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Original

Evidence-based nutritional recommendations for the prevention and treatment of overweight and obesity in adults (FESNAD-SEEDO consensus document). The role of diet in obesity treatment (III/III)

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Abstract

This study is a consensus document of two Spanish scientific associations, FESNAD (Spanish Federation of Nutrition, Food and Dietetic Associations) and SEEDO (Spanish Association for the Study of Obesity), about the role of the diet in the treatment of overweight and obesity in adults. It is the result of a careful and systematic review of the data published in the medical literature from January 1st 1996 to January 31st 2011 concerning the role of the diet on obesity treatment.

The achieved conclusions have been classified into various evidence levels. Subsequently in agreement with these evidence levels, different degree recommendations are established being potentially useful to design food guides as part of strategies addressed to the treatment overweight and obesity.

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RECOMENDACIONES NUTRICIONALES BASADAS EN LA EVIDENCIA PARA LA PREVENCION Y EL TRATAMIENTO DEL SOBREPESO Y LA OBESIDAD EN ADULTOS (CONSENSO FESNAD-SEEDO). LA DIETA EN EL TRATAMIENTO DE LA OBESIDAD (III/III)

Resumen

Se presenta un consenso de la Federación Española de Sociedades de Nutrición, Alimentación y Dietética (FESNAD) y la Sociedad Española para el Estudio de la Obesidad (SEEDO)) sobre la dieta en el tratamiento de la obesidad, tras efectuar una revisión sitemática de los datos de la lilteratura médica desde el 1 de enero de 1996 al 31 de enero de 2011 .

Las conclusiones obtenidas se han catalogado según niveles de evidencia.

Se establecen unas recomendaciones clasificadas según grados que pueden servir de guía y orientación en el diseño de pautas alimentarias dirigidas al tratamiento de la obesidad o el sobrepeso.

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Palabras clave: *Obesidad. Sobrepeso. Tratamiento. Dieta. Nutrición.*

Abbreviations

ADA: American Dietetic Association.
AHT: Arterial hypertension.
BMI: Body mass index.
BP: Blood pressure.
BS: Bariatric surgery.
CH: Carbohydrates.
CI: Confidence interval.
CT: Computerised tomography.
DBP: Diastolic blood pressure.
DF: Dietary fibre.
EFSA: European Food Safety Authority.
EU: European Union.
GI: Glycaemic index.

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GL: Glycaemic load.
HbA1c: Glycated haemoglobin.
HDL: High-density lipoprotein.
HOMA: Homeostatic Model Analysis.
HPD: High protein diets.
HZ: Hazard rate.
IOM: Institute of Medicine.
LCD: Low calorie diet.
LChD: Low-carbohydrate diet.
LDL: Low-density lipoprotein.
LFD: Low-fat diet.
LGID: Low glycaemic index diets.
MRP: Meal replacement products.
MS: Metabolic syndrome.
NMR: Nuclear magnetic resonance.
RCT: Randomised clinical trials.
RD: Royal Decree.
SBP: Systolic blood pressure.
VLCD: Very low calorie diet.
VLCD: Very low calorie diets.
VLDL: Very low-density lipoprotein.

Introduction

In light of the high prevalence of obesity and overweight in our country[1] and the multitude of nutritional approaches proposed to combat them, the Spanish Federation of Nutrition, Food and Dietary Associations (FESNAD) and the Spanish Association for the Study of Obesity (SEEDO) have jointly proposed clarifying the role of the various nutritional factors for both the prevention and treatment of obesity and overweight. For this purpose a FESNAD-SEEDO consensus has been prepared, containing nutritional recommendations based on evidence which will serve as a tool to health professionals when designing prevention strategies or treatment guidelines for obesity or overweight.

It must be noted that the opinions expressed in this document have been agreed upon between the representatives of the different associations listed in the authorship and, as such, they represent the position of all of them.

The consensus is organised into 3 documents published separately. This work covers the review of the dietary aspects of the prevention of obesity and overweight.

Methodology. Levels of evidence

The methodology and working system of this consensus have already been described.[2] Briefly, we can say that for the design of the following recommendations we reviewed the scientific literature which covers the general areas of interest for the consensus, published between 1st January 1996 and 31st January 2011. On the basis of the conclusions obtained from that review, the evidence was classified and recommendations were formulated according to the method proposed in 2008 by the European Association for the Study of Obesity[3] and which consists of a simplified version of the system proposed by the Scottish Intercollegiate Guidelines Network (SING)[4] (tables I and II).

On the basis of the criteria for its preparation, the resulting document is applicable to the adult population (excluding pregnancy and breastfeeding) which, apart from obesity, presents no malnutrition or chronic diseases.

Preliminary anlysis of the reviews and recommendations published

The dietary treatment of obesity has logically been considered in all of the consensuses and clinical guidelines relating to obesity.

The document which is most representative of the international associations is obviously that of the World Health Organisation. In its manifesto of 2007[5] it was considered that there was sufficient evidence to demonstrate the effectiveness for weight loss of hypo-

Table I
Levels of evidence[19]

		Levels of evidence
1	1++	High quality meta-analysis, systematic reviews of RCT's or RCT's with a very low risk of bias.
	1+	Meta-analysis well executed, systematic reviews of RCT's or RCT's with a low risk of bias.
	1-	Meta-analysis, systematic reviews of RCT's or RCT's with a high risk of bias.
2	2++	High quality systematic reviews of case-control or cohort studies.
	2+	High quality case-control or cohort studies with a very low risk of confusion or bias and a high probability that the relationship is causal.
	2-	Well executed case-control or cohort studies with a low risk of confusion or bias and a moderate probability that the relationship is causal.
3		Non-analytical studies (e.g. clinical cases, case series).
4		Opinion of expert(s).

Table II
Levels of recommendation[19]

	Levels of recommendation
A	At a minimum a meta-analysis, systematic review or RCT with a classification of 1++ and directly applicable to the target population, or a systematic review or RCT with a body of evidence consisting mainly of studies graded at 1+, directly applicable to the target population, and demonstrating overall consistency in its outcomes.
B	A body of evidence which includes studies graded at 2++, directly applicable to the target population and which demonstrates overall consistency in its outcomes, or evidence extrapolated from studies graded at 1++ or 1+.
C	A body of evidence which includes studies graded at 2+, directly applicable to the target population and which demonstrates overall consistency in its outcomes, or evidence extrapolated from studies graded at 2++.
D	Evidence of level 3 or 4, or evidence extrapolated from studies graded at 2+.

Studies classified as 1- and 2- must not be used in the process of preparing recommendations because of their high bias potential.

caloric diets, low-fat reduced-calorie diets and low fat diets without a reduction in calories. Furthermore, it recognises the effectiveness of very low calorie diets (VLCD) for short term weight loss in selected patients.

In 2000,[6] American scientific organisations such as the North American Association for the Study of Obesity, the National Heart, Lung, and Blood Institute and the National Institutes of Health, jointly recommended a dietary approach, with a reduction in calorie intake of 500 to 1,000 kcal below calorie needs, following the plan of a conventional hypocaloric diet.

In its subsequent recommendations of 2009,[7] the American Dietetic Association establishes a calorie deficit of 500 to 1,000 kcal to lose weight, by reducing the intake of fat or carbohydrates. It warns of the long term ineffectiveness of diets very low in carbohydrates and of their possible harmful effects. It also considers low glycaemic index diets to be ineffective.

The recent 2010 Dietary Guideless for Americans[8] concludes that, to treat obesity, the initial recommended treatment is a diet with a 500 kcal energy deficit, with the total calorie deficit being considered the important factor, with the proportion of nutrients having little impact on weight. In this sense it adopts the recommendations of the Institute of Medicine on macronutrient distribution (carbohydrates 45-65%, proteins 10-35% and fat 20-35%), although it recognises that it is very difficult to cover the recommendations for dietary fibre intake in the lower range of recommendations for carbohydrates.

Within Europe, in its clinical practice guidelines of 2008,[3] the European Association for the Study of Obesity advocates a reduction in the calorie content of the diet of between 500 and 1,000 kcal. It is not of the opinion that possible variations in the proportion of the immediate principles of the diet offer any advantage over the conventional hypocaloric diet, except in the case of low glycaemic index diets in the short term. It reserves the use of VLCD's for very specific cases and always within an overall weight loss programme being supervised by a specialist. It is also of the opinion that replacing meals with formula diets can improve the dietary balance and help to maintain weight loss.

The British National Institute for Health and Clinical Excellence (NICE)[9] recommends a diet with an overall deficit of 600 kcal by reducing fat intake.

Finally, among the Spanish guidelines, the Spanish Society for Endocrinology and Nutrition of 2004 and the Spanish Association for the Study of Obesity of 2007 recommend hypocaloric diets with a reduction in the proportion of fat content.[10,11]

As we can see, the vast majority of scientific associations continue to recommend the traditional hypocaloric diet. The only different recommendation is in the Canadian Guidelines for the management of obesity,[12] which recommends a balanced hypocaloric diet, although it also suggests the possibility of using a low-fat or high protein diet for 6 or 12 months. It is of the opinion that meal replacement diets can be integrated as part of a hypocaloric diet in some cases.

Objectives of the dietary treatment of obesity

The dietary approach towards treating obesity must aim to meet a series of global objectives in the short and long term. Weight loss will obviously be the aim, but that weight loss must also be accompanied by a set of more ambitious requirements.

In accordance with this approach, the authors of this Consensus understand that the dietary treatment of obesity must meet the conditions which appear in table III.

Obviously, a diet which meets all of the aforementioned conditions would be ideal and, currently, none of the dietary models of obesity fully meet them, but they must be used as a benchmark for what we want to achieve.

It must be considered that selecting an unsuitable diet, contrary to the above, could not only be an ineffective means of achieving the goal of weight loss, but also it could give rise to a whole series of adverse consequences. In table IV there is a list of the possible risks and side effects of an unsuitable diet.

Table III
Conditions which must be met by the dietary treatment of obesity

- It decreases body fat while preserving maximum lean mass.
- It is achievable for a prolonged period of time.
- It is effective in the long term, in other words, maintaining lost weight.
- It prevents future weight gain.
- It involves dietary education which eradicates errors and unsuitable eating habits.
- It reduces the cardiovascular risk factors associated with obesity (arterial hypertension, dyslipidaemia, pre-diabetes or diabetes mellitus).
- It results in improvements in other comorbidities associated with overweight (sleep apnoea, osteoarthritis, neoplastic risk, etc.).
- It induces psychosomatic improvement, with self-esteem being recovered.
- It increases functional capacity and quality of life.

Table IV
Risks of inadequate dietary treatment of obesity

- It results in malnutrition or deficiencies in various types of micronutrients (vitamins, trace elements, etc.).
- It worsens the cardiovascular risk of the patients.
- It stimulates the development of extremely serious eating disorders with a worse prognosis than obesity itself.
- It conveys misconceptions about obesity and its treatment.
- It stimulates a feeling of frustration, having a negative effect on the psychological condition of the patient with obesity.
- It induces changes in energy metabolism which result in "resistance" to weight loss after following successive diets.

Therefore, when assessing the characteristics of the different types of diet, these factors must be considered, and one must not simply limit oneself to quantifying their effect on weight loss.

Dietary factors associated with the treatment of obesity

1. Balanced hypocaloric diet. Eating patterns

The aim of the dietary treatment of obesity is to achieve maintained weight loss for a period which makes it possible to reduce the risk which overweight presents for the health of the patient.

Over the years numerous approaches have been used for the dietary treatment of obesity. The balanced, moderately hypocaloric diet is the type of dietary treatment which is most widely recommended by the scientific organisations and associations for the dietary treatment of obesity.

There is no unanimous agreement on what constitutes a "balanced hypocaloric diet". In general terms it is considered to be a diet which results in a calorie deficit of between 500 and 1,000 kcal/day, with a total calorie intake above 800 kcal per day. The term "balanced" refers to the macronutrient distribution not differing greatly from that which is recommended for the general public. In this sense, it must be taken into account that when a hypocaloric diet is followed it is necessary to increase the proportion of the total calorie intake of proteins. Otherwise it is difficult for the diet to meet its protein requirements, which are established at 0.83 g/kg/day13 for a diet without an energy restriction and which should probably be at least 1 g/kg/day if the diet is hypocaloric. Table V shows the macronutrient distribution suggested by the SEEDO for the dietary treatment of obesity.[11]

Table V
Recommendations on macronutrient distribution for the treatment of obesity[11]

Energy	*500-600 kcal deficit/day on the baseline estimates obtained through equations or on normal intake*
Carbohydrates	45-55%
Proteins	15-25%
Total fats	25-35%
Saturated	< 7%
Monounsaturated	15-20%
Polyunsaturated	< 7%
Trans fatty acids	< 2%
Fibre	20-40 g

The recommended weight loss is approximately between 0.5 and 1 kg per week. Taking into account the energy content of adipose tissue, it is estimated that a daily energy deficit of 500-1,000 kcal/day is necessary to obtain weight loss.[14-16] As remarked above, this type of diet normally contains between 1,000 and 1,200 kcal/day for women and 1,500-2,000 kcal/day for men. The diet plan suggested must be adapted to the clinical characteristics and preferences of each patient, and it must be planned to facilitate long term adherence.

The prescribed calorie intake of the diet must be adapted to the characteristics of each patient. It is not easy to know the energy requirements of obese patients, as they depend on numerous factors associated with body composition, spontaneous and voluntary physical activity and genetic factors. Indirect calorimetry enables an objective assessment of resting energy expenditure. Energy expenditure can also be calculated using equations; that of Harris-Benedict is the most widely used. The American Dietetic Association recommends using the Mifflin-St Jeor formula to calculate resting energy expenditure (table VI).[7] To calculate total energy expenditure, we must use a physical activity correction

Table VI
Equations for calculating resting energy expenditure

Harris Benedict Equation
Men: REE (kcal/day) = 66 + 13.7 weight (kg) + 5 size (cm) – 6.8 age (years)
Women: REE (kcal/day) = 655 + 9.6 weight (kg) + 1.8 size (cm) – 4.7 age (years)
Mifflin St Jeor Equation[7]
Men: REE (kcal/day) = 10 weight (kg) + 6.25 size (cm) – 5 age (years) + 5
Women: REE (kcal/day) = 10 weight (kg) + 6.25 size (cm) – 5 age (years) – 161

REE: Resting energy expenditure.

factor. It must be taken into account that it is estimated that 25% of the composition of the excess weight of a patient with obesity is lean mass and 75% is fat mass. It is also possible to calculate the requirements by analysing the patient's normal diet. It must be taken into account that obese people tend to underestimate their intake.

Conventional hypocaloric diets achieve a weight loss of approximately 8% of the initial weight within a period of 6-12 months.[17] This type of diet is effective in reducing the metabolic risk associated with obesity. Studies over the long term show that this weight loss is difficult to maintain[18] and, in general, long term follow-up studies exceeding one year, show a weight loss of approximately 4%. Close monitoring of the patient including a changed eating behaviour pattern and an increase in physical activity makes it possible to improve these results.

A set of recommendations have been established to facilitate therapeutic adherence to conventional hypocaloric diets. They include measures which are similar to many of those recommended to prevent the development of obesity. The majority of these recommendations are based on epidemiological studies which associate certain eating patterns with the risk of developing obesity. However, there are few studies which have assessed the direct effect of these measures on the treatment of obesity. Those of the greatest importance are:[19]

- Portion size control.
- A reduction in the intake of food with a high energy density.
- Meal distribution throughout the day, reducing the intake late in the evening or at night.

Some studies have prospectively assessed the effect of energy density on the treatment of obesity. In the two-year study by Ello et al.,[20] controlled portions were administered with different energy density. The reduction of energy density was the most important predictive factor for weight loss during the first two months of the study. Other studies have also observed the beneficial effect which controlling energy density has on treating obesity.[21,22-24]

The effect of controlling portion size on weight loss for an obese patient has also been assessed prospectively.[25,26] The reduction of the intake frequency has a negative effect on apetite control and body weight.[27]

EVIDENCE

37. A caloric content reduction of 500 to 1,000 kcal daily might induce a weight loss ranging between 0.5 and 1.0 kg/week, equivalent to an 8% weight loss over an average period of 6 months (Evidence Level 1+).

38. A number of measures exist, such as reducing the size of the consumed portion or reducing the energy density of the diet, which may facilitate adherence to the hypocaloric diet and the weight loss in the obese patient (Evidence Level 3).

RECOMMENDATIONS

16. An energy deficit of between 500 and 1,000 kcal/day from the energy needs of the obese adult patient is enough for inducing an 8% weight loss over the first 6 months of treatment (Recommendation Degree A).

17. Restriction of the size of the consumed portions and/or of the energy density of the diet are effective strategic measures for reducing weight in obese patients through dietary management (Recommendation Degree D).

2. Diet composition

2.1. Low fat *versus* low carbohydrate diets

As opposed to the traditional and classic dietary approach to treating obesity which proposed a reduction in energy intake, chiefly through a reduction in calories originating from fat, for some decades the possibility has been considered of altering this distribution of immediate principles and designing diets which are proportionally low in Carbohydrates (CH). The diffusion of popular diets supporting this design, such as Atkins, has helped to arouse interest in this dietary approach among the scientific community.

There is no absolute uniformity in the relevant literature regarding what is considered to be a diet low in CH (LChD), although the most widely used criterion is that of the American Academy of Family Physicians, which defines a LChD as that which reduces the contribution of carbohydrates to below 20 to 60 g/day (less than 20% of the total calorie intake) and a proportional increase in the intake of fat or proteins to compensate for the decrease in CH28. Restricting carbohydrates to 20 g is considered typical of diets which are very low in carbohydrates or pure ketogenic diets.

Under this criterion, below we review the advantages and disadvantages of LChD's versus conventional low-fat diets (LFD) for the treatment of obesity.

EFFECTIVENESS IN THE WEIGHT LOSS OF OBESE PATIENTS

Its use in the treatment of obesity in comparison with traditional LFD's has been studied in numerous clinical trials and some meta-analyses and reviews. The first systematic review of this aspect was carried out by Bravata et al. in 2003,[29] which included 107 articles, although only 5 of these (neither randomised nor controlled) exceeded a 3 month follow-up; its conclusion was that weight loss mainly depended on the calorie intake, and that this was irrespective of the proportion of CH.

Subsequently, in a meta-analysis published in 2006[30] of 5 randomised controlled trials (RCT)[31-35] (plus an article which was an extension of one of the RCT's36) comparing LChD's without energy restriction with hypocaloric LFD's, observed greater weight loss with the LChD at 6 months (-3.3 kg) but not at 12 months.

In April 2005, the International Life Sciences Institute of North America established a Technical Committee to assess the usefulness of diets low in carbohydrates.[37] It s conclusion was, according to the available studies, that diets low in CH could be more efficient than diets low in fat for short term weight loss, but they had no data beyond 6 months.

Similar results were reported in a systematic review in 2009[38] which included 13 RCT's up to 2007, which compared both types of diet. This review included the studies of the Nordmann meta-analysis[31-35] combined with other subsequent studies.[39-45] At 6 months weight loss in the LChD group was 4.02 kg higher than that of the LFD group, but at 12 months the difference had fallen to 1.05 kg ($p < 0.05$).

Subsequent to the aforementioned RCT's (prior to 2007) several RCT's of varying durations have been published which compare the effects on weight loss of LChD's versus LFD's. There are 2 studies with a follow-up of 5 or 6 months;[46,47] in each case the weight loss was significantly greater in the LChD group than in the LFD group. One of these studies reported its results after a one year follow-up,[48] by which time the differences in weight loss between both groups had disappeared.

Another 1-year RCT was published by Gardner et al.,[42] comparing the effect on weight loss in women of 4 popular diets with a different CH content. The result was that the Atkins diet (which had the lowest glucidic content) was associated with the greatest weight loss (-4.7 kg; CI 95%: -6.3 to -3.1 kg), in comparison with the loss achieved with the Zone diet (-1.6 kg; CI 95%: -2.8 to -0.4 kg), the LEARN diet (-2.6 kg; CI 95%: -3.8 to -1.3 kg) and with the loss achieved with the Ornish diet (-2.2 kg; CI 95%: -3.6 to -0.8 kg). No significant differences were observed between the other three diets in this study. However, in an analysis of the data published subsequently,[49] in which the weight loss of each of these diets was correlated with adherence to treatment, it was possible to confirm that, irrespective of the group to which they were assigned, the weight loss was primarily relative to the degree of adherence to the diet being followed.

Finally, we now have several RCT's with a duration above 1 year. The RCT published by Shai et al. in 2008[50] compared a hypocaloric LFD, a hypocaloric Mediterranean diet and an LChD without calorie restriction. After 2 years, the weight loss was -3.3 kg, -4.6 kg and -5.5 kg, respectively, ($p = 0.03$ for the comparison between LFD and LChD, and no differences were found between the Mediterranean diet and the LCD).

In contrast to the results of this study, three subsequent RCT's have been published which found no differences in weight loss after a two-year follow-up.[51-53] Two of them compared LChD's with LFD's. It must be noted that the study by Dyson et al.[52] was carried out with a very small sample (13 patients), so the results are not very assessable. The third[53] and most complete of the aforementioned studies analysed the influence of isocaloric diets with different CH content (65%, 55%, 45%, 35%) protein content (15% or 25%) and fat content (20% and 40%).

At 2 years no significant differences were observed in weight loss between the groups, with the weight loss being proportional to the number of visits made by the patient or, in other words, the degree of adherence to whichever type of diet they had been assigned.

We also have a three year RCT[54] in which the initial favourable weight loss of LChD's which was observed during the first 6 months, disappeared after 1 year and no further differences were observed after 3 years.

In conclusion, on the basis of the aforementioned results, it can be stated that LChD's result in a greater and more significant weight loss than LFD's in the first 6 months, but this difference is lost after 12 months. If the diets are isocaloric, it does not appear that weight loss is relative to the higher or lower percentage of the macronutrients of which they are composed, but rather the patient's degree of adherence to the diet they have been assigned.

EFFECT ON LIPID PROFILE

Some of the aforementioned studies have detailed the comparative effect of these two types of diet on different lipid parameters.

In the meta-analysis by Nordmann et al.[30] a beneficial effect of the LChD was observed on the levels of triglycerides and HDL cholesterol, although it could have damaging effects on the levels of LDL cholesterol. Hession et al.38 also described beneficial effects on plasma concentrations of HDL cholesterol and Triglycerides with the LChD and a decrease in the levels of LDL cholesterol during the first 6 months with LFD's.

The subsequent short term RCT's (5-6 months)[46,47] have described a reduction in the levels of LDL cholesterol with the LFD's and of the levels of Triglycerides with the LChD's.

The 1-year follow-up of one of these studies[48] demonstrated that a better cardiovascular profile was maintained with an LChD due to the increase in HDL cholesterol and the reduction in triglycerides, although it also presented an increase in LDL cholesterol. Another one-year study[50] also found a significantly higher reduction in total cholesterol and HDL cholesterol with an LChD than with an LFD.

During longer studies, Foster et al.[51] observed an improvement in the lipid profile (HDL and triglycerides) at 6 months with the LChD, but with an increase in the levels of LDL. At 2 years only an improvement in HDL cholesterol remained (with a 23% increase) with the LChD, with all other differences disappearing. Similarly, at 2 years Sacks et al.[53] observed that the LChD had a favourable effect on HDL cholesterol and increased the levels of LDL cholesterol.

Finally, the RCT with the longest duration to date (3 years)[54] found no differences in lipid profile between both diet types.

Together with the aforementioned studies, mostly designed to assess the effect on weight loss, the OmniHeart Study[55] solely assessed the effect of each type of diet on cardiovascular risk. This is a randomised crossover trial which compares 3 types of diet: a diet rich in carbohydrates, a diet rich in proteins and a diet rich in unsaturated fat, with constant weight maintenance at each stage. Their results showed that, in comparison with the diet rich in carbohydrates, the diet rich in unsaturated fats (and low in carbohydrates) reduced systolic blood pressure by 1.3 mm Hg ($P = 0.005$) or 2.9 mm Hg in hypertensive patients ($P = 0.02$), it had no significant effects on LDL cholesterol, it increased HDL cholesterol by 1.1 mg/dL ($P = 0.03$), and reduced Triglycerides by 9.6 mg/dL ($P = 0.02$); overall, these changes represented a lower cardiovascular risk at 10 years, without there being any difference between the diet rich in fat and the diet rich in protein.

Other factors

In addition to the effects of each diet on weight loss and lipid profile, there are other factors to consider such as the degree of adherence, their possible side effects and their nutritional sufficiency or deficiency.

Regarding the adherence to the diet, we have little data. In their revision (studies mostly from 6 to 12 months), Hession et al.[38] describe a greater dropout rate with the LFD. In contrast, no differences were found between both types of diet in other studies after 1 year[30] or two years.[21,53]

Their nutritional content was analysed by Freedman et al.,[56] who found a deficiency of Vitamins A, B6, C and E, thiamine, folate, calcium, magnesium, iron, potassium and fibre in the LChD, to such an extent that they recommend taking multivitamin, fibre and, in the case of women, calcium supplements.

Regarding side effects, Yancy et al.[34] observed a higher frequency of constipation (68% *vs.* 35%; $P < 0.001$), migraine (60% *vs.* 40%; $P = 0.03$), halitosis (38% *vs.* 8%; $P < 0.001$), muscle cramps (35% *vs.* 7%; $P < 0.001$), diarrhoea (23% *vs.* 7%; $P = 0.02$), malaise (25% *vs.* 8%; $P = 0.01$), and skin rashes (13% *vs.* 0%; $P = 0.006$) after 6 months of treatment with an LChD. An uncontrolled observational study[57] also reported a high rate of side effects. In 2 year studies a higher frequency of halitosis, dry skin and constipation were also reported for LChD's, mainly during the 6 initial months of the 2 first years,[51] while in other studies with the same duration, no significant side effects were found with either of the diets.[53]

Regarding the long term safety of these diets, a 1-year RCT comparing LChD's with LFD's[58] did not observe any impact on renal function for either of the diets, or on the parameters of vascular function or endothelial factors, apart from a decreased arterial dilation capacity after hypoperfusion with the LChD.[59]

One factor to consider for the long term safety of these diets is the type of fat consumed. A prospective cohort study[60] demonstrated (after a 26 year follow-up of women and a 20 year follow-up of men) that the total mortality and cancer mortality rates of those following an LChD was higher when the fat consumed was of animal origin, while the consumption of fat of plant origin was associated with a fundamentally lower cardiovascular mortality rate.

Evidence

39. As compared to a low fat one, a low carbohydrate diet achieves in the short term (6 months) a higher weight loss (Evidence Level 1++).

40. In the long term (1 year or more), a low carbohydrate diet achieves a weight loss similar to that achieved with a low fat one (Evidence Level 1+).

41. In the long term (1 year or more), a low carbohydrate diet achieves a greater HDL cholesterol increase and a higher triglyceride reduction than a low saturated fat one (Evidence Level 1+).

42. In the long term (1 year or more), a low saturated fat diet achieves a higher LDL cholesterol reduction than a low carbohydrate one (Evidence Level 2+).

43. Low carbohydrate diets cause more adverse effects than low fat ones (Evidence Level 2++).

44. The very long term mortality with low carbohydrate diets may be increased if the fats are of animal origin (Evidence Level 3).

Recommendations

18. Reducing the proportion of carbohydrates and increasing that of fats is not useful for potentiating the effect of a diet on weight loss (Recommendation Degree A).

19. For controlling the LDL cholesterol levels in an obese patient a low fat diet is effective , while the HDL cholesterol and triglyceride levels are better controlled with a low carbohydrate one (Recommendation Degree B).

20. Low carbohydrate diets should not contain a high proportion of animal origin fats (Recommendation Degree D).

2.2.1. *Diets with modifications to the type of carbohydrates: high-fibre diets*

According to the traditional definition of the Institute of Medicine (IOM)[61] the term "Dietary fibre" (DF) includes non-digestible carbohydrates and lignin which are intact and intrinsic in plants. More recently, the latest scientific update sponsored by the FAO-WHO defines it as the intrinsic polysaccharides of the plant cell walls.[62] The term "Functional fibre" is reserved for isolated, non-digestible carbohydrates which have a beneficial effect on humans. Therefore Total Fibre would be the sum of Dietary Fibre and Functional Fibre.

Within DF, soluble fibre (pectin, guar gum, mucilage and storage polysaccharides) is normally distinguished from insoluble fibre (cellulose, certain hemicelluloses and lignin). Insoluble fibre would stimulate an increase in the volume of faeces and it would be useful for constipation, while soluble fibre has been attributed with positive effects on plasma lipid profile and postprandial glycaemia. However, the solubility of fibre does not always predict its physiological effects, so organisations such as the FAO/WHO[63] and the IOM[61] have proposed that the distinction between soluble and insoluble fibre be abandoned. The viscosity of each type of fibre is of more interest in this respect, as it would contribute to the thickening of fibre after it has been mixed with water and it would slow down gastric emptying and delay the intestinal absorption of nutrients. The fibres with the highest viscosity include many of the soluble fibres such as guar gum, pectin, glucomannans and -glucans.

The Dietary Guidelines for Americans[8] considers the consumption of 14 g of fibre per day and for every 1,000 kcal consumed to be a suitable intake. Similar recommended intakes have been published recently by the European Food Safety Authority (EFSA),[64] which establishes a recommended fibre intake above 25 g/day to achieve the beneficial effects on intestinal function which are derived from its consumption.

The possible benefit for weight loss of a high-fibre diet is based on approaches similar to that of Heaton.[65] According to this author fibre could hinder energy intake through a series of mechanisms: 1) displacing the diet's other nutrients and calories through its lower energy density; 2) increasing chewing, salivation and the secretion of gastric juices, thus resulting in increased gastric distension and greater satiety; and 3) decreasing absorption in the small intestine and increasing the faecal elimination of nutrients. These potential properties of fibre have made it an attractive component of the diet for the treatment of obesity.

Effectiveness of fibre on weight loss when treating obesity

The role of fibre in the treatment of obesity was reviewed by Howarth[66] using data originating from studies published before 2000. A total of 21 studies with an average duration of 3 months were reviewed and it was observed that the "ad libitum" consumption of a diet enriched with 14 g of fibre per day for obese subjects led to a weight loss of 2.4 kg after 3.8 months. The authors were unable to observe differences in the effect on weight loss on the basis of the type of fibre administered. This study comprised trials in which fibre was consumed both as a supplement and as part of a high-fibre diet.

It is worth distinguishing the role of fibre as an additional supplement to the normal diet, usually in the form of viscous fibre capsules or tablets which are consumed between 15 and 60 minutes before main meals, from diets whose composition contains a higher quantity of fibre originating from foods such as pulses and whole grains.

Effectiveness of high-fibre diets

Regarding the role of diets enriched with whole grains, we have a series of RCT's with negative outcomes. In an RCT which compares the effect of hypocaloric diets with different fruit and whole grain content over 48 weeks, Thompson et al.[67] did not observe any differences in weight loss. The results of Katcher et al.[68] which compared whole grains with refined grains for 12 weeks in 50 obese patients being treated with a hypocaloric diet were also negative. The study by Maki et al.[69] was of the same length, with 144 obese subjects following a hypocaloric diet, in which the effect of consuming whole grains was compared with a diet low in fibre, and no differences in weight loss were observed. A recent study by Venn et al.[70] does not demonstrate greater weight loss after 18 months of a hypocaloric diet high in whole grains and red beans when compared with a conventional diet, although it does show a reduction in the abdominal circumference.

Some studies have had positive results, such as that of Lee et al.[71] where greater weight loss was observed (a difference of 2 kg) in a four-week crossover RCT, with normal rice being replaced with rice which was rich in fibre. However, only ten obese subjects were included. There were also positive results in the study by Morenga et al.[72] which compared two diets without calorie restriction in 84 obese subjects: one high in fibre (more than 35 g/day) and in proteins (30% of the

energy intake) compared to a conventional low-fat diet: after 10 weeks of treatment a significant but largely irrelevant decrease in weight (-1.3 kg) and fat mass was observed in the group with the diet high in fibre and proteins.

To date, the longest intervention study has been carried out as part of the Finnish Diabetes Prevention Study,[73] a three-year RCT in which the effectiveness of a series of hygienic-dietary measures for the prevention of type 2 Diabetes Mellitus was studied in overweight or glucose intolerant subjects. One of the analyses carried out was to determine the effect of the different fibre intakes of the participants on their final weight loss. After 3 years, the result was, on comparing those whose fibre intake had remained in the upper quartile (more than 3.7 g/MJ) with those from the lower quartile (less than 2.6 g/MJ), that fibre intake was associated with weight loss (3 kg *vs.* 0.4; $P < 0.001$) and a reduction in the abdominal circumference (29. *vs.* 1.6 cm; $P < 0.033$).

Regarding systematic reviews following the aforementioned review by Howarth, there was one carried out by Van Dam et al.,[74] based on works published before July 2007, which found that high-fibre diets had no significant effect on the treatment of obesity, although they did on its prevention. In 2008, after reviewing the clinical evidence on the use of fibre, the ADA published a Position Statement[75] which provided only limited evidence that a diet containing around 20-27 g/day of fibre may have a modest role in weight loss. The most recent systematic review by the Dietary Guidelines for Americans[8] which included studies up to 2008, recognised that fibre in the diet and the consumption of whole grains play a role in the prevention of obesity, but it did not comment on their role in its treatment. Finally, in the review by Astrup et al.,[76] it was concluded that the majority of the studies which they analysed consistently showed the ineffectiveness of increasing the intake of whole grains or other types of fibre in order to achieve weight loss.

Effectiveness of fibre supplements

A meta-analysis carried out by Pittler et al.[77] on the effects on weight loss of supplementing Guar Gum, including works prior to 2001 (although only 2 lasting for over than 14 weeks) did not show that administering this type of fibre was effective in the treatment of obesity. However, it was observed that they were accompanied by an increase in gastrointestinal side effects. The same author carried out a systematic review up to March 2003[78] which, in addition to Guar Gum, included other types of fibre supplements such as: plantago psyllium, and glucomannan. Once again, the authors did not observe positive results for weight loss after administering different fibres.

Intervention studies which were subsequently carried out also had negative results, for example the study carried out by Kovacs et al.,[79] which did not show that adding a Guar Gum supplement to a semi-liquid hypocaloric diet for 2 weeks benefited weight loss. The study by Salas-Salvadó et al.[80] lasted for longer and had a higher number of patients. It included 200 obese patients who received a supplement of glucomannan and plantago ovata for 16 weeks as part of a hypocaloric diet. These authors did not observe any benefits for weight loss which were attributable to the fibre supplement either.

In contrast to the above, one RCT[81] which analysed the effectiveness of fibre supplements (plantago psyllium) when compared to a diet low in fibre in 72 obese patients for 12 weeks demonstrated that there was greater weight and fat mass loss in the group allocated soluble fibre. The authors concluded that a fibre intake above 30 g/day is necessary to obtain a positive result for weight loss and body composition.

Furthermore, the most recent systematic reviews have observed a moderate effect of fibre supplements on weight loss for obese patients. In this sense, after reviewing the data up to 2007, Van Dam et al.[74] found that the results of studies on weight loss with fibre supplements are inconsistent, but they state that there is some evidence that these supplements increase adherence to the treatment and they stimulate a small additional weight loss. The review by Papathanasopoulos et al.,[82] concludes that fibre supplements can have a minimal effect which favours weight loss through their satiating effect. Similar results were obtained in the review by Astrup et al.,[76] where they state that fibre supplements can favour weight loss by 0.15 kg/week when compared to a placebo. The Position Statement by ADA in 2008[75] provides limited evidence regarding the possible benefits for weight loss of a daily fibre supplement of 20 g.

Among the fibre supplements a special mention must be given to glucomannan, of which we have a meta-analysis[83] which was carried out on 14 RCT's prior to 2008, of which only 2 lasted a minimum of 3 months. The final result was that a supplement of 1.2 to 15.1 g/day of glucomannan led to a significant reduction in weight of 0.79 kg at the end of the trials, mainly when it was part of a hypocaloric diet. Furthermore, a scientific report by the EFSA[84] in 2010 concludes that glucomannan helps weight loss when it is accompanied by a low calorie diet, and to achieve this effect a minimum consumption of 3 g/day is required.

We can therefore confirm that the most recent data does point to fibre supplements having a positive, but limited, effect on weight loss. And of all the types of fibre supplements, this seems to have been demonstrated most with glucomannan.

Effects of fibre on the lipid profile of obese patients during treatment for obesity

Among the results of the aforementioned works, we can occasionally find references to changes in lipid

parameters after treatment with a high-fibre diet. Generally, positive results are consistently described.

In a four-week crossover RCT in which normal rice was replaced with another which was high in fibre, Lee et al.[71] observed a significant reduction in the levels of triglycerides and LDL cholesterol. The Salas-Salvadó et al.[80] study also described a reduction in LDL after 16 weeks of treatment with a glucomannan and plantago ovata supplement. Maki et al.[69] observed an improvement in the levels of LDL cholesterol when taking whole grains. After 10 weeks of treatment with a high fibre and protein diet, Morenga et al.[72] demonstrated a decrease in total cholesterol and LDL in comparison with a conventional low-fat diet. On the completion of the 12 week trial, Pal et al.[81] observed a greater decrease in total cholesterol and LDL in the study diets (59, 31 and 55 g fibre/day) than in the control diet (20 g fibre/day). The meta-analysis by Stood et al.[83] with glucomannan supplements also observed an improvement in total cholesterol, LDL and triglycerides. The Position Statement by the ADA in 2008[75] also concluded that fibre, whether it be present in the diet or originating from supplements, improves lipid profile.

Finally, the EFSA report[84] on the effects of glucomannan supplements recognises that this fibre helps to maintain normal levels of total cholesterol, but no evidence was found about its role in controlling triglycerides. It also establishes that the consumption of β-glucans helps to control cholesterol levels.[85]

EVIDENCE

45. There is no sufficient data that may allow any evidence to be established regarding the role of a fibre or whole grain enriched diet on weight loss.

46. Glucomannan supplements added to the diet may have a discrete effect, via a satiatory mechanism, in favouring weight loss (Evidence Level 1+).

47. Non-glucomannan fibre supplements added to the diet may exert a minimal contribution towards weight loss (Evidence Level 2+).

48. The dietary management of obesity with a glucomannan, Plantago ovata and -glucane enriched or supplemented diet reduces the LDL cholesterol levels in the obese patient (Evidence Level 2+).

RECOMMENDATIONS

21. In the dietary management of obesity, dietary fibre (fundamentally glucomannan) supplements may increase the efficacy of the diet towards achieving weight loss (Recommendation Degree C).

22. Obese patients with hypercholesterolemia alterations may benefit from the prescription of dietary fibre (fundamentally glucomannan) enriched or supplemented diets (Recommendation Degree B).

2.2.2. *Diets with modifications to the type of carbohydrates: low glycaemic index diets*

The concept of the Glycaemic Index (GI) emerged in the 1980's[86] as a method of quantifying the capacity of a food of increasing postprandial glycaemia after it has been consumed and it serves as a tool for controlling type 1 diabetes mellitus. The GI of a specific food is defined as the increase in glycaemia observed after 50 g of that product have been consumed in comparison to the increase observed after consuming 50 g of white bread or glucose. The application of this index to the different types of food made it possible to verify that not all sources of Carbohydrates (CH) are the same when modifying glycaemia and that the type of food containing them also has an impact. Traditionally, to be considered a product with a high GI it must have a GI equal to or greater than 70 units (uu) and a product with a low GI will have less than 56 uu.

Although the GI gives us an idea about the potential of the carbohydrates of a specific food to increase glycaemia, the total glycaemic response depends not only on the type of food (or GI) but also on the quantity (portion) of carbohydrates consumed. Thus arises the concept of the Glycaemic Load (GL) of foods, which is the result of multiplying the GI value by the total quantity of CH (grammes) in that portion of food. A high GL value is 20 or above, while for the food or meal being analysed to have a low glycaemic load it must be below 10.

Dietary treatment of the GI arose from the concept that foods with a high GI induce a higher insulin response. This hyperinsulinism, after consuming food high in CH, could induce the rapid uptake of plasma glucose by tissues and, as a result, a relative postprandial hypoglycaemia which would lead to a higher calorie intake and greater weight gain. In contrast, those products with a lower GI would have a greater satiating effect, thus favouring weight control.

On the basis of this hypothesis, the idea emerged of modifying the GI and the GL in order to reduce the feeling of hunger, the calorie intake and, finally, to achieve greater weight loss. This led to the development of low glycaemic index diets (LGID), with important popular exponents such as the Montignac, South Beach and Sugar Busters diets.

Effects of low GI diets on the treatment of obesity

Regarding its actual effectiveness there is different data in the studies published which compare diets with a low GI or GL with diets with a high GI or GL. The studies prior to 2005 and 2006 were assessed in two important reviews. The first was a systematic review of the Cochrane library[87] which included the results of 6 clinical trials[88-93] prior to July 2006 in which LGID's were compared with subjects who followed any other type of diet for 6 months. The results obtained demonstrated that,

in comparison with other types of diets, there was greater weight loss with the LGID's (-1.1 kg (confidence interval (CI): -2.0 to -0.2; P < 0.05)) and a greater decrease in total fat mass -1.1 kg (CI: -1.9 to 0.4; P < 0.05). However, it is worth highlighting that of the studies included only 2 had a duration of 6 months of treatment and the rest of the studies lasted less than 12 weeks.

Subsequently, a meta-analysis[94,95] which included 45 publications up to 2005 concluded that a lower GI and, above all, a reduction in the GL (above 17 uu) was significantly associated with greater weight loss. The vast majority of these studies were also less than 6 months long.

Some short term RCT's which were subsequently published have corroborated this effect of diets with a low GI on body weight. The study by Abete et al.[96] demonstrated after 8 weeks of treatment that the patients following hypocaloric diets with a lower GI (a difference of 20 units) lost more weight than those whose diets had a higher GI (-5.3 + 2.6% *vs.* -7.5 + 2.9%; P < 0.032). The 12 week study by Philippou et al.[97] observed a greater weight loss (4 kg (CI: 4.4-2.4) vs. 1.5 kg (CI: 3.6-0.8); P < 0.05) and a greater reduction in glycaemia after consuming a hypocaloric diet with 8 units less of GI. After 5 weeks of free diet, De Reugemont et al.98 observed that the subjects who consumed a diet with 20 units less of GI achieved significantly higher weight loss (1.1 ± 0.3 kg *vs.* 0.3 ± 0.2 kg; P = 0.04).

However, other equally short RCT's found no results favouring the role of the GI in the treatment of obese patients. In a 12 week crossover design study comparing two eating patterns without calorie restriction whose GI's only differed by 8.4 units, Aston et al.[99] did not find significant differences in weight or in the satiating effect. Although the study by Maki et al.[100] observes a greater initial impact on weight reduction at 12 weeks when following an ad libitum diet which has a GI which is 5 units lower than a low-fat diet, during the maintenance phase this impact disappears and at week 36 there are no longer any differences.

The long term RCT's do not support the impact of the GI on weight loss either. We have three RCT's each with a duration of at least 1 year. A one-year trial with only 34 patients[101] compared two hypocaloric diets with different GI's (by 33 units) and GL's (by 73 units), without any differences in the quantity of fat administered. On its conclusion, the results of weight loss, adherence to the diet and satiety were similar for both groups. The second study with 302 women and a duration of 18 months[102] compared two hypocaloric diets with a difference of 40 units of GI, and no differences in weight loss were found between each treatment. Finally, after an 18 month follow-up, the study by Ebbeling et al.[103] analysed the effect on weight reduction of a diet with a low GL compared to a low-fat diet (with a difference in GL of 19.8 units). On finishing the study the weight differences were related to the initial basal insulin concentration, but there was no difference between groups.

The results of systematic reviews following those mentioned above did not arrive at the conclusion that there was a consistent relationship between GI or GL and Obesity either. Nor in the Vega et al.[104] review of works published between 2007 and 2008 was it concluded that there was sufficient data which made it possible to establish or reject the link between the GI or GL and obesity. Van Dam arrived at the same conclusion in a review carried out up to July 2007.[74] The most recent systematic review by the Dietary Guidelines for Americans[8] which included studies up to 2008 established that there was strong and consistent evidence that the GI or GL of the diet was not associated with body weight and that they do not lead to greater weight loss or better weight maintenance. However, the European Food Safety Authority (EFSA)[64] is not so categorical when rejecting the role of the GI or GL and, after reviewing scientific data, it has declared that there is no conclusive data which makes it possible to confirm or reject their role in weight control. The latest systematic review to date[105] also recognises this lack of consistency, after analysing all of the evidence available up to June 2009, concluding that the majority of studies do not demonstrate significant difference in weight loss for diets with a low GI or GL.

Finally, observational epidemiological studies have also been analysed in two recent reviews. Gaesser et al.[106] found no relationship between the GI and the Body Mass Index (BMI), but they did observe an inverse and significant relationship between the GL and the BMI. Hare-Bruun et al.[107] concluded that there was no consistent data which made it possible to recommend the reduction of the GI of a diet as a means of losing weight.

In light of the above, we can confirm that the data is not consistent. Generally, the long term RCT's do not describe differences in weight loss between LGID's and diets with high GI's. There is less data on the effect of the GL, but it normally provides similar results. It is possible that the fibre content of LGID's may influence the weight loss results because, in the vast majority of these results, the fibre intake was not considered to be similar in all of the intervention groups. Furthermore, the trials with positive results tend to be short in duration and, both in the case of these RCT's and in the review of the Cochrane library, despite being significant, the weight loss benefits are generally very modest. In the different studies there are also significant variations in the differences between the GI or GL of the control group and that of the intervention group, and between the proportions of different CH macronutrients.

Effects of diets with low GI's on the maintenance of lost weight

In addition to the studies whose aim was to lose weight, work has also been published which analyses the effect of the GI on maintaining weight after the

initial common phase of weight loss with a hypocaloric diet, with the results also being disparate. In the study by Philippou et al.,[108] after an initial period of weight loss, the patients were randomly assigned a diet with a high GI or a low GI (difference of 14 units) which also differed by 47 units of GL. After a 4 month follow-up no differences were observed in the maintenance of weight loss between the subjects from both intervention groups. Recently, the results of the DIOGENES[109] study have been published, comparing the effects of the two diets with different protein content (25% *vs.* 13%) and different GI content (difference of 15 units) on maintaining weight loss after the initial phase of a hypocaloric diet. After a 26-week follow-up, and despite a reduction in GI of 4.7 units being observed (rather than the planned 15), a lower recovery of lost weight was observed (a difference of 0.95 kg in comparison with diets with a high GI).

Cardiovascular effects of diets with a low GI

In addition to the effects of LGID's on weight loss, there are also studies which have described the impact of this type of diet on lipid parameters and cardiovascular risk. The systematic review of the aforementioned Cochrane library[87] reported a beneficial effect of diets with a low GI on the levels of total cholesterol and LDL cholesterol. The meta-analysis by Livesey et al.[94,95] also found an improvement in levels of triglycerides and insulin sensitivity associated with LGID's. The 12-week RCT by Maki et al.[100] confirms the improvement in levels of HDL cholesterol with LGID's.

The results obtained in the long term intervention studies are also contradictory. So while one study carried out with a small group of subjects who were monitored for a year did not observe significant differences in lipid profile between two hypocaloric diets with a different GI and GL,[101] the other two studies carried out to date observed greater benefits for triglycerides and VLDL cholesterol[110] or an improvement in the levels of triglycerides, HDL cholesterol and LDL cholesterol[111] for diets with a low GI or GL. However, the systematic review of the Dietary Guidelines for Americans[8] establishes that there is not enough data to arrive at a conclusion on the effect of LGID's on lipid profile.

There is also an observational transversal study which was carried out in the United Kingdom with 1,152 subjects over the age of 64 which found no relationship at all between the GI of the diet and body weight or other cardiovascular risk factors.[112]

In addition to the foregoing data, there is a study specifically designed for this objective, a randomised crossover trial lasting for 4 weeks at each phase[113] which compared two diets with a difference of 25.5 units of GI and 87 units of GL. The design of the study did not allow differences in weight evolution in order to separately assess the effect of the GI on different parameters (insulin, glycaemia, lipids, markers of inflammation or coagulation). The result was negative, not finding consistent differences for any of the parameters studied.

As we can see, the data from the different studies yield conflicting results in this respect. Possibly the distinct differences in GI or GL in each study or the variability of the proportion of the rest of the immediate principles might explain this heterogeneity.

Evidence

49. Modifications of the glycaemic index or of the glycaemic load of the diet have no lasting effect on weight loss in the dietary management of obesity (Evidence Level 1+).

50. There is no sufficient data for establishing any evidence regarding the role of low glycaemic index or low glycaemic load diets in the maintenance of the weight loss after a hypocaloric diet.

Recommendations

23. A reduction of the glycaemic index or of the glycaemic load cannot be recommended as a specific strategy in the dietary management of obesity (Recommendation Degree A).

2.3. High protein diets

Among the modifications of the proportion of macronutrients in the diet, the option to change the carbohydrates in the diet for proteins has been very popular, with the aim of achieving greater weight loss. This proposal is based on a set of characteristics which are attributed to proteins[114] with potential beneficial effects for the treatment of obesity. Among these properties a possible satiating effect[115] has traditionally been cited, greater than that of carbohydrates or fat, which helps to limit energy consumption, even for a diet with calorie restriction, although this characteristic is in question: although it has been suggested that a higher consumption of proteins could increase short term satiety and, therefore, decrease energy intake,[114] there are studies which do not support this association.[30,116-118] The EFSA is also of the opinion that the evidence in this respect is insufficient.[119] However, proteins constitute the nutrient with the greatest dynamic-specific effect, in other words, it is the immediate principle which consumes the most calories in its rmetabolism and, therefore, the least efficient in terms of energy. It has also been observed in some individuals that a high-protein diet can stimulate protein anabolism and preserve the lean mass, in particular proteins of animal origin. All of the above data is justification for testing this type of diet in the treatment of

obesity, establishing what has come to be known as high protein diets (HPD).

Considering that the proportions normally recommended for protein intake are around 10-15% of the total calorie intake, HPD's would be classified as those which require a protein intake of at least 20% or 20% of the total calorie content of the diet, normally above 25%. Among popular diets, the Atkins diet, which is typically low in carbohydrates and high in fat, is proportionally an HPD. We can also consider this group to include the Zone diet, which recommends a proportion of nutrients of 40-30-30 between carbohydrate, proteins and fat respectively and, most recently, the Dukan diet.[120]

However, it must be taken into account that although the definition of an HPD is based on the percentage of proteins in the diet, variations in their total calorie intake mean that the absolute quantity of proteins (g/day or g/kg weight) can be very variable. This consideration is especially important in the case of hypocaloric diets, for which the decrease in the energy intake of fat and carbohydrates can result in a proportional increase in the intake of proteins, even if the total quantity of these does not differ from that in a balanced normocaloric diet. If we consider that the recommended daily intake of proteins for adults aged above 19 is 0.83 g proteins/kg body weight[13] and that this intake is normally exceeded in the diets of western countries, in order for a high protein diet to be considered as such there would have to be a global minimum intake of 90 g of proteins/day. This factor is not always given enough consideration in many works which study the effects of HPD's.

The effect of high protein diets on weight loss in the treatment of obesity

The effectiveness of this type of diet in controlling obesity has been examined in very diverse studies and documents. In some initial reviews effectiveness for weight reduction was only found in HPD's under free diet conditions[121,122] due to the satiating effect of proteins resulting in a lower energy intake in comparison with following a normal protein diet, and they demonstrated that this favourable effect of the HPD would disappear when calorie restrictions were in place.

In 2001, the Nutrition Committee of the American Heart Association[123] reviewed the role of HPD's and established that the evidence available at that time did not demonstrate that this type of diet, without an associated calorie restriction, induced maintained weight loss or that it was beneficial to health. It even advised against using it because of potential harmful effects.

In 2004, Halton et al.[124] published a critical review which covered 15 RCT's published between 1990 and 2004 and they arrived at the conclusion that scientific evidence suggests that HPD's can be beneficial for short term weight loss, although the majority of the studies are small in size and not conclusive. It must be noted that only 4 of the studies reviewed last for at least 6 months, the rest were more short term.

In 2006 the results of a meta-analysis[125] were published assessing the effects of modifying the quantities of carbohydrates or proteins on the dietary treatment of patients with obesity. They included 87 studies of dietary intervention in obesity, lasting no longer than 6 months and published prior to 2006. A positive effect of reducing carbohydrates on weight loss was demonstrated. However, no benefits were observed when changing protein content (evaluated in g/kg weight).

The subsequent short term (no greater than 6 months) RCT's have yielded disparate results. Among the negative findings we can cite that of McMillan-Price,[91] which compared four hypocaloric diets with different Glycaemic Indices (GI) and proportions of protein, and found no differences in weight loss after 12 weeks between the different types of diet (containing between 63 and 95 g/day of proteins).

In the study by Kerksick et al.,[126] which was of a similar duration (14 weeks), 141 obese women were randomly allocated 4 hypocaloric diets with a different proportion of proteins and carbohydrates: a) a diet very low in carbohydrates and high in protein (185 g/day of proteins), b) an LChD and a moderate protein contribution (125 g/day) or high in carbohydrates, c) a diet low in proteins, or d) a conventional control diet. No differences in weight loss were observed between the 4 types of diet.

In a 5-month follow-up of 100 obese patients with metabolic syndrome, comparing a conventional hypocaloric diet with a hypocaloric diet high in proteins and monounsaturated fat, Muzio et al.[47] did not observe differences in weight. However, the proportion of proteins was below 19% so it cannot strictly be considered an HPD.

In addition to these RCT's, in a non-randomised prospective study of 24 postmenopausal women, Gordon et al.127 found no difference in weight loss after 20 weeks between two hypocaloric diets with different protein contributions (30% [1.2-1.5 g/kg/day] vs. 15% [0.5-0.7 g/kg/day]).

In contrast to the above trials, the following studies did obtain positive outcomes:

- A 12-week study by Meckling et al.[128] comparing 44 obese women with two hypocaloric diets: HPD and a conventional diet, with or without additional exercise, significantly greater weight loss was observed in the HPD group (84-115 g/day proteins) than in the control group with a high carbohydrate diet (-2.5 kg without exercise or 3.0 kg for those associated with exercise).
- Krebs et al.[129] in 46 adolescents over 13 weeks, reported greater weight loss with a free HPD (99 g/day proteins) than a low-fat hypocaloric diet.

– Morenga et al.[72] compared two diets without calorie restriction in 89 patients: one high in fibre (more than 35 g/day) and in proteins (30% of the energy contribution and 107 g/day) compared with a conventional hypocaloric diet. After 10 weeks of treatment greater weight loss was shown (-1.3 kg) with the HPD. In this trial the carbohydrate contribution was the same for both groups with variations, in addition to the protein intake, in the proportion of total fats and saturated fat. The authors did not distinguish whether the results achieved were due to the difference in proteins, fibre or fat between both groups so, the specific impact on weight loss of the increase in proteins in the diet is not clearly individualised.

Regarding longer studies, we have 7 RCT's whose results on final weight loss are basically negative.

– Due et al.[41] compared two ad libitum diets in 50 obese subjects: HPD (25% proteins) compared with a normal protein diet (15%) with a 2-year follow-up. The increased initial weigh loss observed with the HPD was not observed again at one or two years.
– Brinkworth et al.[48] did not find significant differences either between the effect of two hypocaloric diets on 43 obese subjects: standard or HP (110 g/day proteins) on total weight loss, neither during the initial 12-week phase of the hypocaloric diet, nor during the 4 weeks of energy balance, nor on completing the 52nd week of maintenance.
– In the study by McAuley et al.[130] with 93 overweight women, the differences observed at 6 months favouring the HPD (86 g/day) disappeared after a 1-year follow-up.
– After randomly allocating 72 women with two hypocaloric diets (HPD with 109 g/day of proteins vs. a diet high in Carbohydrates) for 12 initial weeks of intensive weight loss and 52 subsequent weeks of follow-up, Clifton et al.[131] observed no significant differences in weight loss. In an analysis of the individual protein intake recorded in each case a significant relationship was found between the consumption of protein and weight loss. This finding leads the authors to conclude that an increase in protein intake can be beneficial for weight loss.
– Sacks et al.[53] studied 4 hypocaloric dietary patterns with different proportions of immediate principles in 811 obese subjects. At 2 years there was no difference in weight loss between the groups.
– Layman et al.[132] were unable to demonstrate significantly greater global weight loss after 1 year of an HPD (1.6 g/kg/day of proteins) when compared to a diet high in carbohydrates and they only demonstrated that the small group of subjects who lost at least 10% of their initial weight was larger in the HPD group.
– The study by Keogh et al.[133] differs from those above as it does not compare an HPD with a diet rich in carbohydrates, but rather both diets in the study are low in carbohydrates and are hypocaloric, with the difference being that one is HP (136 g/day) and the other high in fat. Nevertheless, it also did not demonstrate that one was more beneficial than the other for weight loss after a one-year follow-up.
– The only long term study which truly, clearly shows that HPD's have an advantage was published by Gardner et al.,[42] comparing various types of popular normocaloric diets (Atkins, Zone, Ornish and LEARN). Their results at 12 months show greater weight loss with the Atkins diet (low in carbohydrates and with an increase in protein [27%] and fat intake) than with the rest of the diets which had a higher carbohydrate content and less protein. The study only includes women (311 in total) and, as stated above, the factor of comparison was not a conventional high carbohydrate diet, but different types of popular diets.
– In addition to these RCT's, systematic reviews have been published recently whose long term results, which are detailed below, are essentially negative.
– Hession et al.[38] carried out a systematic review in 2009 which included 13 RCT's up to 2007 which compared an HPD low in carbohydrates (LChD) with every other kind of diet. The majority of the studies used a low-fat diet (LFD) and a conventional hypocaloric diet high in carbohydrates for comparison. At 6 months, weight loss in the LChD/HPD group was 4.02 kg higher than the LFD group, but at 12 months the difference had decreased to 1.05 kg ($P < 0.05$). They also reported lower adherence rates with LFD's. However, the studies included in this review mainly compared carbohydrate or fat content, rather than protein intake.
– Subsequently, Clifton et al.[134] combined the data from 3 twelve-week RCT's,[135-137] comparing the effects of HPD's and normal protein diets on obese subjects with high cardiovascular risk. Globally there was no difference between the diets in weight loss or in the reduction of fat mass. Only in the subgroup of the subjects with the highest cardiovascular risk and with a basal increase of triglycerides was the HPD more effective for weight loss and reducing abdominal fat.
– Furthermore, the European Food Safety Authority[119] reviewed the role of protein in the diet and concluded that there was no evidence that protein intake in the diet had a satiating effect, assisted with weight loss or with maintaining weight loss. However, it did recognise a relationship between protein intake and maintaining muscle and bone mass.

– In contrast, the most recent of these reviews,[138] which includes studies up to the beginning of 2010, does find a positive effect in HPD's both for weight loss and maintenance, although it includes studies of very varied duration, mostly with a follow-up of less than 6 months.

Usefulness of high protein diets in maintaining weight loss

We also have a set of studies which, unlike those discussed above, only study the effectiveness of an HPD in maintaining weight after a common preliminary weight loss phase. Their duration and results are extremely variable.

The study by Claessens et al.,[139] which was only 12 weeks long, assessed the effect on weigh maintenance of 48 obese subjects of two normocaloric diets: one group receiving maltodextrin (high carbohydrate diet) and another receiving casein or whey protein (HPD group); the subjects in the HPD group presented better weight control (difference of 2.3 kg, $P < 0.04$). In the DIOGENES[109] study, with 938 participants, the effects of diets with different GI's and protein content on maintaining lost weight after an initial hypocaloric diet phase were compared; at 26 weeks a significantly higher weight increase was found in the group with a diet low in protein than in the HPD group ($P = 0.003$), although it was quantitatively very modest (0.93 kg [95% CI, 0.31-1.55]).

Furthermore, the aforementioned review by the EFSA[119] did not find sufficient evidence to support this effect and after one year with 180 obese subjects Delbridge et al.[140] found no difference in weight maintenance between both types of diet.

Long term safety of high protein diets

Regarding the safety of HPD's in the very long term, we have 4 fundamental studies. In 2007 two prospective studies were published, one in Sweden[141] which, after a 12-year follow-up of 42,237 women, found that those who consumed the highest quantities of protein and the lowest quantities of carbohydrates had an increase in total mortality (11%) (the majority due to a 37% increase in cardiovascular mortality); this was more pronounced in the group of women between 40 and 49. With a similar design, 22,944 Greek participants from the EPIC study (European Prospective Investigation Cancer and Nutrition) were monitored for 10 years, demonstrating a small but significant increase in total and cardiovascular mortality associated with a smaller intake of carbohydrates.[142]

In order to qualify these results, after a 15-year follow-up of 29,017 from the Iowa Women's Health Study, Kelemen et al.[143] found an inverse relationship between cardiovascular mortality and HPD when carbohydrates were replaced with proteins from vegetables or pulses and a direct relationship with HPD when the protein was consumed via red meat and dairy products. Similar to these findings, recently Fung et al.,[60] in a prospective study of 85,168 women and 44,548 men (monitored for 26 and 20 years respectively) showed that diets low in carbohydrates substituted with protein of animal origin were associated with an increase in total mortality (Hazard Rate [HR] comparing upper and lower deciles; 1.23; CI 95%: 1.11-1.37), cardiovascular mortality (HR: 1.14; CI 95%: 1.01-1.29) and cancer mortality (HR: 1.28; CI 95%: 1.02-1.60). In contrast, diets low in carbohydrates substituted by proteins of plant origin were associated with lower total mortality (HR: 0.80; CI 95%: 0.75-0.85) and cardiovascular mortality (HR: 0.77; CI 95%: 0.68-0.87).

Diets high in protein of animal origin and low in CH can alter the intestinal microbiota and reduce the production of phenolic antioxidants derived from the consumption of fibre (ferulic acid and derivatives) and, as a result, increase the number of N-nitroso compounds which are potential carcinogenic agents from the digestive tract.[144] In the EPIC prospective study a relationship has been demonstrated between the consumption of nitrosamines (e.g. cured or smoked meat) and the risks of various types of digestive cancers, in particular colorectal cancer.[145]

Effect of high protein diets on body composition

Regarding the theoretical effect of HPD's on the preservation of lean body mass in comparison with conventional diets, the available data is not consistent.

In a meta-analysis undertaken by Krieger et al.[125] in 2006, 165 short term interventions (4-24 weeks) with different carbohydrate and protein compositions and their effects on body composition were analysed using linear regression mathematical models. The authors concluded that diets low in carbohydrates induced a greater loss of fat mass and also a higher quantity of fat-free mass in comparison with diets high in carbohydrates. However, when the diets contained more than 1.05 g/kg, they were associated with a fat mass retention of 1.21 kg (0.96% of the body weight) in relation to diets low in proteins.

Among the studies with follow-ups shorter than 6 months which analysed the effect on body compartments, there are several with negative results[128,129,131] which observed no effect on body composition, and there are others which describe HPD's as having a greater impact on the proportional reduction of fat mass.[72,127]

The long term studies which analyse this factor are not consistent either. Due et al.[41] describe a reduction in intra-abdominal fat and in the Abdominal Circumference and Layman et al.[132] describe a reduction in fat mass. However, these are not the findings of the 1-year study by Brinkworth et al.[39]

Among the studies on weight maintenance, on the completion of a 12-week HPD to maintain weight, Claessens et al.[139] found that there was a greater reduction in fat mass (difference of 2.2 kg; $P < 0.02$) in the HPD group which consumed casein or protein in comparison with those receiving maltodextrin (diet high in carbohydrates).

The EFSA's[119] review of this matter did conclude that the protein intake of the diet assisted in maintaining lean mass.

EVIDENCE

51. As compared to a conventional carbohydrate rich diet, a hyperproteic one may induce in the short term (6 months or less) a higher weight loss (Evidence Level 2+).

52. A hyperproteic diet does not induce in the long term (over 12 months) a greater weight loss than a conventional carbohydrate rich one (Evidence Level 1+).

53. There is at present no sufficient data for establishing the efficacy of hyperproteic diets in the maintenance of the weight loss achieved after an initial weight loss phase with other type of diets.

54. A hyperproteic diet favours the preservation of the lean body mass better than a carbohydrate rich one (Evidence Level 2+).

55. Hyperproteic diets can, in the very long term, increase the risk of cardiovascular and overall mortality, mainly when the protein source is of animal origin (Evidence Level 2+).

RECOMMENDATIONS

24. In the dietary management of obesity is not recommended to introduce changes in the protein proportion of the diet (Recommendation Degree A).

25. For ensuring the maintenance or increase of the lean body mass during administration of a hypocaloric diet, it is effective to increase the protein content of the diet to levels above 1.05 g/kg (Recommendation Degree B).

26. Whenever a hyperproteic diet is prescribed, the animal origin protein fraction should be restricted in order to prevent an increased risk of mortality in the very long term (Recommendation Degree C).

3. Meal replacement diets

Adherence to treatment is one of the most important factors which determine weight loss in obese patients. Following this principle, a series of strategies have been developed which attempt to make it easier for a patient to follow a hypocaloric diet. One of these strategies is the direct provision of food to the patient which, according to some studies, can contribute more to therapeutic adherence and weight loss than when the patients select the meals themselves.[146-149] However, other studies have observed greater benefits from prescribing a structured diet with menus, and do not associate the direct provision of food with any additional benefit.[150]

Another type of strategy consists of replacing one or more meals per day (or part of them) with nutritional preparations of a known composition (similar to those used in VLCD's), within a hypocaloric diet which usually provides between 800-1,600 kcal/day. It is therefore possible to totally replace the diet, totally replace one or several meals or partially replace meals or snacks. These products are of a known and constant composition which can facilitate therapeutic adherence and reduce the risk of essential nutrients deficiency. This type of dietary treatment is usually used as part of a structured treatment which also includes exercise and lifestyle behaviour changes.

The composition of the products is very variable, as is the way in which they are presented: milkshakes, bars, biscuits and others. Some of them are intended to replace a main meal, lunch or dinner. In this case they normally contribute 250 kcal and 15-18 g of protein per portion, 18-25 g of carbohydrates and a smaller amount of fat, around 5-8 g per portion. The products are enriched with vitamins and minerals. Many products incorporate fibre in order to induce a potential satiating effect which makes it easier to adhere to the dietary guidelines and prevents constipation.

Other preparations are designed to replace part of a meal or they constitute a snack. In this case the calorie intake usually ranges from 80-150 kcal per ration and they also provide a significant amount of proteins (more than 30% per ration).

The composition and labelling of the food products aimed at the full or partial replacement of the diet, which are to be used in a low-energy diet in order to lose weight, are regulated by Directive 98/6/EC of 26th February of the European Commission, which was incorporated into the Spanish legal system in Royal Decree 1430/1997, of 15th September, approving the specific and technical health regulations for food products intended to be used in low-energy diets in order to lose weight. This Royal Decree regulates the composition of macro and micronutrients and the labelling of these products, which must include specific instructions for use and mention the need for adequate fluid intake. In the advertising and labelling of the products it is not permitted to refer to the extent or speed of the weight loss to be achieved. Replacement products for the full daily diet must provide between 800 and 1,200 kcal/day and include a specific mention that they must not be consumed for more than three weeks without medical indication. Directive 2007/29/EC and Royal Decree 868/2008 modified the initial regulations in order to allow this type of product to make claims about an increase in the feeling of satiety or a

Table VII
Composition of meal replacement products, in accordance with RD 1430-1997

	Unit	*Minimum*	*Maximum*
Energy intake	Kcal	200	400
Protein intake	% of total caloric value	25	50
Fat intake	% of total caloric value		30
Linolenic acid	gramme	1	
Electrolytes/minerals	% of daily recommendations	30*	
Vitamins/trace elements	% of daily recommendations	30	

*Except for potassium: 500 mg/meal.

Table VIII
Composition of complete diet replacement products, in accordance with RD 1430-1997

	Unit	*Minimum*	*Maximum*
Energy intake	Kcal/day	800	1,200
Protein intake	% of total caloric value	25	50*
Fat intake	% of total caloric value		30
Linolenic acid	g/day	4.5	
Electrolytes/minerals	% of daily recommendations	100	
Vitamins/trace elements	% of daily recommendations	100	

*Maximun protein: 125 g/day.

decrease in the feeling of hunger, provided that they are in line with the requirements of Regulation (EC) 1924/2006 regarding nutritional and health claims of food products.

Tables VII and VIII detail the composition of the replacements for one meal or for the whole diet, in accordance with RD 1430/1997. There is no specific legislation in the EU which regulates replacements for part of a meal or snacks. The majority of manufacturers are in line with French regulations in this respect.

In recent years several studies have been published which assess this means of treatment. Most are non-controlled clinical trials which assess weight loss or the effect on the associated pathology presented by patients. Other studies compare this method of treatment with approaches involving a conventional hypocaloric diet or using drugs.

These studies have several limitations. The treatment guidelines they use are extremely variable, especially in terms of patient follow-up, which makes it difficult to compare the results of the different studies. Furthermore, at times the beneficial effect cannot solely be attributed to using MRP's (meal replacement products), because the treatment of the intervention groups also includes other measures, such as the free supply of products, exercise and behavioural modification, in addition to different follow-up patterns. Most of these studies last for less than one year, with the dropout rate being high in some studies. Finally, the clinical applicability of these results outside a clinical trial make it necessary to take into account the financial cost which these therapeutic measures represent for the patient.

Short term effectiveness

Numerous studies have been published on this type of diet.[151-158] In 2003 a meta-analysis was published which assessed their effectiveness and safety for patients with and without diabetes.[159] They included all of the controlled and randomised clinical trials from 1960 to 2001 which compared the effect of diets in which one or more meals were replaced with a conventional hypocaloric diet plan for at least 3 months in patients with a BMI above 25 kg/m^2. 276 studies were assessed, of which only 6 were included in the analysis.[160-165] In total they included 249 patients in the replacement meal group and 238 control subjects. The duration of the studies ranged from 3 to 51 months. In this meta-analysis it was observed that at three months weight loss was significantly higher in the group which received replacement meals than in the group which received a conventional hypocaloric diet: 6.19-6.50 kg vs. 3.23-3.99 kg respectively. This weight loss constituted approximately 7% of the initial weight in the meal replacement group and 4% in the control group. The estimated difference in weight loss between the two forms of treatment was 2.54-3.01 kg ($P < 0.01$). The percentage of patients

who, after three months, achieved at least 5% weight loss was 34% in the conventional group, compared with 72% in the group which was following the meal replacement diet. No adverse effects which were attributable to the treatment were observed. The dropout rate for the treatment was similar in the meal replacement group and the control group (16% and 19% respectively).

The other meta-analysis published by Anderson[166] in 2004 assessed the effectiveness of various dietary treatments for obesity and it contained the results from 4 studies which included diets in which one or two meals were replaced with commercial preparations, two of which had already been assessed in the article by Heymsfield in 2003. In total it included 600 patients (470 women and 133 men), with a BMI between 28 and 34 kg/m^2. Weight loss was 9.3% in women and 8.6% in men; a loss similar to that achieved with other types of diets which included a more thorough follow-up (number of visits, etc.).

Other RCT's have been published on the effectiveness of the MRP's not included in these meta-analyses. Most of them show that using MRP's as part of a clinical trial is associated with higher weight loss, resulting in metabolic benefits167. In a study carried out in Spain[168] during the 6-month maintenance phase following initial weight loss induced by very low calorie diets (VLCD), 83.9% of the patients who received MRP's presented additional weight loss or the maintenance of lost weight, compared with 58.1% of patients receiving a conventional diet. In the study by Davis et al.,[169] the group which received MRP's presented greater weight loss during the 16-week active treatment stage (12.3 *vs.* 6.9 kg). During the 24-week maintenance phase, weight recovery was higher in the group which received MRP's. At the end of the treatment, the percentage of subjects who presented weight loss greater than 5% was higher in the group that receive MRP's (62 *vs.* 30%).

However, other studies have not had positive results. In an 8-week non-randomised, controlled study with weekly follow-ups of patients, Basulto et al. did not observe any increased benefit to weight loss from using MRP's in comparison with a food-based hypocaloric diet.[170]

The 6-month study by Noakes,[156] also observed no increased weight loss when using MRP's. Nor did adherence to treatment with MRP's yield better results during the maintenance phase.[171]

In the study by Lee et al.,[172] the effect of the composition of the preparation was assessed. Weight loss after 12 weeks was similar, but the group which received the highest quantity of protein presented a higher loss of fat mass. Treyon et al. also confirmed this effect on body composition of a higher protein content in MRP's.[173] Anderson[174] observed a more favourable effect on the lipid pattern on using a preparation which contained soy protein as an MRP than when a preparation with dairy protein was used.

LONG TERM WEIGHT LOSS

Some studies have assessed the effect of this kind of diet in the long term. In a non-controlled study, Rothacker observed that subjects who had used MRP's presented significantly greater weight loss after 5 years than a group of people with similar characteristics.[157]

The study by Ditschuneit and Flechtner-Mors[153] consists of 2 phases. During the first 3 months, the patients were randomly assigned to two treatment groups; those on a hypocaloric diet (1,200-1,500 kcal/day) based on conventional foods or those on an isocaloric diet using replacements for two main meals.

In the second four-year phase all patients received the same diet, which included a replacement for one meal and for one snack. Of the 100 patients who started the study 75 completed the 4 year follow-up, although 32 patients had dropped out and joined again in the third year. Weight loss at 3 months was 7.1 ± 3.5 compared with 1.3 ± 2.2 in the control group ($P < 0.001$). The group of patients who had received MRP's during the first 3 months presented greater weight loss in the long term follow-up (8.4 ± 0.8% *vs.* 3.2 ± 0.8%)

The meta-analysis by Heymsfield[159] included four RCT's which lasted for over one year. The treatment dropout rate was higher in the group treated with a conventional diet (64 *vs.* 47%; $P < 0.001$). Weight loss among the patients who completed the treatment was 6.97-7.31 kg in patients who received replacement meals and 2.61-4.35 kg in the control group. The difference in weight loss between the two methods of treatment was estimated at 2.63-3.39, depending on the type of statistical analysis. Overall, it was estimated that weight loss after one year of treatment was 7-8% of the initial weight in the group treated with MRP's and 3-7% in the group treated with a conventional diet. It was also estimated that, after a year of treatment, the percentage of patients achieving over 5% weight loss was 74% and 33% respectively.

The study published by Rock et al.[175] assessed the effectiveness of an intensive programme involving a hypocaloric diet, exercise and lifestyle changes which included the direct provision of food which was prepared for free, and this was compared with a control group. The weight loss at two years of treatment was significantly higher in the group which received intensive treatment with personal check-ups (7.4 kg [6.1-8.7]) or check-ups over the phone (6.2 kg [4.9-7.6]) than in the control group (2.0 kg [0.6-3.3]).

The LOSS study (Louisiana Obese Subjects Study) conducted by Donna Ryan,[176] is a clinical trial which was performed with 400 subjects with morbid obesity who were randomly assigned a conventional diet to follow or an intensive treatment consisting of 3 stages: stage 1: 890 kcal liquid diet (75 g of proteins, 110 g of CH and 15 g of fat) for 12 weeks; stage 2 (4 months) of a conventional hypocaloric diet of 1,200-1,600 kcal, with 2 MRP's, combined with the use of drugs if deemed necessary (orlistat or sibutramine) and 10 group

sessions; stage 3 (month 8-24) the same conventional diet with 1 MRP, combined with drugs and group sessions. After two years those who had completed the study in the intensive group has lost -9.7% ± 1.3% body weight (-12.7 ± 1.7 kg), while in the control group they lost -0.4% ± 0.7% (-0.5 ± 0.9 kg); P < 0.001).

The effectiveness of using replacement diets is greater if they are combined with other, additional measures. Thus, Ashley JM et al.[177] studied the impact of MRP's on premenopausal women with a BMI between 25 and 35 kg/m^2, who were randomly assigned to three nutritional intervention groups for 2 years: A) conventional diet managed by a nutritionist, B) 2 MRP's /day, managed by a nutritionist, C) 2 MRP's /day with instructions in the doctor-nutritionist consulting room. Groups A and B received 26 group sessions in the first year, while group C only received the information provided during these sessions. At the end of the first year, weight loss was similar in groups A and C (4.3 ± 6.5% *vs.* 4.1 ± 6.4%) but lower than group B (9.1 ± 8.9%; P > 0.02). During the second year, in which the patients only attended educational seminars, without personalised visits, group B showed significant differences in the percentage of weight loss (-8.5 ± -7.0%) in comparison with group A (-1.5 ± -5.0%) and group C (-3.0 ± -7.0%; P < 0.001). More studies are necessary in order to be able to assess the long term role of this type of dietary approach.[178]

In 2010 the European Food Safety Authority (EFSA) published a document in which it assessed the possibility of health claims associated with meal replacement products. Based on the meta-analyses of Heysfield and Anderson, the EFSA indicates that, for patients with overweight or obesity, there is a cause and effect relationship between the use of meal replacement products as part of a hypocaloric diet (two preparations per day) and weight loss, and between the use of 1-2 preparations per day and maintaining weight loss. Furthermore, it indicates that their use can achieve similar results to treatment methods which entail a more thorough follow-up.[179]

Effect on comorbidity

Weight loss results in an improved lipid profile, with a fall in triglycerides and an increase in HDL cholesterol.[155,157] Some studies have been published which have directly assessed the effect of this type of dietary treatment on the patient's lipid profile. Ditschuneit et al.[180] observed that, after 4 years, patients presented a fall in plasma cholesterol, the size of which depended more on baseline levels than the amount of weight loss. Patients with hypercholesterolemia presented a significant drop in cholesterol levels after weight loss.

The meta-analysis by Heymsfield[159] provides an analysis of the effect of meal replacement diets on patients with diabetes, based on two of the studies it assesses.[162,163] The dropout rate after a year of treatment was very high, close to 80%, with no difference observed between both groups. The average weight loss after a year of treatment was not significantly different between patients who received MRP's and those that followed the conventional diet.

The other one-year study which was carried out with patients with type 2 diabetes compared the effect of using a conventional hypocaloric diet with a continuous or intermittent meal replacement diet and a sibutramine-associated diet.[181] The three latter alternatives resulted in greater weight loss than the conventional hypocaloric diet. Furthermore, reductions in HbA1c values and in hypoglycaemia treatment requirements were observed for the three active treatment groups.

Cheskin[182] published a controlled study on patients with type 2 diabetes, randomly assigned to follow a hypocaloric diet (75% of energy requirements) with conventional foods or using MRP's, for 34 weeks, followed by a one-year maintenance phase. By using an intention to treat analysis, it was observed that the group which received MRP's had greater weight loss: 40% of the group lost over 5% of their baseline weight, compared to 12% in the conventional group.

Other studies have assessed the effectiveness of a structured and intensive programme of lifestyle modification, which included the use of meal replacement diets. In the LookAHEAD study which was carried out with 5,000 patients with overweight/obesity and type 2 diabetes, the intensive treatment group included the use of MRP's (twice a day from weeks 3-19 and once a day for the rest of the treatment), in addition to an exercise programme and lifestyle modification. After a year,[183] this group lost 8.6% of the initial weight (compared with 0.7% in the control group). After 4 years of treatment, the weight loss was maintained at 6.15% in the active treatment group, compared with 0.88% in the conventional treatment group (P < 0.001).[184] This weight loss was accompanied by better control of glycaemia and vascular risk factors.

Safety

The adverse effects of meal replacement diets are similar to those described for other hypocaloric diets and they include constipation, asthenia, hair loss, etc. There has been no evidence that these effects are more pronounced that those observed with other methods of dietary treatment under isocaloric conditions.

As regards the composition of the diet, various studies have assessed the intake of macro and micronutrients in patients who followed this diet.[156,185] In general, the intake of proteins and micronutrients is higher in patients who receive MRP's than those following a conventional hypocaloric diet.[169] However, fibre intake is variable and depends on the fibre content of the commercial preparation. In comparison with the control group, the subjects who received MRP's presented a greater reduction in the intake of fat and cholesterol.[180]

A recent work has studied the safety of the diets which use MRP's with a high protein content.[186] To do this it has compared two forms of diet based on MRP's with different protein contributions (2.2 g/kg of lean mass/day *vs.* 1.1 g/kg lean mass/day) in a group of 100 patients. After a year of treatment, no adverse effects were observed in hepatic or renal function or in bone mineral density.

Wadden et al. carried out a control study on 123 obese women in which they assessed the effect of several types of hypocaloric diet (MRP's four times a day, conventional 1,200-1,500 kcal/day hypocaloric diet or solely advice without a structured diet) on eating behaviour.[187] At week 28 of treatment, a significantly higher number of patients in the MRP group had developed episodes of binge eating ($P < 0.003$ in comparison with the other two groups). During the subsequent follow-up (weeks 40 and 65) no differences were observed between the groups. None of the patients fulfilled the diagnostic criteria for binge-eating disorder. Bearing in mind that these episodes were moderate and self-limited, the authors conclude that the fear that dietary treatment with MRP's may induce eating disorders is not justified.

Evidence

56. The use of commercial preparations as substitutes or replacements for one or more meals may facilitate correct adherence to the hypocaloric diet, favouring both weight loss and weight loss maintenance (Evidence Level 1–).

57. This beneficial effect is higher when this strategy is used in the context of structured therapies including physical exercise, dietary education and conduct modification of eating habits (Evidence Level 3).

58. No clinically relevant adverse effects have been reported or described in association to the use of meal replacements in the context of hypocaloric diets (Evidence Level 3).

Recommendations

27. The replacement or substitution of some meals with meal replacement preparations, in the context of hypocaloric diets, may be useful for achieving weight loss and for maintaining weight loss in obese or overweight adults (Recommendation Degree D).

4. Very low calorie diets: VLCD

Definition and historical considerations

Very low calorie diets are a method of dietary treatment of obesity which are defined as providing less than 800 or between 450-800 kcal/day. This definition is arbitrary, as the calorie deficit which is the basis of its use depends on the energy requirements of each patient. Therefore, other authors propose that they be defined as those diets which provide less than 50% of the patient's energy expenditure or less than 12 kcal per kg of their ideal weight.[188]

The use of this type of diet requires strict medical supervision, as they can have serious adverse effects.

The most widely-used VLCD's are composed of commercial preparations in liquid or powder form which are reconstituted with water or milk. This type of preparation provides 50-100 g of proteins per day and a variable amount of carbohydrates. Over the last 30 years numerous studies have been published on the short and long term effectives and safety of VLCD's. In 1993 a review was published on this matter at the request of the National Institutes of Health,[188] and it established the fundamental principles for the use of this type of treatment. In 2002 a document was published by experts from several European countries (among which Spain is not included) reviewing the general and legal aspects of this treatment.[189] This document, entitled the SCOOP-VLCD Report, has not resulted in any specific legislation.

As described in the corresponding section, the legislation which regulates dietary products which are to be used to completely replace the diet refers solely to diets with a calorie intake above 800 kcal (RD 1430/1997). Very low calorie diets have no specific regulations to date. In this review we will refer to the directions of RD 1430/1997 regarding the minimum content of some nutrients and the considerations about this type of diet contained in the SCOOP-VLCD Report.

Composition

The composition of VLCD's is variable and is not always expressly described in the studies published. Table IX details the proposed composition in the SCOOP-VLCD Report.[190]

Table IX
Composition of a very low calorie diet SCOOP VLCD (values for one day)[190]

Nutrient	*Minimum*	*Maximum*
Energy	450 kcal	< 800 kcal
Carbohydrates	55 g	
Proteins	50 g*	
Fat	7 g	
– Linolenic acid	3 g	
– α-linolenic acid	0.5 g	
Fibre	10 g	
Micronutrients**	100% of daily recommendations	

*Of high nutritional quality, equivalent to a corrected amino acid score according to the digestibility of the protein of 1.
**Chromium 33 μg/day.

This type of diet induces a negative nitrogen balance, which starts to normalise within two to three weeks. This energy balance mainly depends on the energy deficit and the intake of proteins and carbohydrates.[191] The protein intake is around 70-100 g per day (0.8-1.5 g/kg/day), constituting between 25 and 50% of the total calorie intake. Unlike the initial diets of this type which were used between 1960 and 1970, the preparations currently used contain protein with a high biological value. It must be considered that protein requirements increase in the event of a negative energy balance because part of the proteins will be used by tissues (especially muscles and the liver) to obtain energy.

The carbohydrate intake is variable and, generally, moderate ketosis develops which theoretically helps to reduce the feeling of hunger. Carbohydrates have an effect which "spares" proteins, and this is particularly so with intakes of above 100 g/day. It is recommended that the carbohydrate intake be equal to or above 55 g per day.[189,192] Some types of VLCD significantly limit the amount of carbohydrates in order to induce significant ketosis, in order to stimulate anorexia and facilitate therapeutic adherence. However, this fact has not been demonstrated: some studies have observed that the feeling of hunger is similar when using ketogenic diets and non-ketogenic diets.[193]

No specific recommendations have been established for the intake of essential fatty acids in this type of diet. Current legislation for meal replacement products indicates that at least 1 g of linolenic acid must be provided by each meal replacement product, or at least 4.5 g in the case of a complete diet replacement (> 800 kcal/day). It would appear reasonable to also use this recommendation for very low calorie diets.

The SCOOP-VLCD Report[189] recommends an intake of at least 3 g of linolenic acid and 0.5 g of α-linolenic acid per day. It must be considered that lipolysis which occurs in adipose tissue during slimming constitutes a source of fatty acids for other tissues and limits the risk of deficiency. The incorporation of medium-chain fatty acids can increase energy expenditure and fat oxidation and weigh loss.[194]

Most diets contain fibre in an effort to prevent secondary constipation when following them. Furthermore, the inclusion of fat can help to prevent these patients from developing gallstones. Commercial preparations contain 100% of the recommended intake of micronutrients. Water intake of above 2 litres per day is recommended.

Although they are used less in clinical practice, it is possible to design a very low calorie diet based on conventional foods. This approach requires supplementation with vitamins and electrolytes (including 2-3 g of potassium a day), minerals and trace elements. Some studies have observed that this type of diet leads to weight loss which is comparable to that of a formula diet.[195]

Table X
Contraindications for very low calories diets[196]

- Physiological: infancy, pregnancy, breastfeeding, elderly.
- BMI < 30 kg/m^2.
- Psychiatric disorders: Eating disorder, severe depression, psychosis, drug or alcohol addiction.
- Electrolyte disorders and orthostatic hypotension.
- Protein-losing diseases: Cushing's disease, systemic lupus erythematosus, proteinuria, neoplasia, malabsorption, inflammatory bowel disease, etc.
- Treatment with steroids.
- Situations in which calorie restriction can aggravate or precipitate a disease: porphyria, neoplasia, liver or kidney disease.
- Acute cardiovascular diseases, cardiac arrhythmias, stroke.
- Major surgery or trauma in the last 3 months.

Indications and contraindications

The use of VLCD's must be limited to patients with obesity (BMI > 30 kg/m^2), who present an associated pathology which requires faster weight loss than can be achieved with a conventional approach.[196] Their use is not advised for more than 16 weeks.[197] Ideally, they must be part of a structured programme which facilitates the maintenance of weight loss and, as remarked above, they require precise instructions and close clinical monitoring. Some programmes are used intermittently.[198] In table X their contraindications are indicated.[196]

Effect on weight loss

Patients who follow this type of dietary treatment achieve general weight loss of 1.5-2.5 kg per week, higher than the 0.4-0.5 kg achieved each week with low calorie diets (LCD). The average weight loss in the 12-16 week period is 5-15% of the initial weight, or around 20 kg (compared with the 8 kg achieved on average with a LCD). Various studies have observed that the composition of the weight loss after VLCD consists of 25% lean mass and 75% fat mass. These percentages of lean mass loss depend on various factors, including follow-up time, the degree of obesity, the physical exercise practiced, etc. During the initial weeks, the majority of the weight loss corresponds to water and glycogen, especially if the energy restriction is very pronounced. There are no studies which have directly assessed the effect of different types of diets. A systematic review observed that the studies which use VLCD's show greater lean mass loss than those which use LCD's.[199] A report recently published by the ESFA indicates that, at present, the evidence available does not allow us to assert that VLCD's are associated with more or less lean mass loss in proportion to fat mass when compared with less restrictive hypocaloric diets.[200]

It is interesting to note that various studies have observed similar weight loss when comparing diets with calorie intakes of 400 kcal/day and 800 kcal/day.[201-205] This is probably a consequence of irregular compliance with such energy deficit requirements, but it does indicate that it is probably not necessary to use such restrictive diets in clinical practice.

The long term effects of this type of diet are disparate and most patients are not capable of maintaining the weight loss achieved.[206-207] Approximately 30-50% of patients drop out of treatment between 3 and 6 months. In the absence of a specific follow-up which includes an intensive programme of behaviour modification and lifestyle changes, most patients recover 40-50% of the weight lost within 1-2 years.[208] This weight recovery is higher than that presented by patients who have lost weight by following a conventional hypocaloric diet.[209]

In 2006 a meta-analysis[210] was published which assessed the studies published on this type of long term diet. After reviewing 1,000 studies, six RCT's were selected which compared conventional hypocaloric diets (LCD's), with a follow-up above one year.[211-215] Most of the studies included patients with a BMI between 35 and 40 kg/m^2 and who followed the VLCD's for between 12 and 16 weeks. Two of them only studied women; another two assessed the effect of these diets on people with type 2 diabetes. Five of the six studies reported the outcomes of patients who completed the study and one did so by "intention to treat", using the last available weight. The overall dropout rate was 22.3% for VLCD's and 22.9% for LCD's. Short term weight loss was 16.1 ± 1.6% and 9.6 ± 2.4% of the initial weight, for VLCD's and LCD's respectively. The difference in weight loss between both treatments in the short term was 6.4 ± 2.7% ($P < 0.0001$).

For the long term follow-ups, which ranged from 1-5 years (average 1.9 ± 1.6) the average weight loss was 6.3 ± 3.2 kg or 5.0 ± 4.0% in relation to the initial weight, without significant differences being observed between the two types of treatment. Patients recovered 62% and 41% of the lost weight for VLCD's and LCD's respectively.

Currently most obesity treatment programmes use VLCD's as part of a treatment programme which also includes a controlled transition to a hypocaloric diet with conventional food, eating behaviour modification and physical exercise and which may or may not include the use drugs.

All of these factors affect the long term weight loss maintenance rate. Generally, the patients who adhere to the treatment best and for the longest period of time,[216] those who have check-ups with personal interviews or group therapy or who join an exercise programme obtain the best long term results. Some studies have observed that a slower period of transition to a conventional hypocaloric diet (over 6 weeks) after following a VLCD is associated with better weight loss maintenance than a faster transition.[217]

The study by Marinilli et al.,[218] assessed the effectiveness of a maintenance programme (STOP Regain) in a group of patients who had achieved prior significant weight loss (> 10%) in the last 2 years by using a VLCD, a commercial programme or their own methods. The prior weight loss was 24% of the maximum weight of the VLCD group and an average of 17% in the other two groups ($P < 0.001$). The first group recovered more of the lost weight so, after a 6-month follow-up, the weight loss was similar in all three groups. The patients who had lost weight using their own methods were most capable of maintaining weight loss over time.

Effect on comorbidity

Various studies have shown that weight loss originating from VLCD's results in an improvement in the associated pathology.[219-221]

This fact is especially evident in the case of diabetes. The severe restriction of energy intake results in a drop in baseline glycaemia and glycated haemoglobin.[222]

VLCD's and bariatric surgery

Bariatric surgery is a surgical procedure performed on high risk patients. It is therefore essential to improve the patient's clinical condition prior to surgery. Weight loss prior to surgery facilitates control of comorbidity before surgery (diabetes, AHT, respiratory failure), it is associated with a decreased risk of postoperative complications and a better long term result.[223]

A significant proportion of perioperative complications are conditioned by the presence of hepatic steatosis, which conditions hepatomegaly to varying degrees. This fact, which is associated with the increase in intra-abdominal fat, makes surgery significantly more difficult, with the additional risk of injuring the liver (lacerations, haemorrhages).

In recent years several works have been published which describe the beneficial effect of following a very low calorie diet (VLCD) prior to BS. This type of diet contributes between 400 and 800 kcal/day, with a sufficient quantity of proteins with a high biological value. The use of hypocaloric and high protein commercial preparations achieves greater weight loss than the conventional hypocaloric diet for these patients, it facilitates adherence and it ensures an adequate intake of proteins and other nutrients.

Treatment with VLCD's using hypocaloric and high protein preparations is capable of significantly reducing liver size and the fat content of the liver,[224,225] This reduction in liver size, which is evaluated using CT and NMR, reaches 18.7% (20-51.7).[226] In the subgroup of patients with greater hepatomegaly (liver size above 2.8 L) this reduction is much higher (28.7%).

Various studies have shown that treatment with a VLCD prior to bariatric surgery reduces the complication rate, the average hospital stay, liver volume, the operation

time, blood loss during surgery and the risk of conversion from a laparoscopic procedure to open surgery. It is also associated with greater postoperative weight loss.[227-229] Weight loss immediately prior to bariatric surgery reduces operation time by 23.3 minutes (95% CI 13.8-32.8).[230] A systematic review[231] and a meta-analysis[230] have recently been published on this subject.

This weight loss prior to surgery is well tolerated by the patient, with very few adverse effects. It does not have a negative effect on immune function or scarring.

The Clinical Practice Guidelines for perioperative medical treatment for BS, which have been drafted by several scientific associations, recommend weight loss prior to surgery for patients for whom the reduction in hepatic steatosis and hepatomegaly may improve technical aspects of the surgery.[232]

Patients with more severe obesity or a greater degree of hepatomegaly also receive more benefits from this treatment. In severe cases of patients with extreme obesity with associated complications, it may be necessary to carry out treatment as an inpatient.[233]

Regarding the time during which the very low calorie diet must be maintained prior to surgery, the duration has been variable in different studies, usually between 6 and 12 weeks. In the study by Colles[226] it was observed that 80% of the reduction in liver size took place during the first two weeks. These authors recommend a minimum duration of 2 weeks and they consider a duration of 6 weeks to be adequate.

During the postoperative period, the patient's intake of solid foods is significantly limited as a consequence of the anatomical changes to the digestive tract resulting from the surgery. Therefore, the patient follows a liquid diet for a variable period of time, from one to three weeks, depending on the type of procedure used, digestive tolerance and the appearance of complications. The type of diet followed by the patient is a very low calorie diet, which must include sufficient protein intake.[234]

According to the recommendations of the Clinical Practice Guidelines for perioperative care for bariatric surgery[232] protein intake must be regularly assessed. A recommended minimum intake of 60 g/day is recommended for purely restrictive procedures, which increases to 80-120 g day for procedures with associated malabsorption such as a gastric bypass or biliopancreatic diversion. A protein intake deficiency can result in greater lean mass loss and various degrees of protein malnutrition. Bearing in mind the limited oral intake following bariatric surgery, it is extraordinarily difficult to achieve the recommended protein intake solely with natural foods, especially during the initial weeks following surgery.

In a randomised clinical trial which assessed the evolution of body composition, it was observed that, with identical weight loss, the patients who have undergone restrictive bariatric surgery (gastric band) presented greater lean mass loss than patients undergoing a very low calorie diet with specific products. The authors recommend that the lower protein intake of the patients being treated than those receiving a hypocaloric formula diet is the most likely cause of the drop in lean mass.[235]

Studies carried out in our field[236] have shown that the protein intake does not reach the recommended minimum levels (60 g/day) for a very high proportion of patients. The use of oral nutritional supplements high in protein for these patients helped to make it possible for them to achieve the recommended proteins.

These studies indicate to us that the use of VLCD's with commercial products in the initial postoperative weeks following BS can help the patient to achieve a suitable protein intake.

Safety

The adverse effects of VLCD's include general symptoms (asthenia, weakness, dizziness), digestive symptoms (constipation, nausea) and others such as dry skin, hair loss, menstrual irregularities, intolerance to cold, etc. They are not infrequent but they are not normally serious. At times irritability, depression or difficulty concentrating and even psychotic symptoms can occur. Arrhythmia and other cardiac abnormalities, including sudden death, have also been described. A higher risk of the appearance of gallstones has been described, due to an increase in the concentration of cholesterol in bile and a reduction in the contraction of the gallbladder which is secondary to the low fat intake.

Some clinical studies have observed the appearance of gallstones in 12-25% of patients treated; approximately half of these patients required cholecystectomy. This complication can be partly be prevented by limiting weight loss to 1.5 kg/week, providing a minimum quantity of fat (at least 7 g per day) or the use of ursodeoxycholic acid.[237] The energy deficit and rapid weight loss result in hyperuricemia, which can occasionally lead to an acute gout attack.

The risk of adverse effects with this type of treatment requires, as commented in the foregoing sections, strict medical control.

Evidence

59. In the very short term (less than 3 months), very low calorie diets (400 to 800 kcal/day) achieve a higher weight loss than conventional low calorie (> 800 kcal/day) diets (Evidence Level 1+).

60. In the long term (over 1 year), these diets do not achieve a higher bodyweight loss than conventional low calorie diets (> 800 kcal/day) (Evidence Level 1+).

61. In the preoperative preparation for bariatric surgery in patients with hepatic steatosis and increased surgical risk, the use of a very low calorie diet before surgery diminishes the surgical risk (Evidence Level 1+).

62. There is at present not sufficient data that might allow establishing whether very low calorie-diets using commercial preparations, when used in the postopera-

tive period of bariatric surgery, might contribute to the patient's achieving an appropriate protein intake.

63. Very low calorie diets entail a greater risk of adverse effects than conventional low calorie ones (Evidence Level 1–).

64. At the present time, the evidence available is insufficient for allowing a statement that very low calorie diets might be associated to a higher lean body mass loss in relation to the fatty body mass, as compared to less restrictive hypocaloric diets.

Recommendations

28. The very low calorie diets might be used in the dietary management of patients with obesity, yet always with a concrete clinical indication and under close and strict medical follow-up (Recommendation Degree D).

29. The very low calorie diets should not be used in patients not fulfilling the established medical indications and requirements (Recommendation Degree A).

30. The use of very low calorie diets might be necessary in the preoperative preparation for bariatric surgery in patients with hepatic steatosis and increased surgical risk, always under close medical control and with due consideration of the possible adverse effects that might be observed (Recommendation Degree B).

31. The use of very low calorie diets with commercial preparations might be necessary in the immediate postoperative period after bariatric surgery, so as to contribute to the patients' achieving an adequate protein intake (Recommendation Degree D).

5. Mediterranean diet

The Mediterranean diet is characterised by a high intake of whole grains, fruit, vegetables and pulses, with the use of fish and white meat being favoured over red and processed meat, the use of virgin olive oil both for cooking and garnishing, the low to moderate consumption of wine and the low consumption of milk, cream, butter and sugary drinks. This results in a low intake of saturated and trans fatty acids and added sugar and the high consumption of vegetable fibre and monounsaturated fatty acids. The effects of the Mediterranean diet on health have been extensively studied. Various studies have shown that this eating pattern provides protection against developing cardiovascular disease. It has been observed that following this dietary pattern is associated with lower mortality from any cause, and a decrease in the risk of cardiovascular disease, diabetes and cancer.[238,239]

The effect of the Mediterranean diet on obesity has been evaluated in numerous observational studies and controlled clinical trials, which offer conflicting results. In this section those which use the Mediterranean diet for the dietary treatment of obesity will be described.

A study published by Shai et al. in 2008[50] compared a low-fat diet with a Mediterranean diet, with both being hypocaloric, and a diet low in carbohydrates (CH), without calorie restriction, in 3,222 subjects with moderate obesity (average BMI 31 kg/m^2). After a two-year follow-up, weight was -3.3 kg, -4.6 kg and -5.5 kg, respectively (P = 0.03 when comparing the diets low in fat and carbohydrates, but with the MedDiet and diet low in CH being equally effective). The changes in levels of glycaemia and insulinemia in patients with type 2 diabetes mellitus were more favourable with the MedDiet than with the low-fat diet.

In a recently published meta-analysis there was a specific assessment of the role of the Mediterranean diet in the treatment of obesity.[240] It includes sixteen randomised trials in which 3,436 subjects participated (1,848 assigned to the MedDiet and 1,588 to the control diet). It was observed that the Mediterranean diet resulted in significantly more weight loss, with an average difference from the control group of -1.75 kg (-2.86; -0.64). This positive effect of the Mediterranean diet is greater when associated with energy restriction, increased physical activity and a follow-up greater than 6 months. Despite its higher fat content than other diets, no study observed that the MedDiet induced weight gain.

Another recent study published by Jiménez-Cruz,[241] evaluated the long term studies which lasted for over 24 months and which compared the MedDiet with a control diet, and it includes five RCT's.[50,242,245] This systematic review shows that the Mediterranean diet and a diet low in fat lead to similar outcomes in terms of weight loss when energy intake is restricted and interventions of equal intensity are used. The studies which observed a benefit in the MedDiet had used a hypocaloric diet; other studies applied different follow-up and lifestyle modification patterns in the intervention group and the control group.

This author recommends that people who live in the Mediterranean area should be advised to reduce their overall energy intake, including olive oil when the consumption of this is over 20-25 g per day or when the percentage of fat is over 35% of the total calories. Despite this restriction, the majority of the inhabitants of these areas will continue to consume a suitable amount of monounsaturated fatty acids. The weight loss is due more to the calorie restriction originating from the diet than its composition.

Metabolic effects of the Mediterranean diet

The role of the MedDiet in the various components of metabolic syndrome has also recently been assessed. The meta-analysis published recently by Kastorini et al.,[246] of the same group as above, contains the data from 25 observational studies and 36 clinical trials, which include a total of approximately half a million people.

This meta-analysis includes eight studies (which include 10,399 subjects) which assessed the effect of the Mediterranean diet on the development and progression of metabolic syndrome. Of these, 4 observed a beneficial effect when compared to a control diet.[239,247-250] Follo-

wing the Mediterranean diet is associated with a beneficial effect on MS in 2/2 clinical trials, 1/2 prospective studies and 2/4 transversal studies, in comparison with the subjects with a lower degree of adherence to the diet or with a control diet (low in fat or usual diet). The combined effect of the clinical trials and prospective studies showed that this type of diet has a protective effect (log-hazard ratio -0.69; CI 95%: -1.24 to -1.16).

The effect of the MedDiet on waist circumference has been assessed in 11 clinical trials which include 997 patients assigned to a MedDiet and 669 to a control diet. Overall, it was observed that following a MedDiet is associated with a beneficial effect on waist circumference. This result is particularly evident in one of the studies.[251]

Regarding plasma lipids, twenty-nine studies assessed the effect of the MedDiet on HDL levels; of those 7 observed a beneficial effect. An analysis of these data concludes that, indeed, greater adherence to the MedDiet is associated with an increase in HDL cholesterol.

The effect on triglycerides has been assessed in three observational studies and 29 clinical trials. This meta-analysis concludes that greater adherence to the MedDiet is associated with lower levels of plasma triglycerides.

The effect on arterial hypertension has been assessed in 5 observational studies with disparate results: two of them observed a beneficial effect,[252,253] but another observed an increase in systolic BP in patients with greater adherence to the MedDiet.[254] 14 clinical trials have been published which study the effect of the MedDiet on SBP and DBP. The analysis of the data shows a beneficial effect on BP.

Finally, in this meta-analysis several studies are described which assess the effect of the MedDiet on carbohydrate metabolism. The analysis of the data from two observational studies and 17 clinical trials on a total of 2,373 patients (1,357 assigned to the MedDiet and 1,139 to a control diet) reveals a beneficial effect of the MedDiet on plasma glycaemia. It was also possible to observe lower insulin resistance, evaluated using the HOMA.

The authors of this meta-analysis indicate certain factors which probably affect the heterogeneity of the results. One of the most important factors is the place in which the study is performed; studies carried out in the Mediterranean area observe a positive effect in following this type of diet on all components of MS except waist circumference. However, studies carried out in other geographical locations do not observe a beneficial effect. Short term studies tend to observe an effect on BP and glycaemia, although none is evident on lipids or waist circumference.

EVIDENCE

65. There is at present no sufficient scientific evidence available that might prove that the "Mediterranean" diet, under isocaloric conditions, might achieve a higher body weight loss than other diet types in the dietary management of obesity.

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