de las Cruces Souto-Gallardo, M.a; Bacardí Gascón, M.; Jiménez Cruz, A.
Effect of weight loss on metabolic control in people with type 2 diabetes mellitus: systematic review
Grupo Aula Médica
Madrid, España

Available in: http://www.redalyc.org/articulo.oa?id=309226774008
Revisión

Effect of weight loss on metabolic control in people with type 2 diabetes mellitus: systematic review

M.ª de las Cruces Souto-Gallardo¹, M. Bacardí Gascón²,³ and A. Jiménez Cruz²,³

¹Estudiante del doctorado en Ciencias de la Salud. Profesor de Facultad de Ciencias de la Salud de Ensenada. UABC.

Abstract

Objective: The aim of this systematic review was to examine randomized clinical trials (RCT) regarding long-term effects of weight loss (WL) on biological markers in people with type 2 diabetes mellitus (T2DM).

Methods: We searched for articles published in English and Spanish recorded in the databases of Pubmed and Cochrane, and the journal collections platforms of Ebsco and Scielo between January 1, 2000 and January 1, 2010. Inclusion criteria included RCT with follow-up ≥12 months.

Results: A total of 842 articles were identified, 95 of them contained information on the effect of WL on biological markers. Twenty studies fulfilled the inclusion criteria. WL percentage ranged from 0.8 to 20%. A reduction of A1C was observed in nine studies, blood glucose in seven, of total cholesterol and LDL in four, systolic and diastolic blood pressure in three, and the use of hypoglycemic drugs in four; an increase of HDL was observed in seven studies. Remission of T2DM was reported in only one study, which included surgical treatment. The quality of the studies ranged from very low to high; however, the study with the longest follow-up that did not involve surgical treatment, was 52 months.

Conclusion: The evidence of the beneficial effect of WL on biological markers on long-term studies in people with T2DM is inconclusive. These results warrant longer and better designed studies.

(Nutr Hosp. 2011;26:1242-1249)

Key words: Weight loss. Diabetes. Systematic review. Metabolic control.

Correspondence: Arturo Jiménez Cruz.
Calzada Universidad no. 14418.
Parque Industrial Internacional.
CP 22390 Tijuana B. C. México.
E-mail: a jimenez@uabc.edu.mx
Recibido: 17-II-2011.
Aceptado: 14-III-2011.
Introduction

A worldwide increase in overweight (OW) and obesity (OB) has taken place in the past two decades, which has become a public health problem. Genetic, environmental, biochemical, neurological, physiological, cultural, and socio-economic factors play important roles in the development of OB. Along with the rise of OB, there is an important increase in the incidence of type 2 diabetes (T2DM). The World Health Organization (WHO) reports that more than 220 million people worldwide have diabetes and that in 2005 an estimated 1.1 million people died from diabetes, an estimation that will be doubled by 2030. It has been estimated that up to 75% of the risk of T2DM is attributable to OB. Eighty-six percent of people with T2DM are OW or OB, and 52% are obese. People with OW or OB are at a higher risk of developing T2DM; on the other hand, weight loss has been associated to a decrease in risk. Several weight reduction strategies have been used to improve the metabolic control of diabetes, including lifestyle interventions, drugs, and surgical treatment, which have shown to be effective as a primary prevention and/or as a strategy to delay the onset of T2DM. The benefits of weight reduction in people with T2DM are not thoroughly documented. Weight loss has resulted in the reduction of use of hypoglycemic drugs and/or remission of diabetes. In the review conducted by Autcot (2008), the influences of weight loss on long-term diabetes outcomes were assessed. The author concluded that intentional weight loss reduces the risk of T2DM by lifestyle interventions, drugs or surgical treatment, including in some cases remission of the disease. This study also showed that in order to obtain significant reductions on blood glucose, greater and sustained weight loss is required. Although literature reviews and meta-analyses were included in this study, the results included people with and without T2DM and most of the studies were cohorts. Few randomized clinical trials were evaluated and most of them had less than 12 months of follow-up. Since diabetes is a chronic disease and its implications on other health problems are discovered in the long-term, the conduct of longer follow-up studies is warranted.

The present paper examines the long-term effects of weight loss intervention on people with diabetes.

Methods

The search was conducted in the databases of Pubmed and Cochrane, and the journal collection platforms of Ebisco and Scielo. The studies were searched using the following Mesh descriptors: (“2000/01/01” AND “2010/06/01”) AND (“Diabetes Mellitus, Type 2” AND “obesity” AND “overweight” AND “weight loss” AND “body weight changes”). The MesH descriptors were used to search in Pubmed, Cochrane and Ebisco, and their equivalent in Spanish in Scielo.

Inclusion criteria were the following: randomized clinical trials (RCT), papers written in English, conducted on T2DM people, with at least 12 months of follow-up, which recorded weight changes (BMI or kg), metabolic parameters (A1C, blood glucose, total cholesterol, LDL, HDL, Triglycerides, SBP, DBP) and the use of hypoglycemic drugs (Figure 1). From the initial search, several studies were removed due to the inclusion of people without diagnoses of T2DM (747), lack of BMI or weight data (7) and those with a follow-up less than 12 months.

Given the heterogeneity in study design, a meta-analysis was not appropriate; however, we conducted a systematic review of the available studies. Each study was evaluated according to the number of subjects, age (median), percentage of retention, type of intervention, duration of intervention or follow-up (months), initial and final BMI, percentage of weight change and effects on metabolic parameters.

The quality of the randomized clinical trials was assessed using the GRADE scale. The design of the study, methodological strengths and weakness, and significance of the findings were used to characterize the quality of the evidence of any given study. According to this scale, randomized clinical trials could receive the number four as a maximum score. One point was subtracted when the following occurred: a) significant baseline differences between intervention groups (weight, BMI, age, prevalence of OW or OB), b) percentage of retention ≤ 70%, c) no intention- to -treat analysis, d) uncertainty of directness (questionable validity of instruments/techniques), e) sparse data, f) high probability of reporting bias (sample, population characteristics), g) internal inconsistency (data, values). Two points were subtracted when the study showed: a) very serious design limitations (sample, population characteristics), b) serious uncertainty of directness (validity of instruments). One point was added when: a) the study possessed strong association without plausible confounders, consistent, and direct evidence, b) all plausible confounders would have diminished the effect size. Each study was assessed independently with the criteria recommended by GRADE and mentioned above, by two of the authors (MSG, AJC). When there was no consistency a consensus was reached with the aid of a third author (MBG) using the same criteria for evaluation in quality of the studies.

Results

Our search resulted in 842 articles; 95 of them contained information on the effect of weight loss in metabolic parameters in people with T2DM (fig. 1). Twenty published studies (table I) fulfilled the inclusion crite-
Table I  
Randomized clinical trials on the effect of weight loss in people with type 2 diabetes

<table>
<thead>
<tr>
<th>Authors Country (year)</th>
<th>N</th>
<th>Age (media) (range)</th>
<th>Intervention</th>
<th>Follow-up (months)</th>
<th>RET (%)</th>
<th>Initial BMI (media)</th>
<th>Final BMI (media)</th>
<th>WC (%)</th>
<th>Effects in T2D</th>
<th>Grade</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Pharmacologic therapy</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
| Kelley et al. USA (2002)* | 550 | 57.9 | a) Orlistat 120 mg + reduced calorie diet  
   b) Placebo | 12 | 97 | a) 35.8  
   b) 35.6 | a) NA  
   b) NA | a) ↓ 3.8  
   b) ↓ 1.2 | There was a significant difference in weight loss between groups  
   Greater ↓ of BG, A1C, TC, LDL, LDL/HDL ratio  
   and hypoglycemic drug use in Orlistat group | 4 |
| Hanefeld et al. Germany (2002)** | 492 | 55.7 | a) Orlistat 360 mg/day  
   b) Placebo | 12 | 75 | a) 34.5  
   b) 33.7 | a) NA  
   b) NA | a) ↓ 5.4  
   b) ↓ 3.6 | There was a significant difference in weight loss between groups  
   Greater ↑ HDL in placebo group | 4 |
| Miles et al. USA (2002)** | 516 | 53.1 | a) Orlistat 360 mg/day  
   b) Placebo | 12 | 98 | a) 35.6  
   b) 35.2 | a) NA  
   b) NA | a) ↓ 4.6  
   b) ↓ 1.7 | There was a significant difference in weight loss between groups  
   Greater ↓ in use of metformin and hypoglycemic drugs, A1C, TC, LDL, LDL/HDL ratio and systolic BP in Orlistat groups | 4 |
| McNulty et al. UK (2003)*** | 195 | 49 | a) Sibutramine 15 mg/day  
   b) Sibutramine 20 mg/day  
   c) Placebo | 12 | 99 | a) 36.3  
   b) 35.5  
   c) 36.1 | a) 34.3  
   b) 34.6  
   c) 36.1 | a) ↓ 5.3*  
   b) ↓ 7.7*  
   c) ↓ 0.2 | There was a significant difference in weight loss between groups  
   Greater ↓ systolic and diastolic BP in Sibutramine (15 mg/day) group  
   Pulse in both treatment groups | 4 |
| Redmon et al. USA (2003)** | 61 | 53.5 | a) Standard therapy  
   b) Combination therapy (low-calorie diet + sibutramine 10 mg/day + meal replacement and snack bar) | 12 | 97 | a) 38.6  
   b) 37.8 | a) 38.3  
   b) 35.2 | a) ↓ 0.8  
   b) ↓ 6.4 | There was a significant difference in weight loss between groups  
   Greater ↓ in use of metformin and hypoglycemic drugs, A1C in combination therapy group | 2 |
| Kauliau et al. Finland (2004)* | 236 | 53.5 | a) Sibutramine 15 mg/day  
   b) Placebo | 12 | 98 | a) 35.7  
   b) 35.6 | a) NA  
   b) NA | a) ↓ 7.3  
   b) ↓ 2.4 | There was a significant difference in weight loss between groups  
   Greater ↓ of diastolic BP in Sibutramine group | 3 |
| Berne et al. Sweden (2005)** | 221 | 59.1 | a) Orlistat 120 mg  
   b) Placebo | 12 | 100 | a) 32.6  
   b) 32.9 | a) NA  
   b) NA | a) ↓ 50*  
   b) ↓ 18* | There was a significant difference in weight loss between groups  
   Greater ↓ of, A1C, BG, TC in Orlistat group  
   Greater ↑ HDL in Orlistat group | 4 |
| Scheen et al. USA (2007)** | 1,045 | 55.6 | a) Rimonabant 5 mg/day  
   b) Rimonabant 20 mg/day  
   c) Placebo | 12 | 100 | a) 34.4  
   b) 34.1  
   c) 34.2 | a) NA  
   b) NA  
   c) NA | a) ↓ 2.3  
   b) ↓ 5.5  
   c) ↓ 1.4 | There was a significant difference in weight loss between groups  
   Greater ↓ A1C and systolic BP in both Rimonabant groups  
   Greater ↑ TGL and BG, and greater ↑ HDL in Rimonabant 20 mg group | 4 |
| **Surgical therapy** |   |                     |              |                   |         |                   |                   |       |               |       |
| Dixon et al. Australia (2008)* | 60 | (20-60) | a) Conventional-Therapy Program  
   b) Surgical Program | 24 | 92 | a) 37.2  
   b) 37.0 | NA | a) ↓ 1.4  
   b) ↓ 0.0** | There was a significant difference in weight loss between groups  
   76% and 15% of surgical and conventional program respectively had remission of T2D  
   Greater ↓ BG, AIC and use of hypoglycemic drugs in surgical group | 2 |
Table 1 (continuation)
Randomized clinical trials on the effect of weight loss in people with type 2 diabetes

<table>
<thead>
<tr>
<th>Authors</th>
<th>Country</th>
<th>N</th>
<th>Age media (range)</th>
<th>Intervention</th>
<th>Follow-up (months)</th>
<th>RET (%)</th>
<th>Initial BMI (media)</th>
<th>Final BMI (media)</th>
<th>WC (%)</th>
<th>Effects in T2D</th>
<th>Grade</th>
</tr>
</thead>
<tbody>
<tr>
<td>Brinkworth et al.</td>
<td>Australia</td>
<td>66</td>
<td>61.8</td>
<td>a) Low-protein diet b) High-protein diet</td>
<td>12</td>
<td>58</td>
<td>a) 33.3 b) 33.6</td>
<td>a) NA b) NA</td>
<td>a) ↓ 24+ b) ↓ 39*</td>
<td>Greater ↓ of diastolic BP in high-protein diet</td>
<td>1</td>
</tr>
<tr>
<td>Li et al.</td>
<td>USA</td>
<td>104</td>
<td>55.5</td>
<td>a) Soy-based meal replacement b) Individualized diet plan</td>
<td>12</td>
<td>74</td>
<td>a) 32.8 b) 33.7</td>
<td>a) 31.4 b) 32.9</td>
<td>a) ↓ 46* b) ↓ 23*</td>
<td>Greater ↓ of hypoglycemic drugs in meal replacement group</td>
<td>3</td>
</tr>
<tr>
<td>Aas et al.</td>
<td>Norway</td>
<td>38</td>
<td>57</td>
<td>a) Lifestyle intervention programme b) Lifestyle intervention programme + insulin c) Insulin</td>
<td>12</td>
<td>74</td>
<td>a) 29.8 b) 31.1 c) 30.0</td>
<td>a) 28.9 b) 32.4 c) 29.6</td>
<td>a) ↓ 1.7 b) ↑ 3.0 c) ↓ 2.5</td>
<td>NS</td>
<td>2</td>
</tr>
<tr>
<td>West et al.</td>
<td>USA</td>
<td>217</td>
<td>53</td>
<td>a) Individual sessions of motivational interviewing + weight control program b) Attention control + weight control program</td>
<td>18</td>
<td>93</td>
<td>a) 36.5 b) 36.5</td>
<td>a) NA b) NA</td>
<td>a) ↓ 3.6 b) ↓ 1.8</td>
<td>At 18 months there was a significant difference in weight loss between groups, but not difference was found in AIC</td>
<td>2</td>
</tr>
<tr>
<td>Cheskin et al.</td>
<td>USA</td>
<td>119</td>
<td>55.0</td>
<td>a) Standard diet b) Portion-controlled diet</td>
<td>12</td>
<td>28</td>
<td>a) 35.0 b) 35.7</td>
<td>a) 33.3 b) 33.8</td>
<td>a) ↓ 2.3 b) ↓ 44*</td>
<td>↑ HDL in portion-controlled diet ↓ BG and insulin BP in portion-controlled diet</td>
<td>3</td>
</tr>
<tr>
<td>Davies et al.</td>
<td>UK</td>
<td>824</td>
<td>59.5</td>
<td>a) Structured education programme b) Conventional care</td>
<td>12</td>
<td>68</td>
<td>a) 32.3 b) 32.4</td>
<td>a) NA b) NA</td>
<td>a) ↓ 3.3* b) ↓ 2.0*</td>
<td>NS</td>
<td>1</td>
</tr>
<tr>
<td>Ma et al.</td>
<td>USA</td>
<td>40</td>
<td>53.5</td>
<td>a) Low-GI diet b) ADA diet</td>
<td>12</td>
<td>48</td>
<td>a) 35.6 b) 36.0</td>
<td>a) NA b) NA</td>
<td>a) ↓ 1.3 b) ↓ 0.8</td>
<td>↓ AIC, TC in both groups Greater ↓ of LDL in the low-GI group Low-GI group had much lower likelihood of switching to a new drug or increasing dosage of hypoglycemic drugs</td>
<td>0</td>
</tr>
<tr>
<td>Esposito et al.</td>
<td>Italy</td>
<td>283</td>
<td>(30-75)</td>
<td>a) Low-carbohydrate MED diet b) Low-fat diet</td>
<td>48</td>
<td>76</td>
<td>a) 29.7 b) 29.5</td>
<td>a) 28.5 b) 28.6</td>
<td>a) ↓ 4.4 b) ↓ 0.7</td>
<td>Greater ↓ of BG, AIC and LDL, and ↑ HDL in MED diet group</td>
<td>4</td>
</tr>
<tr>
<td>Baurard et al.</td>
<td>USA</td>
<td>99</td>
<td>55.7</td>
<td>(27-82)</td>
<td>18</td>
<td>88</td>
<td>a) 33.9 b) 33.9</td>
<td>a) 32.3 b) 34.8</td>
<td>a) ↓ 4.4 kg b) ↓ 30 kg</td>
<td>NS</td>
<td>4</td>
</tr>
<tr>
<td>Brehm et al.</td>
<td>USA</td>
<td>124</td>
<td>56.5</td>
<td>(36-75)</td>
<td>12</td>
<td>77</td>
<td>35.9</td>
<td>34.6 b) 34.5</td>
<td>a) ↓ 3.9** b) ↓ 3.7**</td>
<td>↑ HDL, ↓ AIC, BG, diastolic BP, insulin concentration and insulin resistance in both groups</td>
<td>3</td>
</tr>
<tr>
<td>Davi et al.</td>
<td>USA</td>
<td>105</td>
<td>53.5</td>
<td>a) Low-CHO diet b) Low-fat diet</td>
<td>12</td>
<td>81</td>
<td>a) 35.0 b) 37.0</td>
<td>a) 33.7 b) 33.7</td>
<td>a) ↓ 3.3* b) ↓ 3.1*</td>
<td>↑ HDL in low-CHO group</td>
<td>2</td>
</tr>
</tbody>
</table>

N = number of subjects; RET % = retention percentage; BMI = body mass index; WC = weight change; T2D = type 2 diabetes; M = male; F = female; MED = Mediterranean style; NA = not available; BG = blood glucose; A1C = TC = total cholesterol; LDL = low density lipoprotein; HDL = high density lipoprotein; BP = blood pressure; MUFA = monounsaturated fat; CHO = carbohydrate; DSE = Diabetes Support and Education; GI = glycemic index; ADA = American Diabetes Association; ITT = Intention-to-treat.

*p < 0.05.
**p < 0.01.
Abstracts Reviewed from Electronic Databases (RCT from 2000-2010):
PubMED 364
Cochrane Library 454
Ebsco 24
Scielo 0
Total reviewed 842

RCT of effect of weight loss in people with T2DM n = 95

Studies removed due to lack of BMI or weight data n = 7

Studies removed due to the follow-up was less than 12 months n = 68

Studies included that fulfill all inclusion criteria n = 20

Glycemic values

All studies included in this revision assessed the reduction of A1C, but only nine of them (45%) reported a significant reduction after the follow-up period. Of these studies, five were RCT with good quality and had the maximum punctuation using the GRADE scale, four of them used drug therapy, and one used the MED-diet. One of them had zero points using the GRADE scale due to important methodological weaknesses such as differences between groups in baseline characteristics, insufficient samples, retention percentage < 70%, and a lack of intention-to-treat analysis. The rest of the studies also had insufficient samples.

BG was assessed in only 16 studies (80%), seven of which (44%) reported a significant reduction. Four of the studies were evaluated and received four points using the GRADE scale, three of them used drug therapy and one MED-diet. The rest had insufficient samples or low retention rate.

Weight change

All studies included in this revision reported weight loss after the follow-up period. According to the weight reduction strategies, a greater mean reduction was reported using surgical treatment (-20% of body weight (BW)), followed by drug therapy (-2.3-7.7% of BW), and lifestyle interventions (-0.8-4.6% of BW). Greater mean weight reduction was reported using soy-based meal replacements (-4.6% of BW); however, the follow-up of this study was up to 12 months. Esposito et al., using a Mediterranean (MED) diet, reported a weight loss of 4.4% of BW after 48 months of follow-up, and Barnard et al. reported weight loss after 18 months with a vegan diet.
Lipid values

The effect of weight loss on lipid values was assessed in 18 studies (90%). Four of them (20%) reported a significant reduction in total cholesterol, three of them used Orlistat to reduce body weight, and four received four points using the GRADE scale; one study used the low-GI diet or ADA-diet but had important methodological weaknesses. Also, four of them (20%) reported significant reduction in LDL, two used Orlistat (4 points with GRADE scale), and one the low-GI diet (0 points with GRADE scale). Seven studies (35%) reported an elevation of HDL, three using Orlistat, one the MED-diet (4 points with GRADE scale), and one with the high-MUFA and high-CHO diet, and one with low-CHO.

Blood pressure

Sixteen studies (80%) assessed blood pressure, of which only three (19%) reported a significant reduction in systolic BP and three others in diastolic BP. In one study using sibutramine (15 mg/day) a significant elevation of systolic, diastolic BP and pulse rate was reported.

Hypoglycemic drugs use

Nine studies (45%) assessed if there was a reduction in the use of hypoglycemic drugs. A significant reduction was observed in four (44%) of these studies. Two used Orlistat, one used surgical treatment, and one used soy-based meal replacement.

Remission of T2DM

Remission of T2DM was only reported in the study using surgical treatment as the weight control strategy. The remission was observed in four (44%) of these studies. Two used Orlistat, one used surgical treatment, and one used soy-based meal replacement.

Discussion

This revision indicates that the effect of WL on biological markers on long-term studies in people with T2DM is inconclusive. WL percentage ranged from 0.8 to 20%, reduction in A1C was observed in nine out of 20 studies, blood glucose in seven out of 16, total cholesterol and LDL in four out of 18, systolic and diastolic blood pressure in three out of 16 and the use of hypoglycemic drugs in four out of nine; an increase of HDL was observed in seven out of 18 studies. In addition, remission of T2DM was only reported in the study in which subjects underwent bariatric surgery. Most studies had a follow-up of 12 months, four studies had a follow up ≥12 months, and the longest non surgical study had a follow-up of 48 months. One of the studies with the longest follow-up (24 months) reported weight loss, reduction in BG, A1C, and the use of hypoglycemic drugs after bariatric surgery, however, the sample size was insufficient to obtain 80% of statistical power, and no intention-to-treat analysis was used, which resulted in an evaluation score of 2. One of the studies with the follow-up of 18 months reported reductions in weight; however, the quality score of this study was 2 because neither intention-to-treat nor statistical power was reported. One of the longest studies (18 months) had the highest quality score (4) and reported no significant changes in any parameter. The study that included low carbohydrate Mediterranean diet also had the highest quality score and reported a reduction of BG, A1C and LDL and an increase of HDL, after 48 months of follow-up, with no difference in weight lost.

Previous reviews assessed the impact of weight loss in patients with T2DM, but the results included people with and without T2DM; they only assessed one type of intervention, and most of the studies were cohorts. Few RCT were evaluated and most of them had a follow-up of less than 12 months. This study includes RCT with a follow-up ≥ 12 months in order to assess the long term sustainability of the effects on biological markers. The results observed in this study confirm that the metabolic control of people with diabetes is challenging at the long-term.

People with OW or OB have an increased risk of developing T2DM, and weight loss has been associated with a reduced risk. Several large RCT have shown that weight loss might be an important management strategy for OW and OB persons with pre-diabetes, as it may delay or prevent the progression of clinically defined T2DM. Consistently, some studies have shown that weight loss in obese people with T2DM can significantly improve glycemic control, and some subjects can discontinue insulin or oral therapy. However, most studies assessed short-term improvements and long-term effects were less described.

The results of this study suggests that the treatment of OB and OW on people with T2DM should focus on encouraging lifestyle changes and improving biological markers, instead of establishing weight loss goals that are difficult to reach, as an intermediate objective to improve biological markers. However, these results warrant longer and better designed studies.

The strength of this study is the inclusion of studies of ≥ 12 months of follow-up, since diabetes is a chronic disease and its implications on other health problems are discovered in the long-term; therefore, the result are not overestimated by shorter-term intervention (< 6 months). Unfortunately, several studies had to be excluded due to the inclusion of combined data from people with and without diabetes. The main limitation of the study is the lack of a meta-analysis due to the heterogeneous nature of the interventions and outcome measures.
ergoregometry of the studies’ design. In addition, the treatment strategy was mixed, ranging from diet management to stable and flexible doses of insulin or oral hypoglycemic agents. Further, most of the studies did not have specific guidelines regarding physical activity modifications and no objective reports of PA were recorded. The dropout rate in some studies was high, and most of the studies did not performed intention-to-treat analysis. Therefore, the evidence of the beneficial effect of WL on biological markers on long-term studies in people with T2DM is inconclusive.

References


