Obesity

Rimonabant for type 2 diabetes?

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Traditional management of type 2 diabetes advocates rapid achievement of tight glycaemic targets for reduction of associated risks. However, the achievement of tight glycaemic control often leads to weight gain, especially once insulin is initiated. Thus, an important opportunity for improving control through weight loss is often missed. This is an unresolved paradox about contemporary diabetes management.

The other main option, which is seldom pursued, is weight loss. As often highlighted in these commentaries, weight loss is highly beneficial, enhancing glycaemic control, and if sufficient in magnitude, occasionally helping people to achieve diabetes remissions. However, this approach has still to be compared in detail with traditional management, and newer anti-obesity drugs could offer the prospect of even greater and more sustained weight loss.

In the recently reported RIO-Diabetes study on overweight and obese people with type 2 diabetes treated with metformin or a sulphonylurea, Scheen et al (summarised on right) report that the addition of the weight loss drug rimonabant, in a dose of 20 mg daily, compared with placebo, resulted in over three times more people achieving >5 % weight loss, and twice as many reaching glycaemic targets. Clearly, rimonabant might be a useful intervention in this situation. Now the caveats: The study did not answer whether a weight management programme alongside rimonabant was better than the other main alternatives, which were addition of a glitazone or insulin, or a far more aggressive and supervised weight loss intervention than was used.

In the Look Ahead study (Pi-Sunyer, 2006), for example, the intensive lifestyle intervention achieved over 8 % weight loss at 12 months in the group on oral hypoglycaemic agents, which translated into expected improvements in glycaemic control and cardiovascular risk. This is a time of increasing hope for people with type 2 diabetes, as new studies support the use of various weight loss interventions, at least for those people motivated to pursue this option.

Pi-Sunyer X (2006) *The Look Ahead Study.* American Diabetes Association (oral presentation).

OBESITY SURGERY

European budget impact of obesity surgery

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

1 In this study the authors aimed to establish a payer-perspective cost effectiveness and budget impact model for surgery in obese people with type 2 diabetes in the UK, Germany and France.

2 The procedures investigated were adjustable gastric banding and gastric bypass versus conventional treatment. These data were obtained from quoted publications that reflected practice in 2005 .

3 Published sources and authors' institutions were used to find unit costs. These were entered into a deterministic algorithm along with BMI, and resources against time for each of the three treatments.

4 A cost decrease was seen in both Germany and France for gastric bypass surgery and adjustable gastric banding. In the UK a cost increase was found but the treatment was cost effective.

Ackroyd R, Mouiel J, Chevallier J-M et al (2006) Cost effectiveness and budget impact of obesity surgery in patients with type-2 diabetes in three European countries. *Obesity Surgery* **16** 1488–1503

LANCET

Rimonabant gives a significant reduction in bodyweight

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

1 The aim of this trial was to assess the efficacy and tolerability of rimonabant in obese or overweight people with type 2 diabetes that was inadequately controlled by metformin or sulphonylurea.

2 In this study, 1047 overweight or obese people with type 2 diabetes poorly controlled with metformin or sulphonylurea were assigned a mildly hypocaloric diet and were randomised to either placebo, rimonabant 5 mg/day or rimonabant 20 mg/day. The endpoint was weight change after 1 year.

3 Of the 1047 patients, 692 completed the 1 year follow-up and within the 3 groups the numbers on each treatment were similar.

4 The two groups assigned rimonabant achieved a significantly greater weight loss after 1 year than those taking placebo. Within the groups taking rimonabant, those taking 20 mg/day achieved a significantly greater weight loss (5.3 kg) than those on 5 mg/day (2.3 kg).

5 While rimonabant was generally well tolerated, there was a slightly greater incidence of adverse effects in the group with the higher dosage. These included depressed mood, nausea and dizziness.

6 From these results the authors concluded that, alongside a hypocaloric diet and exercise, rimonabant 20 mg/day produces a significant reduction in bodyweight and improves metabolic risk factors for those people with type 2 diabetes that is inadequately controlled by metformin or sulphonylurea.

Scheen AJ, Finer N, Hollander P et al (2006) Efficacy and tolerability of rimonabant in overweight or obese patients with type 2 diabetes: a randomised controlled study. *Lancet* **368:** 1660–72

'...a weight loss of 5 kg over time could account for a reduction of the risk of diabetes of approximately 55 %.'

DIABETES CARE

Weight loss reduces diabetes risk

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

1 This study explored the effect that weight loss and lifestyle intervention had on the risk of developing diabetes by analysing the intensive lifestyle intervention arm of the Diabetes Prevention Program.

2 Weight loss in 1079 people between the ages of 25 and 84 years was used as a predictor of reduced diabetes incidence. Follow-up was for an average of 3.2 years. One hundred and fifty-three participants developed diabetes over the follow-up period, which equates to 5 per 100 person years.

3 The results from the study suggest that at least 150 minutes (approximately) of physical activity per week may be enough to see an effect on diabetes risk.

4 For every 5 % reduction in fat percentage during follow-up, the incidence of diabetes was significantly reduced by 25 %, $P < 0.0007$.

5 The authors postulate that a weight loss of 5 kg over time could account for a reduction of the risk of diabetes of approximately 55 % over the follow-up period.

6 An increase in the amount of physical activity undertaken helps to sustain the weight loss needed to reduce the risk of diabetes. In those that do not lose weight but increase their exercise levels there was still a risk-reduction of 44 %.

7 The authors conclude that the most successful interventions to reduce the risk of diabetes will be those that primarily target weight loss.

Hamman RF, Wing RR, Edelstein SL et al (2006) Effect of weight loss with lifestyle intervention on risk of diabetes. *Diabetes Care* **29**: 2102–7

DIABETES CARE

Weight loss improves arterial stiffness

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

1 This single-centre, randomised, double blinded, placebo-controlled clinical trial assessed arterial stiffness at baseline and after a 1-year weight-loss intervention.

2 Assessment of arterial stiffness was done by measuring aortic pulse wave velocity at baseline, metabolic control of type 2 diabetes was also assessed.

3 Thirty-eight out of 52 participants completed the 1-year intervention, which required at least a 7 % weight loss. This was achieved through reduced calorie consumption, increased exercise and healthy food selection. In addition, participants were randomised to receive orlistat or placebo.

4 Fasting blood samples were also taken at baseline and 1-year to assess lipids, glucose, insulin, HbA_{1c}, inflammatory markers and liver enzymes. BMI was also recorded.

5 Weight loss was equivalent in both the placebo and orlistat arms of the investigation at both 6 months and 1 year.

6 There were improvements in HbA_{1c}, LDL cholesterol, insulin resistance, inflammatory markers and also in aortic pulse wave velocity.

7 The authors conclude that moderate weight loss improves arterial stiffness in people with type 2 diabetes.

Barinas-Mitchell E, Kuller LH, Sutton-Tyrrell K et al (2006) Effect of weight loss and nutritional intervention on arterial stiffness in type 2 diabetes. *Diabetes Care* **29**: 2218–22

NEW ENGLAND JOURNAL OF MEDICINE

Pioglitazone improves fatty liver

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

1 In this study the authors tested the effect of pioglitazone on non-alcoholic steatohepatitis (fatty liver), which is characterised by insulin resistance, steatosis and necroinflammation with or without centrilobular fibrosis.

2 Fifty-five people with type 2 diabetes or impaired glucose tolerance and non-alcoholic steatohepatitis were subjected to a hypocaloric diet plus either pioglitazone or placebo.

3 This study lasted for 6 months and hepatic fat content and glucose turnover were assessed both before and after this period.

4 A hypocaloric diet plus administration of pioglitazone rather than placebo improved glycaemic control and glucose tolerance, decreased hepatic fat content, increased hepatic insulin sensitivity and normalised liver aminotransferase levels.

5 Pioglitazone was also found to have benefits of improving histological markers of fatty liver. These benefits were seen with regard to steatosis, ballooning necrosis and inflammation.

6 The investigators found that in subjects with non-alcoholic steatohepatitis, pioglitazone led to both metabolic and histological improvements.

Belfort R, Harrison SA, Brown K et al (2006) A placebo-controlled trial of pioglitazone in subjects with nonalcoholic steatohepatitis. *New England Journal of Medicine* **355**: 2297–307