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DEMENTIA AND NUTRITION. INTERVENTION STUDY IN INSTITUTIONALIZED PATIENTS WITH ALZHEIMER DISEASE

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Abstract: Objectives: To know nutritional status of a group of institutionalized patients with moderate Alzheimer's Disease (AD), and to ascertain the effects of an intervention with nutritional supplements on morbidity and mortality after one year follow-up. Patients and Methods: 99 patients (mean age: 86.5 years), 80 women, with a diagnosis of AD according with NINCDS/ADRDA criteria, were recruited from 8 nursing-homes. 25 were included in an intervention group and received a nutritional supplements along 12 months. Evolution was evaluated according to the Functional Assessment Staging Test (FAST). Patients with FAST levels 5-6 were included. General clinical variables as well as variables reflecting cognitive state and nutritional status: anthropometric, biochemical data and Mini Nutritional Assessment (MNA) were analysed. Statistical analysis was carry out with the SPSS 10.0 package. Results: Mean time since diagnosis was 49 months, with a 20.2 months duration of institutionalization. Mean value of MNA was 20.1 ± 3.5. 16.5% of patients had a BMI equal o lower than 21. After one year the intervention group showed higher levels of albumin (P=05), pre-albumin (P=05), iron (P=01), zinc (P=05), and beta-carotene (P=05) than the control group. The same response in BMI (P=05), MNA (P=05), and triceps skinfold (P=01). Mortality was lower (16% vs. 22.7%), without statistical significance, in the intervention group, as it was the number of infectious events (47% vs. 66% P=05), and the days in bed (7.5±2.1 vs. 17.3±5.6 P=05). Conclusion: Nutritional supplements applied to a group of patients with AD living in nursing-homes can reduce morbidity and mortality after one year follow-up.

Key words: Malnutrition, nutrition, nutritional supplements, dementia. Alzheimer's disease, institutionalization.

Introduction

Recent studies have demonstrated that malnutrition is a common condition among elderly people, and is associated with low nutrient and calorie intake (1-3). When comparing with younger groups, it must be concluded that age seems to be an important risk factor for the development of malnutrition. Furthermore, among the elderly there are subgroups with a higher risk of undernutrition, e.g., patients institutionalized in hospitals and nursing homes, and those with chronic illness. A recent review in our country emphasises this point (4).

Elderly patients with dementia are a group with a special interest in this field (5). Alois Alzheimer in his work notes described a slow but progressive weight loss in his first patient. Nevertheless, only recently have investigators studied this issue in longitudinal studies, and they found that weight loss is apparently inexorable. Some studies have observed a significant weight loss, even in the initial stages of the disease, regardless of the caloric content of the diet (6-10). Weight loss has been included in the NINCDS-ADRDA criteria for Alzheimer disease (AD) (11). Several studies have shown that weight loss correlates with the severity and progression of AD (12).

Nutrition not only influences the individual's health status, but it's also important in the maintenance of the immune system function, production of blood elements, and for the synthesis of serum proteins (13,14). Various studies have established that malnutrition is associated with increased morbidity and mortality rates due to, urinary tract infections, dehydration, and with the development of pressure sores (15-17). However, another study showed no correlation between malnutrition and decreased life expectancy in patients with AD (18).

It is not yet clear what determines undernutrition in demented patients (19). Some hypothesis have been proposed:

1. Inadequate intake. Anorexia usually occurs in the final stages of the disease, definitely contributing to weight loss. This anorexia has been attributed to physical changes such as olfactory disturbances or a decrease in the levels of endogenous estrogens. Neuropsychiatric disturbances associated with the disease may also contribute, such as memory loss, impaired judgement, autonomic adaptation, changes in eating habits, or simply the presence of dysphagia (20-21).

2. Increased body requirements as a consequence of metabolic alterations (22,23). Energy consumption may rise with increased physical activity due to agitation, motor conduct disturbances, or elevation of cortisol levels due to a hypercatabolic state (24).

3. Medial temporal cortex atrophy. Patients with AD have significant atrophy of the medial temporal cortex, which plays an essential role in eating behavior and in the regulation of memory and emotions. Another study has described a correlation between the degree of atrophy and weight loss in patients with AD (25).

Other studies have correlated cognitive function in the presence of AD with serum levels of vitamin C, E, B12, B6, folic acid, and beta-carotenes (26, 27). High serum levels of these substances may be associated with better results in cognitive tests scores. Nutritional state appears to condition the integrity of cognitive functions in two ways, through the anti-oxidative effect of certain vitamins and by ensuring adequate levels of vitamin B12 and folic acid (28).

Free radicals have also been implicated in the etiology and pathogenesis of AD in different studies. Oxidative stress refers to the consequences of cellular energy metabolism, which causes oxidative damage and increases the levels of hazardous substances such as nitric oxide and other free radicals. Substances that compensate for defects in energy metabolism and improve mitochondrial function act to reduce free-radical formation, thus increasing anti-oxidative capacity. Such substances could be of therapeutic value in AD.

The use of antioxidants, such as fruits and vegetables rich in vitamins A, C, and E, presumably improves health and has a positive effect on AD and other neurodegenerative diseases (29-33).

The aim of this study was to know the nutritional status of institutionalized patients with moderate AD type dementia and to ascertain the effects of an intervention with nutritional supplements on morbidity and mortality in a one-year follow-up.

Methods

Patients

Ninety-nine patients were recruited from eight nursing homes in Madrid (Spain). All patients had a diagnosis of AD according to the National Institute of Neurological and Communicative Disorders and Stroke / Alzheimer's Disease and Related Disorders Association (NINCDS/ADRDA) (11).

The evolution of the disease was evaluated with the Functional Assessment Staging Test (FAST) (34). We selected patients with a FAST score of 5-6, corresponding to patients with moderate to severe AD.

Patients with a FAST score of 7, corresponding to severe AD, were excluded from the study. Patients with an associated severe illness that interferes with follow-up and patients receiving enteral or parenteral nutrition at the beginning of the study were excluded.

Variables

1. General data: Age, gender, time living in nursing home, duration of AD, associated diseases, and drugs used.

2. Cognitive impairment: Measured by Folstein's Mini-Mental State Evaluation (MMSE) (35). Functional Status was measured using the Blessed scale (36). Disorders in conduct were evaluated with the Cummings' Neuropsychiatry Inventory (NPI), which measures the frequency and severity of behavior changes (37).

3. Nutrition:

a. Nutritional risk: We used the Mini Nutritional Assessment (MNA) test, which has demonstrated in several studies to be of great help in the institutionalized older persons, especially in those with cognitive impairment. MNA results were used to establish three groups: < 17, high risk of malnutrition; 17 – 23, moderate risk; and > 24, no risk of malnutrition (38).

b. Anthropometric data: Weight, height, brachial and calf circumference, biceps, triceps and scapular skin folds. To measure skin folds we used a previously calibrated Holtein foldometer. Using this data to calculate the Body Mass Index (BMI) (39), we established four groups by BMI measurement: < 19, severe malnutrition; 19 – 21, moderate malnutrition; 21 – 23: borderline; > 23 good nutritional status.

c. Biochemical data: Proteinogram, total serum proteins, pre-albumin, lymphocyte count, cholesterol, calcium, phosphorus, uric acid, iron, magnesium, zinc, vitamin A, B, and E levels, and flavonoids (lutein, cryptoxanthine, and lycopene). All blood samples were obtained from the cubital vein in fasting conditions. All samples were analyzed by the Blood Analysis Laboratory of the Hospital Clínico San Carlos of Madrid.

Follow up

Twenty-five patients were randomly assigned to a group which received Nutrison", a nutritional supplement. This supplement was chosen because it is a rich calorie and protein formula, enriched with arginine, glutamine, minerals, and most antioxidants (see nutritional information for this product in Appendix). After one year, all patients were evaluated for cognitive, nutritional, biochemical, and anthropometric data. During this period of follow-up, hospitalization, duration of hospital stays, infections, and deaths were recorded.

Statistical analysis:

All data were analyzed with the SPSS 10.0 package. The dispersion of measurements was measured by standard deviation. All quantitative variables had a normal distribution using the Kolmogorov-Smirnoff test. We parted from the hypothesis that all measurements between groups were equal, rejecting X when the value of T for n-2 degrees of liberty was less than 0.05 alpha.

Results

Ninety-nine patients were included in the study, all with Alzheimer's disease of moderate to severe stage, corresponding to FAST 5-6. General data are shown in table 1. We want to underline the advanced mean age and the dominance of women. The most frequent associated diseases were hypertension, falls and fall-related fractures, constipation, and urinary incontinence. Neuroleptics and benzodiazepines were the most commonly used drugs. Cognitive, conductual, and nutritional findings are shown in table 2. The MMSE and Blessed scores corresponded to moderate to severe dementia.

The most significant biochemical parameters are summarized in table 3. This table shows the percentage of patients with lower-than-normal results in laboratory tests. A large percentage of patients had lower-than-normal total protein, albumin, pre-albumin, iron, zinc, vitamin E, and various flavonoids.

Table 1
General data, indicating a predominance of women and advanced age in the sample.

Data	AD
Sample	99
Women	79.8%
Median age	86.5 ± 6.1
Duration of institutionalization	20.2 ± 18.8
Time from diagnosis (months)	49.1 ± 24
Number of diagnoses	4.5 ± 2
Number of drugs	3.9 ± 1.7
FAST 5	48.5%

Table 2
Cognitive, conductual and nutritional evaluation.

MMSE	12.7 ± 5.3
Blessed	13.8 ± 4.4
NPI	10.2 ± 6.9
MNA	20.1 ± 3.5
< 17	17.5%
17 – 23.5	68.1%
>24	14.4%
BMI	24 ± 3.4
< 19	8.3%
19 – 21	8.2%
21 – 23	27.8%
> 23	55.7%

Regression analysis of MNA and BMI basal results was made with various parameters, the results are shown in table 4. There is a significant positive relation between MNA and BMI, albumin, and the MMSE score, and a negative relation with the Blessed, FAST, and NPI scores. There was a significant positive relation between BMI, brachial circumference, and MMSE score, and a significant negative relation with the Blessed, FAST, and NPI scores.

Table 3
Biochemical data, standard deviation and percentage of patients with lower-than-normal laboratory results.

Parameter	Data
Proteins (g/l)	6.46 ± 0.58
< 6.5	52%
Albumin (g/l)	3.63 ± 0.42
< 3.5	30%
Pre albumin (mg/dl)	19.2 ± 4.8
< 18	27%
Lymphocytes	1,722 ± 533
< 1,200	34%
Cholesterol (mg/dl)	193.3 ± 44.6
< 140	6%
Lutein (mg/l)	0.43 ± 0.22
< 0.32	27%
Cryptoxanthine	0.43 ± 0.25
< 0.27	28%
Iron (mg/dl)	66.7 ± 23.4
< 68	47%
Zinc (mg/dl)	54.3 ± 9.1
<70	80%
Vitamin A (mg/dl)	0.63 ± 0.21
< 0.43	14%
ß-Carotene (mg/l)	0.62 ± 1.32
< 0.14	18%
Vitamin E (mg/l)	6.77 ± 1.32
< 5.8	23%
Lycopene (mg/l)	0.53 ± 0.26
< 0.32	14%

Table 4
Positive and negative relation between nutritional parameters.

MNA	P	r	BMI	p	R
BMI	0.001	+ 0.6	Brachial	0.001	+ 0.52
Albumin	0.005	+ 0.32			
MMSE	0.05	+ 0.20	MEC	0.03	+ 0.23
Blessed	0.001	- 0.5	Blessed	0.02	- 0.24
FAST	0.001	- 0.4	FAST	0.05	- 0.23
NPI	0.002	- 0.3	NPI	0.05	- 0.22

Two groups were established for follow-up: a) A control group of 74 patients, mean age 85.6 ± 4.6 years, 78% women. b) Twenty-five patients who received nutritional supplements (Nutrison“), mean age 84.7 ± 3.8 years, 75% women. All the patients of this group had a very high nutritional supplement compliance. This can be explained because they are institutionalized and had a very close surveillance. The differences between groups in the anthropometric and biochemical findings at baseline and after 1 year follow-up are shown in tables 5 and 6. The difference between the two groups in albumin, pre-albumin, iron, zinc, beta-carotene, and lycopene are statistically significant. No other parameter showed statistically significant results. With regard to anthropometric differences between the two groups, BMI,

bicipital skin folds, and calf perimeter showed statistically significant differences. The other variables had no statistical significance. MNA was also statistically significant.

Table 5
Differences in biochemical data between study and control group.

Data	Intervention	Control	p
Total proteins	+ 0.5	+ 0.4	NS*
Albumin	+ 0.44	+ 0.12	0.05
Pre albumin	+ 2.2	+ 0.7	0.05
Lymphocytes	- 97	+ 119	NS
Cholesterol	+ 11	- 18	NS
Calcium	- 0.2	+ 0.1	NS
Iron	+ 4.9	- 0.2	0.01
Zinc	+ 4.9	- 0.2	0.05
Vitamin A	+ 0.2	- 0.05	NS
Vitamin E	+ 1.1	+ 0.6	NS
b carotene	+ 0.76	+ 0.26	0.05
Cryptoxanthine	+ 0.12	+ 0.11	NS
Lycopene	+ 0.9	- 0.9	0.01
Lutein	+ 0.3	+ 0.3	NS

* NS, No statistical significance.

Table 6
Anthropometric differences between the study and control group.

Data	Intervention	Control	P
BMI	+ 1.6	- 0.3	0.05
MNA	- 0.2	- 3.2	0.05
Brachial (cm)	+ 0.7	- 1.2	NS
Biceps (cm)	+ 1.2	- 0.2	NS
Triceps (cm)	+ 2.4	- 1.5	0.01
Sub scapular (cm)	- 0.8	- 1.5	NS
Calf (cm)	- 0.7	- 1.4	NS

The differences in mortality, infections, and days in bed are shown in table 7. The group that received the nutritional supplement had fewer infections and spent fewer days in bed.

Table 7
Variable analysis of morbidity and mortality.

Data	Intervention	Control	p
Mortality	16%	22.7%	NS
Infections	47%	66%	0.05
One	47%	21%	
Two		30%	
> three		15%	
Days in bed	7.5 ± 2.1	17.3 ± 5.6	0.05

Discussion

Nutritional problems are common in AD. Weight loss is a good indicator of calorie and protein malnutrition in the elderly and has a predictive value of mortality (40).

The baseline biochemical findings in the studied population revealed lower-than-normal total protein, albumin, and pre-albumin levels. These findings confirm the presence of malnutrition in the institutionalized elderly persons with dementia described in different studies. We found that one-fourth of the patients had vitamin and flavonoid deficiency. Flavonoids (cryptoxanthine, lycopene, and lutein) are considered highly antioxidant elements. The high percentage of patients with plasma deficit of iron and zinc was noteworthy. Zinc is important in the aging process. Zinc deficits particularly affect immunological processes (40). The relation between zinc and impaired immunity could explain the reduction in infections in the intervention group. Further studies of lymphocytes are needed in order to explain the relation between nutritional supplements, infections, and immunology.

Vitamin deficits seen in patients with AD could be a consequence of the disease rather than a cause. These patients had a monotonous diet, which could be related with nutritional deficits. In a recent study the administration of selergine and alpha-tocopherol delayed the progression of moderate AD, reduced mortality, and increased functionality (41). In our study we observed important changes in various markers of oxidation, anti-oxidation systems like vitamin E levels, and other antioxidants like flavonoids. The influence of this factors on the evolution and natural history of AD has yet to be defined.

In the intervention group, anthropometric and biochemical parameters improved, although there were no statistically significant differences in cognitive, functional or conduct variables. Similar results have been found in other studies, although more studies with a longer follow-up are needed (41).

Mortality, infections, and days in bed decreased in the intervention group. As remarked, these results can be attributed to the decrease in the number and severity of infections. These findings support the administration of nutritional supplements to moderate and severely demented patients (42-43).

In conclusion, Institutionalized patients with moderate to severe AD have a high risk of malnutrition and vitamin and mineral deficiency. Nutritional supplements do not modify cognitive function, but they do lower morbidity and mortality in these patients. Nevertheless, we still have questions regarding nutritional status and intervention programs in patients with AD in relation to time and duration of intervention, and the kind of supplement to be given. To understand this, longer studies of a larger patient samples, including both patients living at home and institutionalised patients, are needed.

APPENDIX

Nutrison“ Nutritional information.

Presentation	500 µl	Fiber	0.9 g	Vitamins	
Volume	100 µl	- Soluble	0.43 g	- A	133 µg-RE
Energy	125 Kcal	- Insoluble	0.47 g	- ß carotene	67 µg-RE
Proteins	7.5 g (24% energy)	Minerals	- D	0.5 µg	
- Glutamine	1.3 g	- Na	0.11 g	- E	6.7 mg
- Arginine	0.89 g (0.67 g free)	- K	233 mg	- K	4 µg
- Cysteine	0.07 g	- Cl	125 mg	- C	13.3 mg
Carbohydrates	14.5 g (46% energy)	- Ca	67 mg	- B1	0.1 mg
- Lactose	0.01 g	- P	67 mg	- B2	0.11 mg
- Dextrinomaltose	13.96 g	- Mg	20 mg	- Niacin	1.2 mg
- Other	0.52 g	- Fe	1 mg	- B6	0.13 mg
Lipids	4.17 g (30% energy)	- Zn	1 mg	- Folic acid	13.3 µg
- Saturated	2.09 g	- Mn	0.3 mg	- B12	0.2 µg
- MCT	1.72 g	- Cu	0.15 mg	- Pantothenic acid	0.4 µg
- Mono-saturated	0.68 g	- I	10 µg	- Biotin	10 µg
- Poly-unsaturated	1.4 g	- F	0.1 mg	- Colin	20 µg
- ω-6	1.08 g	- Mo	8 µg		
- ω-3	0.3 g	- Cr	7 µg		
		- Se	5 µg		

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