

Can We Stop the Progression of Diabetes? DREAM

Abstract

People with type 2 diabetes are at high risk of serious morbidity and premature death. Risk factors for diabetes include: a) a westernized society; b) glucose levels that are modestly elevated within the nondiabetic range; c) prior gestational diabetes; d) aboriginal or South Asian origin; e) abdominal obesity; f) cardiovascular disease; g) hypertension or smoking; or e) family history of diabetes or cardiovascular disease. Lifestyle interventions (i.e. activity and weight loss), metformin, acarbose and orlistat can reduce diabetes incidence of diabetes. Thiazolidinediones enhance hepatic and peripheral insulin sensitivity, lower glucose levels in dysglycaemic individuals, increase hepatic insulin clearance, reduce hepatic fat and inflammatory cytokines, increase adiponectin and promote preadipocyte differentiation into adipocytes. They may also prevent damage to beta cells and preserve insulin secretion.

In the DREAM trial 5269 people age 30 or older (mean age 55; 59% women, mean weight 85 kg) with impaired fasting glucose alone (14%), impaired glucose tolerance alone (57.5%) or both abnormalities (28.5%) were randomly allocated to ramipril 8 mg/day or placebo and/or rosiglitazone 15 mg/day or placebo, and followed for a median of 3 years. Rosiglitazone significantly reduced the primary outcome of diabetes or death by 60% and increased regression to normoglycemia; 0.5% of participants on rosiglitazone developed nonfatal heart failure.

Whether preventing diabetes also prevents its consequences is unknown. The 60% risk reduction with rosiglitazone may lead to a reduction in some of the consequences of diabetes. Ongoing analyses of DREAM data will report on the atherosclerosis and renal effects of rosiglitazone.

DREAM

Diabetes REduction Assessment with
ramipril and rosiglitazone Medication

New Engl J Med 2006; 355:1551-1562
Lancet 2006; 368:1096-1105

Why Prevent Type 2 Diabetes?

- **Strong belief that if type 2 DM is prevented, its consequences will also be prevented ...**
 - **true** for morbidity/cost of high glucose, home monitoring, surveillance for DM consequences, labeling effects
 - **likely true** for eye, kidney & nerve disease
 - **no trial evidence** for CVD, CHF, amputations, cognitive decline, mortality, ED, & other chronic consequences
- **Possibility that if dysglycaemia is treated people at risk (i.e. abnormal glucose levels are normalized)...**
 - may reduce CVD & other chronic consequences

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DREAM

- Aims:** Does ramipril 15 mg/d prevent diabetes?
Does rosiglitazone 8 mg/d prevent diabetes?
- Design:** 2 X 2 factorial, double-blind RCT
- Sample:** Age 30+; IGT (FPG <7 & 2 hr 7.8-11) &/or IFG (FPG 6.1-6.9)
- Pts:** 5269 in 191 sites, 21 countries, & F/U 3 yrs
- Outcome:** Incident DM (confirmed FPG \geq 7 or 2 hr \geq 11.1; or MD diagnosis) or death*

*because undiagnosed diabetes may be more frequent in those who die than in those who do not

DREAM

Rosiglitazone & Primary Outcome

	Rosi N=2635	Placebo N=2634	HR (95% CI)	P
Primary Composite	306 (11.6)	686 (26.0)	0.40 (0.35-0.46)	<0.0001
Diabetes	280 (10.6)	658 (25.0)	0.38 (0.33-0.44)	<0.0001
Dx by FPG/OGTT	231 (8.8)	555 (21.1)	0.38 (0.33-0.44)	<0.0001
MD Diagnosed	49 (1.9)	103 (3.9)	0.47 (0.33-0.66)	<0.0001
Death	30 (1.1)	33 (1.3)	0.91 (0.55-1.49)	0.70

