Why Are We Missing Chances to Prevent Diabetes?

Prevalence, Diagnosis, and Treatment of Impaired Fasting Glucose and Impaired Glucose Tolerance in Non-diabetic US Adults

Using data from a nationally representative sample of the US population 3 years after publication of the Diabetes Prevention Program results (Fourth National Health and Nutrition Examination Survey [NHANES IV]), Karve and Hayward assessed the proportion of 1547 adults who met the criteria for impaired fasting glucose (IFG) or impaired glucose tolerance (IGT) and the proportion of adults with these conditions who (1) reported receiving a formal diagnosis from their physicians, (2) reported having lifestyle modification recommended or were prescribed an oral hypoglycaemic agent (OHA), and (3) were actively modifying their lifestyle or taking an OHA.

Individuals were considered prediabetic if they reported that a physician told them had "borderline diabetes, prediabetes, impaired fasting glucose, or impaired glucose tolerance." Receipt of an anti-hyperglycaemic agent was considered pharmacotherapy for prediabetes, and vigorous or moderate activity for about 30 minutes daily for the previous 30 days was considered "compliant" with ADA recommendations for treatment of IFG/IGT. Participants were also asked whether their physicians recommended diet or exercise modification.

Only 3.4 % of the study sample reported receiving a previous diagnosis of IFG, IGT, borderline diabetes, or prediabetes, but 584 persons (38 %) had IFG or IGT (or both conditions). Of the persons who reported a diagnosis, 38.5 % no longer met the criteria for prediabetes. No individuals diagnosed with prediabetes reported receiving oral anti-hyperglycaemic medications. Of the 584 prediabetic individuals, 31.7 % (95 % confidence interval [CI], 23.3 %-40.2 %) reported receiving counselling for exercise, 33.4 % (95 % CI, 26.4 %-40.5 %) for diet, and 25.9 % (95 % CI, 17.9 %-34.5 %) for both. However, adherence to counselling was relatively high - 86 % of those who received a recommendation to control their diet or weight reported engaging in that behaviour and 70 % of those who received an exercise recommendation reported exercising.

Viewpoint

Studies from around the world have firmly established that diabetes can be prevented or delayed with lifestyle modification or pharmaceutical interventions in patients with IFG / IGT.\(^1-4\) Despite this abundance of evidence, the current study suggests that physicians in the United States are rarely diagnosing prediabetes.

Of course, considering patients' imperfect recall, coupled with the fact that what goes in the chart and what is discussed with the patient may not be identical, the diagnosis rates may not be as poor as reported in this study. Still, these findings show that fewer than one third of patients with prediabetes are given (or recall being given) advice on diet and exercise, and pharmacotherapy is rarely given. Thus, it is difficult to conclude anything other than that the results of well-publicized diabetes prevention trials are not being translated into clinical practice.

The news is not all bad. It is encouraging to see in the current findings that 70 % to 86 % of patients who received diet or exercise recommendations actually followed this advice. Given that success, however, the relatively low proportion of patients who received such counsel is all the more glaring.

We know that diabetes prevention is possible, and we now know that patients will attempt the necessary lifestyle changes. All we have to do is ask.

SOURCE: Karve A, Hayward et al. Diabetes Care. 2010;33:2355-2359

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Major Milestones in Diabetes: 2010

Year’s Worth of Diabetes Research

The diabetes epidemic continues while research into its aspects, from prevention to therapy to complications, is mounting. Although it is not possible to cover all of the important developments here, a brief summary of the best of 2010 follows.

In January, the American Diabetes Association (ADA) issued its annual update of its Standards of Medical Care in Diabetes. The notable change was the introduction of A1C as a suitable test for diagnosing diabetes, using an A1C threshold for diagnosis of ≥ 6.5 %.

New Risk Factors Identified

The February issue of Diabetes Care contained 2 important studies. Landman and colleagues used data from the ZODIAC [Zwolle Outpatient Diabetes project Integrating Available Care] study to conclude that although people with type 2 diabetes are at increased risk for cancer, metformin use was linked with lower cancer mortality compared with non-use (hazard ratio 0.43, 95 % CI 0.23-0.80). A second study provided information about a different type of lifestyle risk for diabetes - sleep. The meta-analysis showed that both short and long duration of sleep (5-6 and 8-9 hours,resp.) were associated with greater risk for incident diabetes. Furthermore, difficulty initiating and maintaining sleep also increased diabetes risk.

Another meta-analysis was published in March, examining statin use and risk for diabetes. Combining data from 13 trials, 174 more cases of diabetes occurred in the groups on statin treatment than on placebo or standard-care groups, i.e. a 9 % increase in the development of diabetes during follow-up, or 1 additional case of diabetes per 255 statin-treated patients over 4 years. The risk was stronger in trials with older participants, but baseline BMI and percent change in LDL-cholesterol did not seem to be important factors.

ACCORD: Unexpected Findings

The BP and lipid arms of the ACCORD trial published their main results in April. In ACCORD BP, targeting a SBP < 120 mmHg did not reduce the rate of major CVEs compared with targeting a BP < 140 mmHg. The ACCORD Lipid trial tested the combination of fenofibrate and simvastatin compared with simvastatin alone and failed to find a difference in the primary outcome of nonfatal MI, nonfatal stroke, or death from CVD.

In an effort to understand the unexpected finding that tight glycaemic control increased risk for mortality in the ACCORD trial, a post-hoc epidemiologic analysis of the data was published in May. Higher average A1C was associated with greater risk for death, as each 1 % greater mean A1C was associated with an approximate 20 % increase in all-cause mortality. The original ACCORD finding that mortality risk was greater with the intensive strategy than with the standard strategy appeared to hold only when average A1c was > 7 %.

Intensive Treatments Bring Small Gains

In July, the Lifestyle Over and Above Drugs in Diabetes (LOADD) study, investigated if dietary advice could improve glycaemic control and risk factors for CVD in people with persistent hyperglycaemia (A1C > 7 %) despite drug treatment optimized according to current guidelines. After 6 months, A1C in the intervention group declined from 8.9 % to 8.4 % but remained unchanged (8.6 %) in the control group. Significant favourable differences were also observed in weight, BMI, and waist circumference.

ACCORD finally reported some favourable findings in August. Although intensive treatment of hyperglycaemia did not improve the primary outcomes, secondary outcome measures favoured intensive therapy. Thus, whereas risks for advanced microvascular composite outcomes that included renal dialysis or transplantation and retinal photocoagulation were not reduced, intensive therapy did delay onset of albuminuria, some eye complications, and neuropathy.

Diabetes Drugs Pose Risks

The debate over whether rosiglitazone is safe for patients with diabetes was rendered irrelevant in September when the US FDA restricted access to the drug. Rosiglitazone will be available to new patients only if other drugs have failed and the patient has medical reasons for not taking pioglitazone. Meanwhile, the European Medicines Agency banned rosiglitazone. Cont Page 3...
Another concern about thiazolidinediones (TZDs) in general has been fracture risk. In October, an observational case-control study using data from the Translating Research into Action for Diabetes (TRIAD) study reported that in women aged 50 years+, exposure to TZDs increased the odds of fracture by 71% (odds ratio [OR] 1.71, 95% CI 1.13-2.58). The OR of fracture was also dramatically increased among men taking TZDs, but only if they did so in conjunction with loop diuretics (OR 3.46, CI 1.06-11.28).

Recently, pioglitazone has been removed from the French and German Markets due to concerns over bladder cancer, and the FDA has released warnings about its long-term use >1 yr.

Prevention Falling Short

November was National Diabetes Prevention Month, yet diagnosis of individuals with IFG or IGT and subsequent prevention efforts remain woefully inadequate. In a study of 1547 adults, 3.4% reported receiving a previous diagnosis of "IFG, IGT, borderline diabetes, or pre-diabetes," but 584 (38%) had IFG and/or IGT. No patient with pre-diabetes reported receiving oral antihyperglycaemic medications, and less than one third reported receiving counselling for exercise, diet, or both.

Depression and Diabetes

December brought us several studies of the apparently bidirectional link between depression and diabetes. Although this link has long been recognized, the real story here was that treatment with antidepressants was implicated as a risk factor in 3 of those studies, confirming an earlier report from the Diabetes Prevention Program. Unlike statins, which were associated with a relatively small increased risk for diabetes (9%), the risk associated with antidepressants was up to 2.5 times greater.

This recap only scratches the surface of the depth and breadth of diabetes research in 2010.

NICE Publishes Guidelines on Lipid-Lowering Treatments

Physicians should prescribe statins as part of a prevention strategy for all patients with at least a 20% chance of developing CVD in the next 10 years, under a practice guideline (May 28) by the clinical effectiveness agency for England and Wales. The guideline from the National Institute for Health and Clinical Excellence said physicians should first seek to modify other risk factors, such as smoking or excess weight, before prescribing statins to prevent cardiovascular disease, which accounted for one in three deaths in the United Kingdom in 2005.

For secondary prevention, the NICE guideline calls on physicians to immediately prescribe statins or other cholesterol-lowering drugs, regardless of efforts to change modifiable risk factors. The guideline recommends prescribing statins for patients with clinical evidence of cardiovascular disease.

The guideline on lipid modification should help guide physicians to provide more consistent care nationwide, Dr. Gillian Leng, NICE deputy chief executive, said in a written statement. “This guideline will provide needed clarity for healthcare professionals, many of whom report uncertainty in how to manage blood lipids in patients both with and without pre-existing cardiovascular disease,” Leng said. “As a result, the guideline should also help to reduce the current variation in prescribing lipid modifying drugs in primary care. The guideline recommends treatment based on overall cardiovascular risk rather than on isolated lipid levels.”

The guideline recommends that physicians make use of existing medical records databases to identify their patients aged 40-75 who are likely to be at high risk of cardiovascular disease. For primary prevention, statin therapy should begin with 40 mg of simvastatin. A lower dose or an alternative such as pravastatin may be necessary in case of contraindications or potential drug interactions.

For secondary prevention, treatment should start with 40 mg of simvastatin. If total cholesterol does not drop below 4 mmol/L or LDL cholesterol does not drop below 2 mmol/L, physicians should consider increasing to 80 mg of simvastatin or another drug of similar efficacy.

The guideline was one of several NICE published May 28, including: Promotion of physical activity in the workplace, through development of workplace programmes and encouraging employees to walk or cycle to work rather than drive.
Whether fructose is a panacea for people with diabetes (because of its low glycaemic index [GI]) or a plight (because of its adverse metabolic effects) is an ongoing controversy. It has its roots in its complicated and taxing metabolism: needing to be phosphorylated, having no auto regulation for this process, thus depleting ATP stores and leading to transient ischemia and cell exhaustion (the majority of this brunt being borne by the liver). (1) Administration of 1 mmol of fructose in vitro can effectively paralyze cell metabolism. (2,4) Then we get studies from gastroenterologists, highlighting that one of the most important and overlooked causes for non-alcoholic steatohepatitis seen in the metabolic syndrome and in people with diabetes is possibly overconsumption of fructose. (3) (Admittedly, it makes sense) Some authors even propose a “fructose index” over a “glycaemic index” stating that a high fructose diet is instrumental in causing the metabolic syndrome. (4) Not all sugars are equal it seems.

However, the very animal studies that give us this information on fructose also possibly underestimate its harmful effects on human consumption, the reason being the test subjects themselves. Biologically rats have the capacity to synthesize uricase and vitamin C, which is notably absent in humans. (4) Fructose is thought to mediate its effects via uric acid, which rises minutes after its consumption. Hyperuricaemia has been shown to be an independent predictor of hypertension in 15 of 16 studies, to predict insulin resistance (5), and to predict the development of diabetes (6) and obesity (7). Through uricase, rats can break down uric acid and vitamin C negates some of the metabolic effects of fructose and uric acid particularly in neutralizing oxidative stress.

So, do rats have the advantage? Admittedly with a big Mac available just a phone call away, it would seem so, but change the setup and we may have something else altogether. There is an interesting hypothesis (8) about how fructose is the ideal substrate for the animal undergoing prolonged periods of fasting due its ability to encourage triglyceride production and increase lipid stores. Loss of vitamin C synthesis may have represented an additional survival advantage by augmenting the effects of uric acid (and fructose) in this regard.

So in the end, comparative physiology may tell “why?”, but we are still left with “what now?” and more problems than solutions in an evolving epidemic.

REFERENCES


By Dr Zaineb Vakil