Clinical Nutrition (2005) **24**, 390–397

ELSEVIER

Clinical Nutrition

http://intl.elsevierhealth.com/journals/clnu

ORIGINAL ARTICLE

Effect of oral administration of a whole formula diet on nutritional and cognitive status in patients with Alzheimer's disease

Jordi Salas-Salvadó[a,b,*], Míriam Torres[a], Mercè Planas[c], Salvador Altimir[d], Carlos Pagan[e], María Eloina Gonzalez[f], Susan Johnston[g], Carolina Puiggros[c], Anna Bonada[b], Pilar García-Lorda[a]

[a]*Unitat de Nutricio Humana, Facultat de Medicina de Reus, Universitat Rovira i Virgili, C/San Llorenc 21, 43201 Reus (Tarragona), Spain*
[b]*Nutrition and Dietetics, Hospital Universitari de Sant Joan, Reus, Spain*
[c]*Nutritional Support Unit, Hospital Universitari Vall d'Hebron, Barcelona, Spain*
[d]*Geriatrics Unit, Hospital Germans Trias i Pujol, Badalona, Spain*
[e]*Geriatrics Unit, Llar d'Ancians, Palma de Mallorca, Spain*
[f]*Geriatrics Unit, UADG Manso, Barcelona, Spain*
[g]*Unit of Dietetics, Hospital Germans Trias i Pujol, Badalona, Spain*

Received 17 August 2004; accepted 16 December 2004

KEYWORDS
Alzheimer's disease;
Malnutrition;
Albumin;
Body weight;
Oral supplements

Summary *Aims*: To evaluate the effect of a whole formula diet on nutritional and cognitive status in Alzheimer's disease patients.

Methods: Patients were randomly assigned to two interventions: a whole formula diet based on lyophilised foods (Treatment Group, $n = 24$) or nutritional advice (Control Group, $n = 29$). Energy intake, body weight, biochemistry, Mini Nutritional Assessment (MNA) and Pfeiffer's tests were determined at baseline and at 3 months of treatment.

Results: No differences were observed between groups at baseline. Energy intake tended to increase in the Treatment Group and to decrease in the Control Group, although differences were not significant. The improvement in MNA and Pfeiffer test scores was not significantly different between groups. Body weight increased by 2.06 ± 1.9 kg in the Treatment Group and by 0.32 ± 3.04 kg in the Control Group ($P = 0.007$). The increases in albumin ($P = 0.007$), haemoglobin ($P = 0.002$) and serum ferritin ($P = 0.009$) were higher in the Treatment Group than in controls. A similar rate of serious adverse events (hospitalisation or death) was observed in both groups.

*Corresponding author. Tel.: +34 977 75 9313; fax: +34 977 75 93 22.
E-mail address: jss@fmcs.urv.es (J. Salas-Salvadó).

0261-5614/$ - see front matter
doi:10.1016/j.clnu.2004.12.006

Conclusions: Administration of this whole formula has a positive impact on nutritional status. The great diversity in textures and tastes enable these formulations to be administered to a wide range of patients with or without liquid dysphagia.

Introduction

Life expectancy and, consequently, the proportion of elderly people are increasing in developed countries. As a result, the incidence of age-related diseases, such as dementia of different causes is also increasing spectacularly. Nowadays, the prevalence of dementia is estimated to be between 5% and 6% in subjects more than 65 years old.[1]

During the course of this chronic disease, a large subset of patients suffer from unintentional weight loss and malnutrition.[2,3] In fact, according to the criteria of the National Institute for Neurological and Communicative Disorders and the Stroke and Alzheimer's Disease and Related Disorders Association,[4,5] body weight loss is one of the main symptoms of Alzheimer's disease. Furthermore, body weight loss tends to augment in parallel with the progression of the disease and is a predictor of mortality in Alzheimer's disease patients.[6,7]

The aetiology of body weight loss and malnutrition in the context of Alzheimer's disease is multifactorial. Alzheimer patients show a progressive inability to make correct nutritional choices, a loss of autonomy to feed themselves and, frequently, negative attitudes related to intake. The presence of anorexia, other problems related to ageing and dementia such as dysphagia, and the increase in nutritional requirements associated to the disease also contribute to the development and maintenance of malnutrition.[8,9]

Several authors have made studies to determine how effective nutritional supplementation with liquid formulas is on energy intake and nutritional status in this kind of patients. Some studies have shown that such liquid supplements can lead to an increase in body weight and plasma albumin levels,[10–14] whereas other studies have failed to demonstrate any effect.[15] This discrepancy is probably explained by the heterogeneity of the populations studied, the different formulas used and the variable length of the nutritional interventions.

Furthermore, the degree of compliance with these liquid formulas is highly variable, which can also affect the results obtained. Between 15% and 20% of elderly patients dislike liquid formulas[16] or dropout for this reason in clinical trials.[17] Furthermore, some authors have described that more than 40% of subjects did not comply with prescribed liquid supplements in clinical settings.[18] Most of these commercialised products are liquid sweet formulas with monotonous flavours. Hence, a high percentage of patients abandon the treatment shortly after supplementation is started. On the other hand, the liquid consistency of most of these products makes tolerance difficult in demented patients with liquid dysphagia. At present, complete formulas based on lyophilised natural foods with liquid or semi-solid consistency (depending on the amount of water used for their dilution) are available. These formulas offer a wide range of savoury and sweet flavours. These formulas will probably be easier for geriatric populations to accept and can be easily administered to patients with liquid dysphagia. Therefore, it can be hypothesised that these formulas will have better effects on the nutritional status of patients with dementia.

Hence, the present study conducted in patients with Alzheimer's disease aims to: (a) evaluate the compliance to a complete nutritional formula of liquid or semi-solid consistency; (b) analyse the total energy intake in patients receiving this nutritional intervention in comparison with patients fed with a traditional home-made diet; and (c) evaluate the effect of this nutritional intervention on body weight, nutritional markers and cognitive parameters in comparison to the Control Group.

Patients and methods

Patients

The study evaluated 56 patients older than 65 years with Alzheimer's disease diagnosed on the basis of the DSM-IV criteria, who fulfilled the following inclusion criteria: (a) to score 3 and above on Pfeiffer's cognitive questionnaire, (b) to need a semi-solid or liquid diet, and (c) to present or refer a weight loss higher than 5% of body weight in the previous year.

Exclusion criteria were: (a) terminal care or severe acute illness, cancer or history of cancer in

the last 5 years; (b) severe gastrointestinal disease; (c) respiratory or urinary infection or any other acute illness potentially able to affect the nutritional status at the moment of study; (d) significant hepatic or renal disease; (e) enteral or parenteral nutritional support at the moment of the study; (f) chronic treatment with corticoids, antibiotics or antineoplastics; (g) diabetic patients under insulin treatment; (h) use of nutritional supplements in the last 15 days prior to entering the study.

Study design

The present study is a prospective multicentric 3-month randomised clinical trial. Subjects were recruited in six geriatric institutions from Catalonia (Spain).

A total of 53 out of the 56 patients first selected took part in the study and were randomised to receive: (a) a complete formula based on natural lyophilised foods (Treatment Group, $n = 24$), or (b) standard dietetic advice (Control Group, $n = 29$). Randomisation process was centralised and both groups were stratified by the initial body mass index (BMI). Three patients did not take part in the study because they did not like the product, particularly because they claim for food of solid consistency.

First degree relatives or legal tutors and, if possible, the patients gave their written informed consent to participate. The study protocol was approved by the Ethics Committee of the Hospital Universitari Sant Joan de Reus.

Table 1 Nutritional composition of the complete formula Vegenat®-med.

Nutrients	330 g	100 g
Energy (kcal)	1490	451.52
Carbohydrates (g)	186.86	56.62
Protein (g)	69.07	20.93
Fat (g)	52.27	15.84
Saturated fatty acids (g)	13.39	4.06
Monounsaturated fatty acids (g)	26.72	8.10
Polyunsaturated fatty acids (g)	12.08	3.66
Vitamin A (μg)	743.49	225.30
Vitamin D (μg)	10.89	3.30
Vitamin E (mg)	10.56	3.20
Vitamin K (μg)	52.8	16.00
Vitamin B1 (mg)	1.65	0.50
Vitamin B2 (mg)	0.99	0.30
Niacin (mg EN)	23.76	7.20
Pantotenic acid (mg)	7.26	2.20
Vitamin B6 (mg)	5.61	1.70
Folic acid (μg)	166.32	50.40
Vitamin B12 (μg)	1.65	0.50
Biotin (μg)	73.92	22.40
Vitamin C (μg)	59.4	18.00
Sodium (mg)	1095	331.82
Potassium (mg)	1860	563.64
Calcium (mg)	820.16	248.53
Phosphorous (mg)	614.46	186.20
Magnesium (mg)	268.62	81.40
Iron (mg)	11.55	3.50
Zinc (mg)	11.55	3.50
Copper (μg)	1254	380.00
Selenium (μg)	5412	1640.00

Note: Composition is expressed per 100 g and 330 g (corresponding to three packets).

Intervention

Patients from the Treatment Group received a complete diet based on natural lyophilised foods with liquid or semi-solid consistency depending on the amount of added water. They were administered orally 3 packets/d (450 kcal/packet) of Vegenat®-med, which substituted breakfast, lunch and supper. A wide range of savoury and sweet flavours was provided to the patients (lentils, chickpeas, ham, fish, beef, chicken, vegetables, apple, honey, orange and chocolate). They also received recommendations directed to increase energy intake. They were also allowed to consume as a dessert or as snack the following items: baked apple or pea fruit juices, yoghurt, crème caramel, milk or cookies. Patients in the Control Group received the same dietetic advice as the Treatment Group. No nutritional supplements, but the Vegenat®-med in the intervention group, were allowed during the study in any group. Caregivers from both groups received written information about balanced diet recommendations and advice on how to increase energy intake by using home-made food as well as recommendations on how to prevent liquid dysphagia if necessary. The nutritional composition of the complete natural lyophilised formula is shown in Table 1.

Nutritional and cognitive evaluation

Before randomisation, subjects underwent a screening which recorded information about usual body weight, weight loss in the previous 3 months, height, waist circumference and systolic (SBP) and diastolic (DBP) blood pressure. Waist circumference was measured at the midpoint between the last rib and iliac crest.[19] When height and weight could not be measured in the standard way, specially adapted

weight scales were used and height was estimated by measuring the non-dominant leg.[20]

At the beginning of the study and at 1 and 3 months of intervention, energy intake, body weight and nutritional status were evaluated and a blood sample was obtained. Energy intake was recorded using a 24-h dietary record of three non-consecutive days including one non-working day. Dietary records were completed by the caregivers and checked by a trained dietician. The energy and nutrient intake were estimated with the French Regal composition table.[21] Nutritional status was assessed by the Mini Nutritional Assessment (MNA) Test.[22] Venous blood was drawn from fasted subjects. Fasting glucose, plasma lipid profile, haemoglobin, albumin and prealbumin were measured enzimatically. Lymphocyte count and erythrocyte sedimentation rate (ESR) were determined by routine technique. Serum ferritin and C-reactive protein (CRP), vitamin B12 and folic acid were determined by chemiluminescence.[23,24]

Cognitive performance was evaluated at the beginning of the study with Pfeiffer's mental status questionnaire validated for a Spanish population by García-Montalvo. On the basis of this test subjects were classified as having: (a) preserved cognitive status (scores between 0 and 2); (b) slight cognitive impairment (scores between 3 and 4); (c) moderate cognitive impairment (scores between 5 and 7); and (d) severe cognitive impairment (scores between 8 and 10).[25,26] The Blandford scale codified eating disorders and was used to evaluate eating behaviour.[2]

The degree of cognitive and functional impairment was evaluated at the beginning and at the end of the study by the GDS scale, validated for the Spanish population by Peña-Casanova in 1997.[27] This scale determines the severity of the dementia and classifies patients according to the degree of cognitive affection (GDS) and functional impairment (FAST).[28,29]

Statistical analyses

Statistical analyses were performed with the statistical package SPSS® version 11.5 for Windows. Results are expressed as mean $\pm$ SD.

For comparisons between groups, non-parametric tests were used for quantitative variables (Mann–Whitney *U*-test) and the Chi-square test was used for categorical variables. Changes in the studied parameters from the beginning to 3 months of intervention were calculated and compared among groups using non-parametric tests (Mann–Whitney *U*-test). A *P*-value of <0.05 was considered to be statistically significant.

Results

Baseline

All the patients studied scored above 5 on the GDS scale, and a high percentage (51.7% in the Control Group and 54.2% in the Treatment Group) scored 7. Hence, the population studied consisted of patients with a severe cognitive impairment or advanced dementia. No significant differences in GDS scoring were observed between the intervention and the Control Group.

Tables 2–4 show the baseline demographic, biochemical characteristics and the intake of energy and nutrients (protein, carbohydrates, lipids and alcohol) of the studied sample. No significant differences in any of the studied variables were observed between groups at baseline. In addition, the prevalence of concurrent or previous

Table 2 Baseline characteristic of the study groups.

	Control Group ($n = 29$)	Treatment Group ($n = 24$)
Gender (male/female)	4/25	5/19
Age (years)	83.9 $\pm$ 6.9	85.6 $\pm$ 6.6
Height (cm)	149.6 $\pm$ 11.9	151.8 $\pm$ 9.9
Weight (kg)	48.6 $\pm$ 10.7	51.5 $\pm$ 10.4
BMI (kg/m^2)	21.7 $\pm$ 3.6	22.3 $\pm$ 10.4
Usual body weight (kg)	56.1 $\pm$ 11.3	58.5 $\pm$ 12.4
Waist circumference (cm)	79.4 $\pm$ 9.4	83.1 $\pm$ 13.0
SBP (mmHg)	118.2 $\pm$ 12.6	122.3 $\pm$ 18.6
DBP (mmHg)	65.7 $\pm$ 13.8	66.4 $\pm$ 10.1
MNA score	16.5 $\pm$ 3.6	15.1 $\pm$ 4.8

SBP, systolic blood pressure; DBP, diastolic blood pressure; MNA, Mini Nutritional Assessment Test.

Table 3 Biochemical parameters at baseline.

	Control Group ($n = 29$)	Treatment Group ($n = 25$)
Haemoglobin (g/dL)	12.4±1.6	11.6±1.7
Lymphocytes ($\times 10^9$/L)	2.2±1.4	1.8±0.76
Cholesterol (mg/dL)	175.7±50.2	187.8±35.2
Tryglicerides (mg/dL)	93.9±32.6	108.3±45.8
Albumin (mg/dL)	33.8±5.3	32.8±7.0
Prealbumin (g/L)	0.18±0.04	0.16±0.04
Glucose (mg/dL)	86.5±13.2	91.0±20.3
Ferritin (μg/dL)	132.2±122.2	120.2±84.0
Folic acid (μg/mL)	7.0±5.0	7.5±5.7
Erythrocyte sedimentation rate (mm/h)	30.2±19.0	40.0±35.8
Vitamin B12 (pg/mL)	321.5±95.5	287.7±93.5
C reactive protein (mg/dL)	1.4±1.6	1.7±2.4

Table 4 Energy and nutrient intake at baseline.

	Control Group ($n = 28$)	Treatment Group ($n = 22$)
Energy (kcal)	1903.4±478.7	1841.6±640.4
Protein (g)	88.3±32.2	87.4±39.3
Carbohydrates (g)	234.0±68.6	213.0±71.0
Fat (g)	68.7±22.0	70.5±28.5
Alcohol (g)	0.73±2.7	0.27±1.1

diseases (diabetes, dyslipidaemia, hypertension, history of cancer or cardiovascular disease) was not significantly different between groups.

Although the prevalence of malnutrition was high in the studied population, no significant differences among groups were observed. At baseline, 13.2% of the patients presented a BMI $< 18\,kg/m^2$, 52% had albumin levels < 35 mg/dL and 50.9% showed MNA scores suggestive of malnutrition.

No significant differences between groups were observed in the cognitive status as measured by Pfeiffer's test or in their eating behaviour as measured by the Blandford scale.

Evolution

While, at the end of the study, mean energy intake tended to increase in the Treatment Group (124±833 kcal/d), a tendency to decrease was found in the Control Group (−46±402 kcal/d); however, the changes were not significantly different. No significant differences were observed in relation to changes in protein, carbohydrates, fat or alcohol intake between groups during the intervention period. In the intervention group, 32% of the total reported energy intake came from other food sources different from the prescribed supplements.

Severe adverse events were not significantly different between groups. A total of 11 patients did not end the study since they presented severe adverse events, five in the Control Group (three deaths and two acute diseases that required hospitalisation) and six in the Treatment Group (five deaths and one acute disease requiring hospitalisation). Ten out of these 11 patients who had severe adverse events presented an advanced degree of dementia at baseline (GDS score = 7).

Table 5 shows the differences in the evolution of body weight and biochemical parameters between groups. Mean body weight increased by 2.06±1.9 kg in the Intervention Group and by 0.32±3.04 kg in the Control Group ($P = 0.007$). The Intervention Group showed a significant increase in albumin levels compared to the Control Group (3.76±5.03 mg/dL versus 1.13±5.7 mg/dL; $P = 0.007$). Similar trends were observed in haemoglobin levels ($P = 0.002$) and serum ferritin ($P = 0.009$). No significant differences were observed between groups in relation to the changes in other biochemical parameters. The MNA score increased more in the Treatment Group than in the Control Group (3.6±4.16 versus 0.7±5.05, respectively) although the differences between groups were not significant. No significant differences were observed in cognitive parameters such as GDS test and Pfeiffer's scores (Table 6).

Discussion

The main objective of the present study was to evaluate how a new complete nutritional formula

Table 5 Changes in biochemical and nutritional parameters during the study period time in both groups.

	Control Group ($n = 23$)	Treatment Group ($n = 15$)
Weight (kg)	0.32 ± 3.04	2.06 ± 1.90*
Haemoglobin (g/dL)	-0.18 ± 0.95	1.10 ± 1.47**
Lymphocytes ($\times 10^9$/L)	-0.33 ± 1.53	0.03 ± 0.31
Cholesterol (mg/dL)	7.46 ± 40.73	0.92 ± 28.50
Tryglicerides (mg/dL)	15.50 ± 22.52	7.73 ± 31.64
Albumin (mg/dL)	1.13 ± 5.70	3.76 ± 5.03*
Prealbumin (g/L)	0.02 ± 0.03	0.02 ± 0.04
Glucose (mg/dL)	2.78 ± 15.34	-4.55 ± 12
Ferritin (ng/dL)	8.58 ± 90.82	25.38 ± 35.50*
Folic acid (ng/mL)	2.63 ± 8.49	0.64 ± 1.80
Erythrocyte sedimentation rate (mm/h)	2.45 ± 13.76	-0.31 ± 14.86
Vitamin B12 (pg/mL)	14.09 ± 58.43	4.15 ± 27.16
C reactive protein (mg/dL)	-0.05 ± 0.45	0.06 ± 0.13

*$P < 0.05$; **$P < 0.005$.

Table 6 Changes in cognitive parameters evaluated by GDS scale and Pfeiffer's test during the study period time in both groups.

	Control Group		Treatment Group	
	Baseline ($n = 24$)	Final ($n = 23$)	Baseline ($n = 15$)	Final ($n = 15$)
Pfeiffer's test score	7.8 ± 1.7	7.8 ± 1.8	7.5 ± 2.5	7.0 ± 2.4
GDS (number of patients)				
<5	0	0	0	0
5	0	0	2	1
6	12	10	7	7
7	12	13	6	7

Note: No significant differences among groups were observed.

based on natural lyophilised foods with liquid or semi-solid consistency affected body weight and other nutritional parameters in patients with Alzheimer's disease.

As shown in the Results section, baseline clinical and nutritional characteristics as well as mental status were similar between groups which is essential if the trial design is to be suitable.

In these conditions, the present study demonstrates that this kind of intervention for 3 months is able to improve the nutritional status in these Alzheimer's disease patients. The use of this formula associated to dietetic advice on how to increase energy intake leads to a higher increase in body weight and a greater improvement of several nutritional parameters than traditional dietetic advice.

In fact, mean body weight increased while the formula was administered by 2.06 ± 1.9 kg in the Treatment Group and by only 0.32 ± 3.04 kg in the Control Group ($P = 0.007$). This is important because body weight change is an important indicator of health status, and a decrease in body weight has been associated to an increased morbimortality in different chronic conditions.[30,31]

The mean increase in body weight observed in the present study is similar to that reported in Gray-Donald's study[32] in which the administration of a nutritional supplement over a period of 12 weeks was accompanied by a 2.1 kg increase in body weight. It was also higher than that observed in a similar period of time by other nutritional intervention studies on psycho-geriatric nursing home patients[12,17] or hospitalised geriatric patients.[13]

Albumin, haemoglobin and serum ferritin levels also improved more in the nutritional Intervention Group, suggesting that this kind of nutritional formula is more effective at improving nutritional status. Albumin has been shown to be a strong predictor of mortality in several conditions and a

specific and sensitive nutritional marker in chronic conditions.[33] The use of ferritin and albumin as nutritional markers could be impaired by the presence of inflammatory conditions. However, in our study, no changes in inflammatory markers such as ESR and CRP occurred that could explain such differences in albumin and ferritin.

The improvement in nutritional status achieved in the present study might be explained by an increase in energy and protein intake associated with a nutritional intervention that offers a wide variety of presentations and flavours. The wide range of savoury and sweet flavours probably contributes to increasing its acceptability in the long term. Additionally, the fact that the texture can be easily changed from liquid to semi-solid makes them adaptable to all kinds of patients including those with liquid dysphagia. The formula used in the present study was well accepted and patients adhered well to the intervention. In our study, patients from the Intervention Group tended to increase their energy intake whereas the Control Group showed a slight decrease. However, no significant differences could be observed between groups. This lack of significance could be due to the large standard deviation observed in energy intake leading to an inadequate statistical power for the present sample size which was initially calculated taking body weight changes as the main study variable.

Our study sample consisted of patients with advanced dementia and a considerable impairment of mental status. It could be hypothesised that the improvement in nutritional status is accompanied by an improvement in mental functioning. However, no significant improvement in Pfeiffer's test or in the GDS scale was observed in our study. This could be explained by the short intervention time and does not necessarily rule out a potential effect. Additionally, the severe baseline mental impairment of our patients could also explain the difficulty in observing any scoring change in tests evaluating cognitive status.

The nature and design of the present study does not make it possible to analyse the effect of the nutritional intervention on other hard end points such as morbidity or mortality. Longer studies with larger samples are needed to determine whether this improvement in nutritional status is maintained over time and to evaluate its effect on morbimortality.

In conclusion, our study showed that the nutritional status of advanced Alzheimer disease patients can be improved by providing dietary advice and, specially, a high dense complete formula based on natural lyophilised food.

Acknowledgments

This study was supported in part by Vegenat S.A. and by a grant from the FIS of the Instituto de Salud Carlos III, Red de Centros RCMN (C03/08), Madrid, Spain. We thank Rocío Figueredo, Mónica Bulló, and Núria Guillen for their commitment to the study and the IRCIS foundation (Reus, Spain) for the administrative support provided.

References

1. López-Pousa S, Vilalta J, Llinas J. Epidemiología de las demencias en España. *Rev Gerontol* 1995.
2. Blandford G, Watkins LB, Mulvihil MN, Taylor B. Assessing abnormal feeding behaviour in dementia: a taxonomy and initial findings. In: Vellas B, Riviere S, Fiteen, editors. *Research and practice in Alzheimer's disease. Weight loss and eating behaviour in Alzheimer's patients*. New York: Springer; 1998.
3. Esteban M, Fernández J, Salas-Salvadó J. Estado nutricional de la población anciana en función del régimen de institucionalización. *Nutr Hosp* 2000;**15**:105–13.
4. Mckhann G, Drachman D, Folstein M. Clinical diagnosis of Alzheimer's disease: report of the NINCDS-ADRDA Work Group under the auspices of Department of Health and Human Services. Task force on Alzheimer's disease. *Neurology* 1984;**34**:939–43.
5. Poehlman ET, Dvorak RV. Energy expenditure, energy intake, and weight loss in Alzheimer disease. *Am J Clin Nutr* 2000;**71**:650S–5S.
6. Cronin-Stubbs D, Beckett LA, Scherr PA, et al. Weight loss in people with Alzheimer's disease: a prospective population based analysis. *Br Med J* 1997;**314**:178.
7. White H, Pieper C, Schmader K. The association of weight change in Alzheimer's disease with severity disease and mortality: a longitudinal analysis. *J Am Geriatr Soc* 1998;**46**:1223–7.
8. Folstein M. Nutrition and Alzheimer's disease. *Nutr Rev* 1997;**55**:23–5.
9. García-Lorda P, Foz M, Salas-Salvadó J. Estado nutricional de la población anciana de Cataluña. *Med Clin (Barc)* 2002;**118**:707–15.
10. Lauque S, Arnaud-Battandier F, et al. Protein-energy oral supplementation in malnourished nursing-home residents. A controlled trial. *Age Ageing* 2000;**29**:51–9.
11. Payette H, Boutier V, Coulombe C, Gray-Donald K. Benefits of nutritional supplementation in free-living, frail, undernourished elderly people: a prospective randomized community trial. *J Am Diet Assoc* 2002;**102**:1088–95.
12. Wouters-Wesseling W, Wouters AEJ, Kleijer CN, Bindels JG, de Groot CPGM, van Staveren WA. Study of the effect of a liquid nutrition supplement on the nutritional status of psycho-geriatric nursing home patients. *Eur J Clin Nutr* 2002;**56**:245–51.
13. Gazzotti C, Arnaud-Battandier F, Parello M, et al. Prevention of malnutrition in older people during and after hospitalisation: results from a randomised controlled clinical trial. *Age Ageing* 2003;**32**:321–5.
14. Planas M, Conde M, Audivert S, et al. Micronutrient supplementation in mild Alzheimer disease patients. *Clin Nutr* 2004;**23**:265–72.

15. Beck AM, Ovesen L, Schroll M. Home-made oral supplement as nutritional support of old nursing home residents, who are undernourished or at risk of under nutrition based on the MNA. A pilot trial. Mini Nutritional Assessment. *Aging Clin Exp Res* 2002;**14**:212–5.
16. Bruce D, Laurance I, McGuiness M, Ridley M, Goldswain P. Nutritional supplements after hip fracture: poor compliance limits effectiveness. *Clin Nutr* 2003;**22**:497–500.
17. Wouters-Wesseling W, van Hooijdonk C, Wagenaar L, de Groot L, van Staveren W. The effect of a liquid nutrition supplement on body composition and physical functioning in elderly people. *Clin Nutr* 2003;**22**:371–7.
18. Remsburg R, Sobel T, Cohen A, Koch C, Radu C. Does a liquid supplement improve energy and protein consumption in nursing home residents? *Geriatr Nurs* 2001;**22**: 331–5.
19. Sociedad Española para el Estudio de la Obesidad (SEEDO). Consenso SEEDO'2000 para la evaluación del sobrepeso y la obesidad y el establecimiento de criterios de intervención terapéutica. *Med Clin (Barc)* 2000;**115**: 587–97.
20. Chumlea WC, Steinbaugh ML, Roche AF, Mukherjee D, Gopalaswamy N. Nutritional anthropometric assessment in elderly persons 65 to 90 years of age. *J Nutr Elderly* 1985;**4**:39–51.
21. Favier J-C, Ireland-Ripert J, Toque C, Feinberg M. *Répertoire général des aliments. Composition table*. Paris: CIQUAL-REGAL; 1995.
22. Soini H, Routasalo P, Lagström H. Characteristics of the mini-nutritional assessment in elderly home-care patients. *Eur J Clin Nutr* 2004;**58**:64–70.
23. Obey R, Schorr H, Eckert R, Herrmann W. Vitamin B12 status in the elderly as judged by available biochemical markers. *Clin Chem* 2004;**50**:238–41.
24. Clarke R, Grimley EJ, Schneede J, Nexo E, Bates C, Fletcher A. Vitamin B12 and folate deficiency in later life. *Age Ageing* 2004;**33**:34–41.
25. Pfeiffer E. A short portable mental status questionnaire for the assessment of organic brain deficit in elderly patients. *J Am Geriatr Soc* 1975;**23**:433–41.
26. García-Montalvo JI, Rodríguez L, Ruipérez I. Validación del cuestionario de Pfeiffer y la escala de incapacidad mental de la Cruz Roja en la detección del deterioro mental en los pacientes externos de un servicio de geriatría. *Rev Esp Geriatr Gerontol* 1992;**27**:129–33.
27. Peña-Casanova J, Aguilar M, Bertran-Serra I, et al. Normalization of cognitive and functional assessment instruments for dementia (NORMACODEM) (I): objectives, content and population. *Neurology* 1997;**12**:64–8.
28. Reisberg B, Ferris SH, De León MJ, Crook T. The Global Deterioration Scale for assessment of primary degenerative dementia. *Am J Phys* 1982;**139**:1136–9.
29. Auer S, Reisberg B. The GDS/FAST staging system. *Int Psychogeriatr* 1997;**9**:167–71.
30. Sullivan DH, Patch GA, Walls RC, Lipschitz DA. Impact of nutrition status on morbidity and mortality in a select population of geriatric rehabilitation patients. *Am J Clin Nutr* 1990;**51**:749–58.
31. Turic A, Gordon KL, et al. Nutrition supplementation enables elderly residents of long-term-care facilities to meet or exceed RDAs without displacing energy or nutrient intakes from meals. *J Am Diet Assoc* 1998;**98**:1457–9.
32. Gray-Donald K, Payette H, Boutier V. Randomized clinical trial of nutritional supplementation shows little effect on functional status among free-living frail elderly. *J Nutr* 1995;**125**:2965–71.
33. Fuhrman MP, Charney P, Mueller CM. Hepatic proteins and nutritional assessment. *J Am Diet Assoc* 2004;**104**(8):1258–64.