

Sugar Lowering Drugs for Asymptomatic Diabetes

By

David K. Cundiff, MD

LA County + USC Medical Center

Internal Medicine Dept. Retired

University Group Diabetes Program

- Trial arms
 - Insulin fixed dose
 - Insulin adjusted dose
 - Phenformin
 - Tolbutamide
 - Diet
 - Placebo
- Results (JAMA:1971-1992)
 - Phenformin causes lactic acidosis (taken off the market)
 - Tolbutamide + diet or insulin related to CV mortality
 - Clinical outcomes: drugs not better than placebo

United Kingdom Prospective Diabetes Study (UKPDS)

- 3,867 *asymptomatic* newly diagnosed patients with type 2 diabetes
- Study endpoints
 - 14 clinical endpoints ($P = \text{NS}$)
 - Retinopathy requiring photocoagulation ($P < 0.01$)
 - All microvascular endpoints 25% reduction, (95% CI 7-40, $P=0.0099$)
 - All diabetes endpoints 12% reduction (95% CI 1-21, $p=0.029$)
- UKPDS Conclusion: insulin injections or pills to lower blood glucose (metformin and sulfonylureas) reduced the long-term complications of diabetes.

Adverse Effects with Intensive Treatment

- Major hypoglycemic episodes per year
 - Conventional treatment = 0.7%
 - Chlorpropamide = 1.0%
 - Glibenclamide 1.4%
 - Insulin = 1.8%.
- Weight gain (2.9 kg more, $P < 0.001$)
- Metformin-sulfonylurea compared with sulfonylurea alone: 96% increased risk of diabetes-related death
- Increased heart failure complications

Deaths with Tight Sugar Control: 2 RCTs

Intervention: Intense as compared to less intense blood sugar control (goal: hemoglobin A1C < 6%)

1. 10,251 patients followed 3.5 yrs
 - Increased deaths with intensive-therapy: 257 versus 203 (HR: 1.22; CI, 1.01 to 1.46)
 - *N Engl J Med.* June 12, 2008;358(24):2545-2559.
2. 11,140 patients followed 5 years
 - NS: (0.88; CI, 0.74 to 1.04; P=0.12)
 - *N Engl J Med.* June 12, 2008;358(24):2560-2572

Diabetes Treatment Costs USA 2010

- Cost of treating people with diabetes: \$212 b
- Reduced national productivity: \$70 b
- Excess medical expenditures: \$141 b
 - Costs to directly treat diabetes: \$33 b
 - Diabetes-related chronic complications: \$70 b
 - Excess general medical costs: \$38 b
- Average cost/yr for diabetics: \$11,744
 - Part attributed to diabetes: \$6,649
 - 2.3 times higher than in the absence of diabetes

Trends in Diabetes Outcomes/Costs

- Change in complication incidences: 1997 to 2002
 - People diagnosed with diabetes: + 43%
 - Visual impairment: + 24%
 - Hospitalization for foot ulceration: + 50%
 - Hospitalization for painful neuropathy: + 81%
 - Initiation of kidney dialysis: + 24%
 - Prevalence of cardiovascular disease: + 34%
 - U.S. population: + 5%
- Costs of treatment of diabetes and complications
 - 1997 - \$11b
 - 2007 - \$116b
 - + 1050%

Rates of Preventive Care Practices in Adults with Diabetes 2004 (USA)

Preventive Care Practice	Compliance
• Annual dilated eye exam:	68.6%
• Daily self-monitoring of blood glucose:	59.8%
• Annual foot exam:	67.7%
• Daily self-exam of feet:	65.8%
• Two or more HbA1c tests in last year:	71.9%
• Attended diabetes self-management class:	53.7%
• Annual influenza vaccine:	56.8%
• Ever had pneumococcal vaccine:	50.3%

ADA's nutrition recommendations to treat diabetes

Year	Distribution of calories (%)		
	Carbohydrates	Protein	Fat
Before 1921	Starvation diets		
1921	20	10	70
1950	40	20	40
1971	45	20	35
1986	< or = 60	10 – 20	< 30
1994	varies ^a	10 – 20	varies ^b

^a Based on a dietitian's nutritional assessment and the patient's treatment goals.

^b Less than 10% of calories from saturated fats

Conclusion

- The Diabetes Control and Complications Trial results in type 1 diabetics not applicable to type 2 diabetics.
- Drug treatments for asymptomatic type 2 diabetics are not proven to improve clinical outcomes
- The ADA diet is not evidence-based to reduce complications of diabetes.
- Diabetics need dietary recommendations that are based on science rather than opinion and food politics.
- The potentially beneficial effects of a more plant-based diet in people with type 1 and type 2 diabetes should be explored.