases per 10,000 persons; 95% CI, 76.6 to 114.6), and the smallest absolute decline was in the number of deaths from hyperglycemic crisis (−2.7; 95% CI, −2.4 to −3.0). Rate reductions were larger among adults with diabetes than among adults without diabetes, leading to a reduction in the relative risk of complications associated with diabetes. When expressed as rates for the overall population, in which a change in prevalence also affects complication rates, there was a decline in rates of acute myocardial infarction and death from hyperglycemic crisis (2.7 and 0.1 fewer cases per 10,000, respectively) but not in rates of amputation, stroke, or end-stage renal disease.

Rates of diabetes-related complications have declined substantially in the past two decades, but a large burden of disease persists because of the continued increase in the prevalence of diabetes.

Edward W. Gregg, *et al*. *N Engl J Med* 2014;370:1514–1523.

Corneal Confocal Microscopy to Assess Diabetic Neuropathy: An Eye on the Foot

EDITOR'S VIEW

There is no real early marker of diabetic peripheral neuropathy. The corneal confocal microscopy can be a real solution

Accurate detection and quantification of human diabetic peripheral neuropathy are important to define at-risk patients, anticipate deterioration, and assess new therapies. Easily performed clinical techniques such as neuro-logical examination, assessment of vibration perception or insensitivity to the 10 g monofilament only assess advanced neuropathy, i.e., the at-risk foot.

Techniques that assess early neuropathy include neurophysiology (which assesses only large fibers) and quantitative sensory testing (which assesses small fibers), but they can be highly subjective while more objective techniques, such as skin biopsy for intra-epidermal nerve fiber density quantification, are invasive and not widely available. The emerging ophthalmic technique of corneal confocal microscopy allows quantification of corneal nerve morphology and enables clinicians to diagnose peripheral neuropathy in diabetes patients, quantify its severity, and potentially assess therapeutic benefit.

MitraTavakoli *et al*. *J Diabetes Sci Technol* 2013;7(5):1179–1189

Does dipeptidyl peptidase-4 inhibition prevent the diabetogenic effects of glucocorticoids in men with the metabolic syndrome?

EDITOR'S VIEW

Treatment of drug induced diabetes are very risky. If the diabetogenic drug is stopped and the antidiabetic drug is continued in the same pattern hypoglycaemia can result. Gliptin is very ideal in this situation, because their effect is dependent upon the blood sugar level and do not commonly produce hypoglycemia. This study has also shown that treatment with sitagliptin improved various aspects of pancreatic islet-cell function.

Anti-inflammatory glucocorticoid (GC) therapy often induces hyperglycemia due to insulin resistance and islet-cell dysfunction. Incretin-based therapies may preserve glucose tolerance and pancreatic islet-cell function. In this study, we hypothesized that concomitant administration of the dipeptidyl peptidase-4 inhibitor sitagliptin and prednisolone in men at high risk to develop type 2 diabetes could protect against the GC-induced diabetogenic effects.

Men with the metabolic syndrome but without diabetes received prednisolone 30mg once daily plus sitagliptin 100mg once daily (n=14), prednisolone (n=12) or sitagliptin alone (n=14) or placebo (n=12) for 14 days in a double-blind 2×2 randomized-controlled study. Glucose, insulin, C-peptide, and glucagon were measured in the fasted state and following a standardized mixed-meal test. β-cell function parameters were assessed both from a hyperglycemic–arginine clamp procedure and from the meal test. Insulin sensitivity (M-value) was measured by euglycemic clamp.

Prednisolone increased postprandial area under the curve (AUC)-glucose by 17% (P<0.001 vs placebo) and postprandial AUC-glucagon by 50% (P<0.001). Prednisolone reduced 1st and 2nd phase glucose-stimulated- and combined hyperglycemia–arginine-stimulated C-peptide secretion (all P≤0.001). When sitagliptin was added, both clamp-measured β-cell function (P=NS for 1st and 2nd phase vs placebo) and postprandial hyperglucagonemia (P=NS vs placebo) remained unaffected. However, administration of sitagliptin could not prevent prednisolone-induced increment in postprandial glucose concentrations (P<0.001 vs placebo). M-value was not altered by any treatment.

Fourteen-day treatment with high-dose prednisolone impaired postprandial glucose metabolism in subjects with the metabolic syndrome. Concomitant treatment with sitagliptin improved various aspects of pancreatic islet-cell function, but did not prevent deterioration of glucose tolerance by GC treatment

Eur J Endocrinol 2014;170:429–439.

Are SGLT 2 Inhibitors effective in Type 1 DM ?

EDITOR'S VIEW

So long majority of the trials have established the role of SGLT2 inhibitors in Type 2 diabetes. This trial is a unique one to show the efficacy of the drug in Type 1 diabetes.If severallarge multicentric trials can establish the efficacy the Type 1diabetics will ultimately get one oral drug in addition to insulin.

Adjunctive-to-insulin therapy with sodium-glucose cotransporter 2 (SGLT2) inhibition may improve glycemic control in type 1 diabetes (T1D).

The glycemic efficacy and safety of empagliflozin 25 mg daily in 40 patients treated for 8 weeks in a single-arm open-label proof-of-concept trial (NCT01392560) was evaluated. Mean A1C decreased from 8.060.9% (64610mmol/mol) to 7.660.9% (60610 mmol/mol) (P < 0.0001), fasting glucose from 9.0 6 4.3 to 7.0 6 3.2 mmol/L (P =0.008), symptomatic hypoglycemia (<3.0 mmol/L) from 0.12 to 0.04 events per patient per day (P = 0.0004), and daily insulin dose from 54.7620.4 to 45.8618.8

units/day (P < 0.0001).Mean urinary excretion of glucose increased from 19 619 to 134 6 61 g/day (P < 0.0001). Weight decreased from 72.6 6 12.7 to 70.0 6 12.3 kg (P < 0.0001), and waist circumference decreased from 82.9 6 8.7 to 79.1 6 8.0 cm (P < 0.0001). This proof-of-concept study strongly supports a randomized clinical trial of adjunctive-to-insulin empagliflozin in patients with T1D.

Diabetes Care 2014;37:1480–1483.

Peripheral arterial disease in patients with type 2 diabetes mellitus in South India: The urban vs rural divide

EDITOR'S VIEW

The study is very interesting to compare the scenario of PAD in rural and urban diabetics. Complications in rural patients are occurring earlier and the rural patients with PAD had two and a half times higher risk of IHD.

Peripheral arterial disease (PAD) is a variant of for macrovascular disease and complicated by lower limb amputations, in patients with diabetes. The aim of this study was to screen for asymptomatic PAD using ankle brachial index (ABI) in order to characterize and compare risk factors associated with it and to look for the presence of ischemic heart disease (IHD) in rural and urban populations.

This was an observational, cross-sectional study involving type 2 diabetic patients attending the diabetes clinic in an urban and rural hospital. Two hundred rural (R) and 400 urban (U) patients were screened for PAD over a period of 1 year. An ABI ≤0.9 or >1.3 was considered abnormal. Patients with known PAD and or claudication were excluded as the aim was to look for PAD in asymptomatic patients.

Out of them, 17.8% of patients had an ABI suggestive of PAD (R 20% vs U 16.8%). 63.6% were male. Known risk factors of PAD were identified and included dyslipidemia (85%; R 92.5% vs U 80.6%; OR 1.61), obesity (84.1%; R 85% vs U 83.6%; OR 0.75), hypertension (59.8%;R 47.5% vs U 67.2%; OR 1.26), and age >50 years (64.5%; R 55% vs U 70%; OR1.24).

Except for smoking (22.4%; R 32.5% vs U 16.4%; OR 1.03), none of the other risk factors were different between groups. Mean duration of type 2 diabetes mellitus (T2DM) was 7.95±7.50 (R 4.66±5.22 vs U 9.61±7.93; P<0.001). Electrocardiogram (ECG) changes consistent with IHD were found in 25.3% of patients with PAD (R 20% vs U 28.3%; OR 3.06; confidence interval (CI) 1.81-5.18; P=0.001).

The study demonstrates that one in six asymptomatic South Indians with T2DM have PAD. One in four patients with PAD had ECG changes of IHD which was statistically significant.

Based on the odds ratio, the rural patients with PAD had two and a half times higher risk of IHD, even though there was no statistically significant difference in cardiovascular risk factors, age, sex, and mean hemoglobin A1c (HbA1c) in both groups.

Bhavana Sosale,*et al*. *Journal of Academy of Medical Sciences* 2012;105(2).

Impact of Visit-to-Visit Glycemic Variability on the Risks of Macrovascular and Microvascular Events and All-Cause Mortality in Type 2 Diabetes: The ADVANCE Trial

EDITOR'S VIEW

It has been recently been thought of that beyond blood sugar values and the HbA1c values glycaemic variability is also a determining factor for developing complications in diabetes.This study shows adefinite association between VVV of fasting glucose and increased risk of vascular events, variability of HbA1c with the risk of macrovascular events and glucose variability with both macro- and microvascular events. The study population is a bigger one and the message cannot be neglected.

There is no definite opinion on the importance of visit-to-visit glycemic variability in diabetes. The study group assessed the effects of visit-to-visit variability (VVV) in HbA1c and fasting glucose on major outcomes in the ADVANCE (Action in Diabetes and Vascular Disease: Preterax and Diamicron MR Controlled Evaluation) trial.

The trial ADVANCE was a factorial randomized controlled trial of intensive glucose control

and blood pressure lowering in patients with type 2 diabetes. VVV in the intensive glucose treatment group was defined using the SD of five measurements of HbA1c and glucose taken 3–24 months after randomization. The outcomes were combined macro- and microvascular events and all-cause mortality occurring post 24 months.

Out of the 4,399 patients in the intensive group, an increase in VVV of HbA1c was associated with an increased risk of vascular events ($P = 0.01$) and with mortality ($P < 0.001$): highest versus lowest tenth hazard ratio (95% CI) 1.64 (1.05–2.55) and 3.31 (1.57–6.98), respectively, after multivariable adjustment. A definite association was noted between VVV of fasting glucose and increased risk of vascular events ($P < 0.001$; 2.70 [1.65–4.42]). HbA1c variability was positively associated with the risk of macrovascular events ($P = 0.02$ for trend), whereas glucose variability was associated with both macro- and microvascular events ($P = 0.005$ and $P < 0.001$ for trend, respectively). Sensitivity analyses using other indices, and

patients in the standard glucose treatment group, were broadly consistent with these results.

Consistency of glycemic control is important to reduce the risks of vascular events and death in type 2 diabetes.

Yoichiro Hirakawa, Hisatomi Arima, Sophia Zoungas, *et al*.
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