

THERAPEUTICS

Review: Lifestyle or pharmacologic interventions prevent or delay type 2 diabetes in impaired glucose tolerance

Gillies CL, Abrams KR, Lambert PC, et al. Pharmacological and lifestyle interventions to prevent or delay type 2 diabetes in people with impaired glucose tolerance: systematic review and meta-analysis. *BMJ*. 2007;334:299.

Clinical impact ratings: GIM/FP/GP ★★★★★☆ Endocrinology ★★★★★☆

QUESTION

In persons with impaired glucose tolerance, do lifestyle or pharmacologic interventions prevent or delay type 2 diabetes mellitus (DM)?

METHODS

Data sources: MEDLINE (1966 to July 2006), EMBASE/Excerpta Medica (1980 to July 2006), Cochrane Central Register of Controlled Trials, Cochrane Database of Systematic Reviews (Issue 2, 2006), references of relevant articles, and experts in the field.

Study selection and assessment: Randomized controlled trials (RCTs) that evaluated an intervention to delay or prevent type 2 DM in persons with impaired glucose tolerance and had an outcome measurement of diabetes. 21 RCTs met the selection criteria, and 17 RCTs (*n* = 8084, mean age range 39 to 57 y, mean body mass index range 24 to 36 kg/m², average follow-up range 0.4 to 4.6 y) were included in the meta-analysis. Among the 17 RCTs, 8 had quality scores ≥ 3 out of 5 on the Jadad scale, and 2 had allocation concealment.

Outcomes: Development of type 2 DM and adverse events.

MAIN RESULTS

Meta-analysis using a random-effects model showed that both lifestyle interventions (diet, exercise, or both) and pharmacologic interventions (oral diabetes drugs [acarbose, flumamine, glipizide, metformin, or phenformin] or an antiobesity drug [orlistat]) reduced the incidence of type 2 DM (Table); 2 RCTs assessing troglitazone were excluded from the meta-analysis because the drug had been removed from several markets worldwide because of liver toxicity. In 1 RCT, jiangtang bushen (a Chinese herb) did not reduce DM (Table). Adverse events related to

the pharmacologic interventions (gastrointestinal and hypoglycemic symptoms) were more common in the treatment groups (no statistical tests reported).

CONCLUSION

In people with impaired glucose tolerance, lifestyle or pharmacologic interventions prevent or delay type 2 diabetes mellitus.

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Lifestyle or pharmacologic interventions vs placebo to prevent or delay type 2 diabetes mellitus in persons with impaired glucose tolerance at mean follow-up range 0.4 to 4.6 y*

Outcome	Comparisons	Number of trials (n†)	Hazard ratio (95% CI)	NNT (credible interval)
Type 2 diabetes mellitus	Lifestyle vs placebo‡	10 (4452)	0.51 (0.44 to 0.60)	7 (5 to 9)
	Oral diabetes drug vs placebo§	8 (4580)	0.70 (0.62 to 0.79)	11 (9 to 15)
	Orlistat vs placebo	2 (814)	0.44 (0.28 to 0.69)	6 (5 to 8)
	Jiangtang bushen vs placebo	1 (51)	0.32 (0.03 to 3.07)	Not significant

*Abbreviations defined in Glossary.

†Sample sizes provided by author.

‡Lifestyle interventions included diet, exercise, or both.

§Oral diabetes drugs were acarbose, flumamine, glipizide, metformin, or phenformin.

COMMENTARY

The systematic review by Gillies and colleagues provides pooled estimates of effectiveness of pharmacologic and lifestyle interventions in preventing type 2 DM in persons with impaired glucose tolerance. Lifestyle (diet, exercise, or both) interventions reduced progression to type 2 DM by 50% and were at least as effective as drugs.

Sustained effects from preventive interventions are clinically important. For instance, rosiglitazone (RG) has been associated with a 60% reduction in progression to type 2 DM in the DREAM trial (1). However, the unpublished washout data suggest a similar incidence of type 2 DM in RG and placebo-treated groups soon after discontinuation of RG (2). Other drugs have also been reported to lack sustained diabetes prevention properties after washout (3). On the other hand, sustained effects have been reported from intensive lifestyle interventions (4). Drugs used in type 2 DM prevention trials are also more commonly associated with side effects (e.g., gastrointestinal upset, liver function decline, and hypoglycemia) than lifestyle interventions. RG has been associated with weight gain, excess fractures, and a 7-fold incidence of nonfatal heart failure (1, 2).

Cost, adverse effects, and nonsustained efficacy associated with diabetes prevention drugs suggest that lifestyle interventions remain the mainstay of diabetes prevention.

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References

- Gerstein HC, Yusuf S, Bosch J, et al. Effect of rosiglitazone on the frequency of diabetes in patients with impaired glucose tolerance or impaired fasting glucose: a randomised controlled trial. *Lancet*. 2006;368:1096-105.
- Bilous R. DREAM and ADOPT: rosiglitazone does what it says on the packet [Editorial]. *Diabet Med*. 2007;24:107-9.
- Diabetes Prevention Program Research Group. Effects of withdrawal from metformin on the development of diabetes in the diabetes prevention program. *Diabetes Care*. 2003;26:977-80.
- Lindström J, Ilanne-Parikka P, Peltonen M, et al. Sustained reduction in the incidence of type 2 diabetes by lifestyle intervention: follow-up of the Finnish Diabetes Prevention Study. *Lancet*. 2006;368:1673-9.