Preventing the development of type 2 diabetes with orlistat

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We know that people with impaired glucose tolerance (IGT) have a 50% chance of developing type 2 diabetes in 10 years. Studies in Finland and the US have shown that in people with IGT lifestyle change with weight reduction and increased exercise can reduce the risk of developing type 2 diabetes by 58%, whilst the study from the US showed that taking metformin reduced this risk by 31%.

The XENDOS study investigated the role that lifestyle change and the drug orlistat have on reducing the development of diabetes. It is a randomised controlled trial of 3305 obese people who were randomly allocated to lifestyle changes plus either 120 mg orlistat or a placebo three times a day for 4 years. Of the study group, 21% had IGT and 79% had normal glucose tolerance.

Treatment was completed by 52% of the orlistat patients and 34% of those who took the placebo. After 4 years, the cumulative incidence of diabetes was 9% in the placebo group and 6.2% in the orlistat group, corresponding to a risk reduction of 37%. Mean weight loss was greater in the orlistat group than in the placebo group (5.8 kg vs 3.0 kg).

The weight loss in the lifestyle plus placebo group was comparable to that in the intensive intervention arm of the US study and the Finnish study, both of which were in people with IGT.

The addition of orlistat to lifestyle changes resulted in a significantly greater weight loss which was the same in people with impaired or normal glucose tolerance. In the IGT population it can be estimated that treating 10 people for 4 years with orlistat plus lifestyle, rather than lifestyle alone would prevent the development of one case of diabetes.

The results of this trial suggest that lifestyle change plus orlistat therapy is effective in preventing the development of type 2 diabetes.

CLINICAL THERAPEUTICS

A clinical review of metformin

Readability	✓ ✓ ✓
Applicability to practice	✓ ✓ ✓ ✓
WOW! factor	✓ ✓ ✓

1 The aim of the article was to review the pharmacokinetics, pharmacology, drug-interaction potential, adverse effects and dosing guidelines for metformin, and pharmcoeconomic considerations.

2 Primary research and review articles were identified through a MEDLINE search. Abstracts were identified through a search of International Pharmaceutical Abstracts and Web of Science. Package inserts for metformin and metformin consultation products were consulted.

3 All identified articles and abstracts were assessed for relevance and priority was given to the clinical trial reports and primary medical literature.

4 Metformin is the only currently available oral antidiabetic/hypoglycaemic agent that acts predominantly by inhibiting glucose release.

5 Metformin is effective in lowering HbA_{1c} by 1–2% when used as a monotherapy or in combination with other blood glucose lowering agents or insulin, positively affects lipid profiles and improves vascular and haemodynamic indices.

6 Bodyweight can be maintained or slightly reduced through the use of metformin.

7 Adverse effects are generally tolerable and self-limiting.

Setter SM, Iltz JL, Thams J, Campbell RK (2003) Metformin hydrochloride in the treatment of type 2 diabetes mellitus: a clinical review with a focus on dual therapy. *Clinical Therapeutics* **25**(12): 2991–3020

DIABETES CARE

Orlistat reduces type 2 diabetes in obese people

Readability	✓ ✓ ✓ ✓
Applicability to practice	✓ ✓ ✓ ✓
WOW! factor	✓ ✓ ✓ ✓

1 Previous research has shown that lifestyle changes can reduce the incidence of type 2 diabetes.

2 The researchers investigated if adding a weight-reducing agent to lifestyle changes could lead to a greater decrease in bodyweight (and the incidence of type 2 diabetes) in people with obesity.

3 A total of 3305 people were randomised to lifestyle changes plus either 120 mg of orlistat or a placebo, three times daily in a 4-year, double-blind prospective study.

4 Participants had a BMI ≥ 30 kg/m^2 and normal (79%) or impaired (21%) glucose tolerance (IGT).

5 The cumulative incidence of diabetes was 9.0% with placebo and 6.2% with orlistat, corresponding to a risk reduction of 37.3%.

6 An exploratory analysis indicated that the preventive effect was explained by the difference in people with IGT.

7 Mean weight loss after 4 years was significantly greater with orlistat than placebo, and similar between orlistat recipients with impaired or normal glucose tolerance at baseline.

8 A second analysis in which the baseline weights of participants who dropped out of the study was carried forward also showed greater weight loss in the orlistat group than in the placebo group.

9 Orlistat plus lifestyle changes resulted in a greater reduction in type 2 diabetes over 4 years and produced greater weight loss in obese people compared with lifestyle changes.

Torgerson JS, Hauptman J, Boldrin MN, Sjostrom L (2004) XENical in the prevention of diabetes in obese subjects (XENDOS) study. *Diabetes Care* **27**(1): 155–61