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Original article

Effect of essential amino acid supplementation on quality of life, Amino acid profile and strength in institutionalized elderly patients

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SUMMARY

Background & aims: This study assessed the efficacy of supplemented essential amino acids on depressive symptoms, nutrition, muscle function, daily physical activity, and health-related quality of life (HRQoL) of institutionalized elderly patients.
Methods: Forty-one patients (58.5% women; mean age 79.8 yrs) with sequelae of coronary artery disease (73%), femoral fracture (34%), were randomly assigned to receive oral essential amino acids 4 gr 2 times a day for 8 weeks or isocaloric placebo. Before randomization and 8 weeks after the protocol started, the following variables were measured: depressive symptoms (Geriatric Depression Scale, GDS), nutritional panel (Mini Nutritional Assessment, MNA; serum albumin and prealbumin levels), muscle strength (Hand Grip, HG), Activity Daily Life (ADL), Quality of Life (SF-36, HRQoL) and amino acid profile.
Results: Compared with the placebo group, EAA patients improved nutrition (MNA score 22.6 $\pm$ 1.5 post *vs* 21.8 $\pm$ 1.6 pre; $p < 0.04$, albumin g/dl 4.04 $\pm$ 0.35 post *vs* 3.88 $\pm$ 0.3 pre; $p < 0.01$), GDS(score 10.3 $\pm$ 1.75 post vs 13.85 $\pm$ 3.37 pre; $p < 0.001$), HG (Kg 19.75 $\pm$ 1.7 post *vs* 18.68 $\pm$ 1.36 pre; $p = 0.001$), ADL ($p < 0.04$) and both physical and mental components of SF-36 ($p < 0.002$).
Conclusions: Oral supplementation with essential amino acids improved several determinants of quality of life in institutionalized elderly patients, including depressive symptoms, nutrition, muscle function and daily life activity.
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1. Introduction

Health-related quality of life (HRQoL) is the perception patients have of the impact of a disease (s) from the physical, psychological, social and somatic domains of functioning and well-being.[1]

Improving HRQoL is one of the primary objectives of health care in institutionalized elderly patients, as survival becomes less important than HRQoL as experienced by the patient.

Besides socio-economic status, a number of health-related conditions including bad nutrition,[2] low physical function,[3] depression[4] may affect the HRQoL of elderly patients.

In several studies, depression, present principally in elderly patients living in residential care homes (6–11% for major depression, 30% for depressive symptoms)[5] has been documented to be linked with HRQoL. In surgery hip-fractured patients, HRQoL was more related to depressed-risk groups than physical recovery.[6] In another study, oral supplementation with nutritionally complete formula improved depressive symptoms in acutely hospitalized older patients and during convalescence/rehabilitation periods.[7] Provision of a nutrient dense protein-energy liquid supplement to community-living, frail, undernourished elderly people positively affected their emotional role functioning.[8]

Here, we tested the hypothesis that depression, nutrition, muscle function, daily physical activity and HRQoL could be improved in institutionalized elderly patients by supplementing simple nutritional substances such as essential amino acids (EAAs).

Abbreviations: EAAs, essential amino acids.

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Both biochemical and practical considerations were the rationale behind using EAAs.

First, EAA-induced protein synthesis leads to increased muscle mass/function and physical functioning,[9] a factor that positively affects HRQoL. Second, several EAAs are precursors of brain neurotransmitter synthesis[10] including serotonin, dopamine, norepinephrine, relevant for mood and behavior. Moreover, in clinical practice, increasing protein intake in order to improve body protein synthesis may be challenging for elderly patients since even healthy subjects (from 15% to 41%),[11,12] may eat less protein than their minimal requirement (0.8 g/kg/day) and even if they take adequate protein supplementation, they might be ingesting proteins less efficiently.,[11,12] Finally, recent studies demonstrated that supplementation of the diet with EAAs improves lean body mass, strength and physical function in elderly subjects[13] and it is potentially an efficient method of increasing protein intake without affecting satiety.[14] So, using EAAs may be an obliged method to boost protein synthesis in elderly patients. In order these latter may improve several determinants of quality of life, including depressive symptoms, nutrition, muscle function and daily life activity.

2. Material and methods

2.1. Subjects

Subjects were recruited from a nursing home in Pavia (RSA "F. Pertusati"), where they had been institutionalized for at least 3 months before enrollment; the eligible participants were male and females aged between 75 and 95 years.

Patients with altered glycometabolic control, diabetes mellitus, dis thyroidism and other endocrinopathies and renal failure were excluded.

Indeed these diseases per se may potentially have a negative impact on protein synthesis.

In addition, the selected patients had to have normal nutritional status (BMI$>19<25$ kg/m^2; associated with serum albumin levels >3.5 g/dl), similar physical ability (activity daily living, ADL), normal cognitive function (Mini Mental State Examination, MMSE, score higher than 24).[15] The reason for adopting these latter criteria was to reduce confounding factors influencing depression and HRQoL.[2]

Data were gathered from the end of January 2008 to the end of December 2009. The protocol was approved by the Ethics Committee of the Azienda Sanitaria Locale (ASL) of Pavia and all participants gave their written consent to the study.

2.2. Supplementation protocol

The intervention treatment was an oral Essential Amino Acid (EAA) mixture (Table 1). The control group was treated with an equicaloric amount of maltodextrin placebo (4 g) with the same flavour and appearance as for the intervention product. Subjects were randomized to receive one portion containing 4 g of EAAs, orally twice a day, as snacks at 10:00 a.m. and 5:00 pm, or an identical portion of placebo for 8-week. The oral EAA mixture (Aminotrofic) was manufactured by Professional Dietetics, Milan, Italy. Identical preparation for each treatment group were assigned a subject number according to a coded (AB) block randomization table, prepared by an independent statistician. Investigators were blinded to the randomization table, the code assignments and the procedure. As subjects were enrolled, they were assigned a progressive subject number. Safety was based on the absence of serious side effects from the supplement i.e., gastrointestinal symptoms, such as nausea and diarrhea. Everyday the caregivers, after giving the supplement, asked about the occurrence of unwanted side effects.

Table 1
Nutritional composition of an individual packet containing 4 g of an amino acid mixture used in this study.

Kcal	35.3
Kj	149.9
Total amino acids of which:	4 g
L-Leucine	1250 g
L-Lysine	650 mg
L-Isoleucine	625 mg
L-Valine	625 mg
L-Threonine	350 mg
L-Cysteine	150 mg
L-Histidine	150 mg
L-Phenylalanine	100 mg
L-Methionine	50 mg
L-Tyrosine	30 mg
L-Tryptophan	20 mg

2.3. Procedures

Depressive symptoms were assessed through using the Geriatric Depression Scale (GDS)[16] before and after the treatment period (week 0 and 8). The GDS Long Form is the most widely used scale to evaluate depression in the elderly. This is a 30-item questionnaire in which participants are asked to respond by answering yes or no to how they felt over the past week. Scores of 0–9 are considered normal, depending on age, education and complaints; 10–19 indicate mild-moderate depression and a score over 20 would suggest severe depression. The GDS can be used with healthy, unhealthy and mild to moderately cognitively impaired elderly subjects. It has been extensively used in community, acute and long-term care settings. The validity and reliability of the test has been supported through both clinical practice and research evidence.[17] The scale is commonly used as a routine part of our comprehensive geriatric assessment.

In addition, the subjects were tested with the Short-Form 36-Item Health Survey (SF-36),[18] in order to evaluate their quality of life. The SF-36 questionnaire is a valid generic measure for rating health-related quality of life in several research fields, on the basis of its validity, high internal consistency and high test-retest reliability.[18]

The SF-36 is easy to administer and to compile for respondents, it has extensive psychometric validation and is responsive to treatment in several medical conditions. Response items are usually arranged into eight domains reflecting physical and mental health-related quality of life: physical functioning (10 items), role limitations due to physical functioning (role-physical limitation) (4 items), bodily pain (2 items), general health (5 items), vitality (4 items), social functioning (2 items), role limitations due to emotional functioning (role-emotional limitation) (3 items) and mental health (5 items). The 8 scales were scored between 0 and 100 (worst to best possible health status). For each dimension, the score was the mean of item values obtained by the subject when all items were completed or when the number of missing values was no more than half of the total items. Otherwise, the score was recorded as missing. Moreover, the scales of SF-36 were summarized into two dimensions. The first five scales make up the "physical health" dimension, and the last five form the "mental health" dimension. The vitality and general health scales are parts of both dimensions. Hence, each dimension includes three specific and two overlapping scales. The standardized summary scores for physical (PCS) and mental (MSC) components were calculated and separately used as outcome measures. Also QoL SF-36 was assessed

before and after the treatment period. The capacity of the patients to care for themselves was assessed by the Katz Index of Independence in activities of Daily Living (ADL)[19] prior to enrollment.

The hydraulic Hand dynamometer Jamar (Sammons Preston Rolyan, Bolingbrook, Canada) was used to evaluate muscle function. The dynamometer is an instrument which can objectively and quantitatively evaluate physical parameters of the muscle function in different joints.[20] Both hands were tested three times, the best results for each hand was used in the comparison. The measurement was performed in the sitting position with the arm held in a comfortable position as described by Spijkerman et al .[21] All measurements were made at approximately the same time of day (between 14:00 and 16:00 h).

Ongoing pharmacological treatment at the inclusion time (such as drugs for insomnia, hypertension, diabetes, etc.) was maintained during the study.

2.4. Body composition and nutritional status

Nutritional status was assessed using anthropometric measurements. Body weight and height were measured and Body Mass Index (BMI) (kg/m^2) was calculated. The Mini Nutritional Assessment (MNA) was also performed in all subjects.[22] MNA, which comprises simple measurements and brief questionnaire involves the following: an anthropometric assessment (weight, height and weight loss), a general assessment (lifestyle, medication and mobility) and a dietary assessment (number of meals, food and fluid intake, autonomy of eating self assessment, self-perception of health and nutrition). Patients ate three meals daily, with breakfast between 07:00 and 08:00 a.m., lunch between 12:00 and 1:00 and dinner between 6:00 and 7:00 pm. The food intake was based on a well balanced diet (with standard caloric and macro and micronutrient content) provided by the hospital kitchen that consists of a 4-week rotating menu that repeats itself, so during the study the diet remained similar. Foods served and return by subjects were weighed on a dietetic spring scale by a dietician during meals of a three consecutive days at the beginning and at the end of the study. Nurses who served foods to the subjects between meals recorded the quantity of food consumed in household measurements. A computer program was used to calculate the energy and the macronutrients content of food consumed.

2.5. Biochemical analysis

Venous blood samples, taken at 8:00 a.m., were drawn from the antecubital vein in fasting patients to determine plasma amino acid concentrations, although we focused on Branched Chain Amino Acids (BCAAs: leucine, valine, isoleucine), phenylalanine (Phe), tyrosine (Tyr) and tryptophan (Trp), precursors of brain neurotransmitters. We then calculated the tryptophan ratio:

$$\text{teyptophan ratio} = \text{Trp}/(\text{Tyr} + \text{Phe} + \text{BCAAs})$$

The tryptophan ratio reflects the brain tryptophan concentration, which is related to brain serotonin synthesis and concentration.[23] Insulin resistance was estimated using the Homeostasis Model Assessment (HOMA)[24] as follows:

$$\text{HOMA} = \frac{\text{blood glucose level (mmol/1)} \times \text{fasting serum insulin level}(\mu\text{U/ml})}{22.5}$$

The normal value of HOMA in healthy elderly patients aged 61–81 years is <2.4.,[25,37] The concentration of free amino acids in the plasma was measured using the AminoQuant II amino acid analyzer based on the HP 1090 HPLC system with fully automated pre-column derivatization using both ortho-phtalaldehyde (OPA) and 9-fluorenylmethyl-chloroformate (FMOC) reaction chemistry according to the manufacturer's protocol.

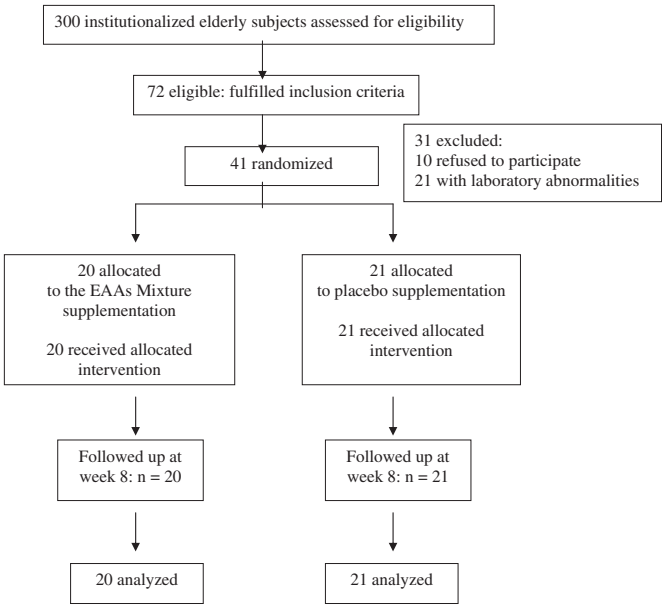

Fig. 1. Flow diagram of a trial supplementation with EAAs mixture vs placebo to treat eld**erly subjects with lower health-related qu**ali**ty of life and mild depressive symptoms. The diagram includes the number of patients analyzed for the main outcome (effect on quality of life).**

Amino acid detection was performed measuring UV absorbance at 338 and 262 nm, respectively. The procedure used was as follows: 2 ml samples of plasma were de-proteinized by adding 500 μl of 0.5 N HCl and, after centrifuging at 5,000 g for 10 min at 5 °C, the supernatant was concentrated up to 200 μl under a nitrogen stream and further filtered on a 0.45 μm Millipore filter. Aliquots (1 μl each) were automatically transferred to the reaction coil and derived with the reagents mentioned above. The remaining de-proteinized serum was stored at 20 °C. Analyses were performed in duplicate, and the value reported for each amino acid was the mean of two independent measurements. The average minimum detectable level of amino acid was 3–5 pmol for each microliter of material injected. Amino acid concentration was expressed as mmoles per liter.

2.6. Statistical analysis

Descriptive statistics were performed reporting means and standard deviations for all recorded variables. An unpaired *t*-test was used to compare the two groups for baseline demographic-, and nutritional intake characteristics.

A repeated measure analysis of variance model with one factor was applied to test differences in trend over time (baseline *vs* 8-weeks) of all variables between amino acid-supplemented patients and controls. In particular, a significant interaction term indicated by the analysis supported the finding of a difference in trend over time between groups.

Table 2
Baseline demographics and nutritional intake of studied subjects.

	Control group	EAAs supplemented group	*p* value
Variables			
Age (year)	79.9 ± 6.2	83.5 ± 7.6	ns
Level of schooling (year)	9.5 ± 3.8	9.7 ± 1.7	ns
Body weight (kg)	64.1 ± 8.9	60.8 ± 5.9	ns
Body Mass Index (kg/m^2)	22.1 ± 2.6	21.8 ± 2.3	ns
Daily nutritional intakes			
Energy			
Kcal/day	1920 ± 350	1550 ± 215	ns
Kcal/kg	30.1 ± 6.8	25.5 ± 1.5	ns
Proteins			
g/day	59 ± 8	50.1 ± 12	ns
g/kg	0.92 ± 0.16	0.82 ± 0.2	ns
Fat			
g/day	54 ± 12	46 ± 9	ns
g/kg	0.84 ± 0.18	0.75 ± 0.15	ns
Carbohydrates			
g/day	225 ± 44	204 ± 32	ns
g/kg	3.5 ± 0.7	3.35 ± 0.5	ns

Data are expressed as mean ± standard deviation (SD).
Statistical analysis: Unpaired *t*-test placebo group vs EAAs supplemented group.
ns: not significant.

3. Results

All 300 patients institutionalized in the nursing home were assessed for eligibility: 72 were eligible participants. A total of forty-one subjects were enrolled, out of 72 eligible participants: 10 cases were excluded because they refused to participate and 21 had laboratory abnormalities (severe ischemic heart disease in eight cases, uncontrolled diabetes in seven cases, hypertension not properly controlled by pharmacological treatment at the observation time in four case, and increased creatinine value compared to baseline in two cases) as shown in Fig. 1. Following the randomization model, 20 subjects were included in the intervention group (males/females: 9/11), and 21 in the placebo group (males/females: 8/13). The groups were similar for distribution of major diseases: stable coronary artery disease 70% in intervention-, 76% in placebo group; proximal femoral fracture 30% in intervention-, 38% in placebo group; hypertension 50% in intervention, 57% in placebo group. For all patients the hip fracture had occurred at least 45 days before the beginning of the study (49 ± 4 days before for treated group and 51 ± 6 before for placebo group).

3.1. Baseline characteristics

The two groups of patients at enrollment were similar in demographic, education, daily nutritional intake (Table 2). The results showed that the 2 groups, at the start of the study were similar in biohumoral (including amino acids) variables, muscle functioning (grip strength), physical performance (ADL), quality of life (PCS and MCS) depression levels (GDS) (Table 3).

3.2. Time courses of variable changes

Two months after protocol started, patients on EAAs improved their depression levels, while, those on placebo tended to have deteriorated depressive symptoms (GDS score) (interaction $p < 0.001$) (Fig. 2).

Nutritional intakes of experimental and control patients did not change over time (Table 4).

Both groups improved their nutritional status. Among nutritional variables, MNA score and serum prealbumin levels improved in both groups but there was more increase for patients on EAAs. Serum albumin levels tended to be lower in placebo group and higher in EAA group (interaction $p = 0.014$).Both groups improved

Table 3
Variables analyzed in the two study groups at baseline and eight-weeks after protocol started.

	Control group		EAAs supplemented group		Overtime global changes	Interaction
	baseline	8 weeks	baseline	8 weeks		
Variables						
Blood glucose (mg/dl)	80.7 ± 7.8	78.8 ± 5.9	76.1 ± 8	74 ± 7	ns	ns
HOMA model (score)	2.2 ± 1.1	2.1 ± 1.3	2.3 ± 0.9	2.1 ± 1.2	ns	ns
Nutritional variables						
BMI (kg/m^2)	22.19 ± 2.67	22.26 ± 2.67	21.80 ± 2.33	21.87 ± 2.34	ns	ns
MNA (score)	22.55 ± 1.71	22.83 ± 1.48	21.80 ± 1.6	22.65 ± 1.50	<0.001	0.047
Serum albumin (g/dl)	3.88 ± 0.39	3.83 ± 0.43	3.88 ± 0.30	4.04 ± 0.35	ns	0.014
Serum prealbumin (mg/dl)	17.90 ± 3.081	18.19 ± 3.043	17.05 ± 4.58	19.40 ± 3.016	0.002	0.015
Muscle function						
Hand Grip (kg)	18.46 ± 1.14	18.50 ± 1.04	18.68 ± 1.36	19.75 ± 1.7	0.001	0.001
Physical performance						
ADL (score)	5.38 ± 0.59	5.38 ± 0.59	5.30 ± 0.65	5.55 ± 0.51	0.044	0.044
Cognition						
MMSE (score)	27.10 ± 2.04	27.14 ± 2.21	26.05 ± 2.089	26.05 ± 2.089	ns	ns
Plasma amino acids						
Tyrosine (μmol/L) (nv 52 ± 5.7)	51.17 ± 20.69	52.29 ± 16.14	45.58 ± 10	56 ± 15.10	ns	ns
Valine (μmol/L) (nv 154 ± 13)	149.24 ± 49.36	173.45 ± 36.66	164.32 ± 16.46	182.49 ± 36.61	ns	ns
Methionine (μmol/L) (nv 20.5 ± 7.9)	28.39 ± 8.47	19.23 ± 8.93	7.60 ± 0.62	8.60 ± 1.47	0.001	<0.001
Tryptophan (μmol/L) (nv 51 ± 4.6)	20.59 ± 2.44	21.35 ± 8.68	27.25 ± 5.54	32.47 ± 5.64	0.067	ns
Phenylalanine (μmol/L) (nv 46 ± 5.6)	31.81 ± 10.68	39.10 ± 13.90	42.92 ± 5.34	57.03 ± 15.18	0.015	ns
Isoleucine (μmol/L) (nv 46 ± 5)	45.64 ± 11.53	45.34 ± 11.47	37.33 ± 5.95	46.16 ± 10.36	ns	0.049
Leucine (μmol/L) (nv 78 ± 6.3)	75.51 ± 22.17	86.13 ± 20.75	65.23 ± 7.40	76.66 ± 19.77	0.028	ns
Trp ratio (μmol/L) (nv 9.3 ± 1.1)	6 ± 1.5	5.7 ± 3.3	7.6 ± 1.4	8.1 ± 1.6	ns	0.05

Data are expressed as mean ± standard deviation (SD).
Statistical analysis: Anova test; Overtime global changes = comparison between values at baseline and 8 weeks irrespective of treatment; Interaction = comparison in trends over time between control and EAAs supplemented groups.
ns = not significant.
nv = normal value.
HOMA = homeostatic model assessment; BMI = Body Mass Index; MNA = Mini Nutritional Assessment; ADL = Activity Daily Life; MMSE = Mini Mental State Examination test.

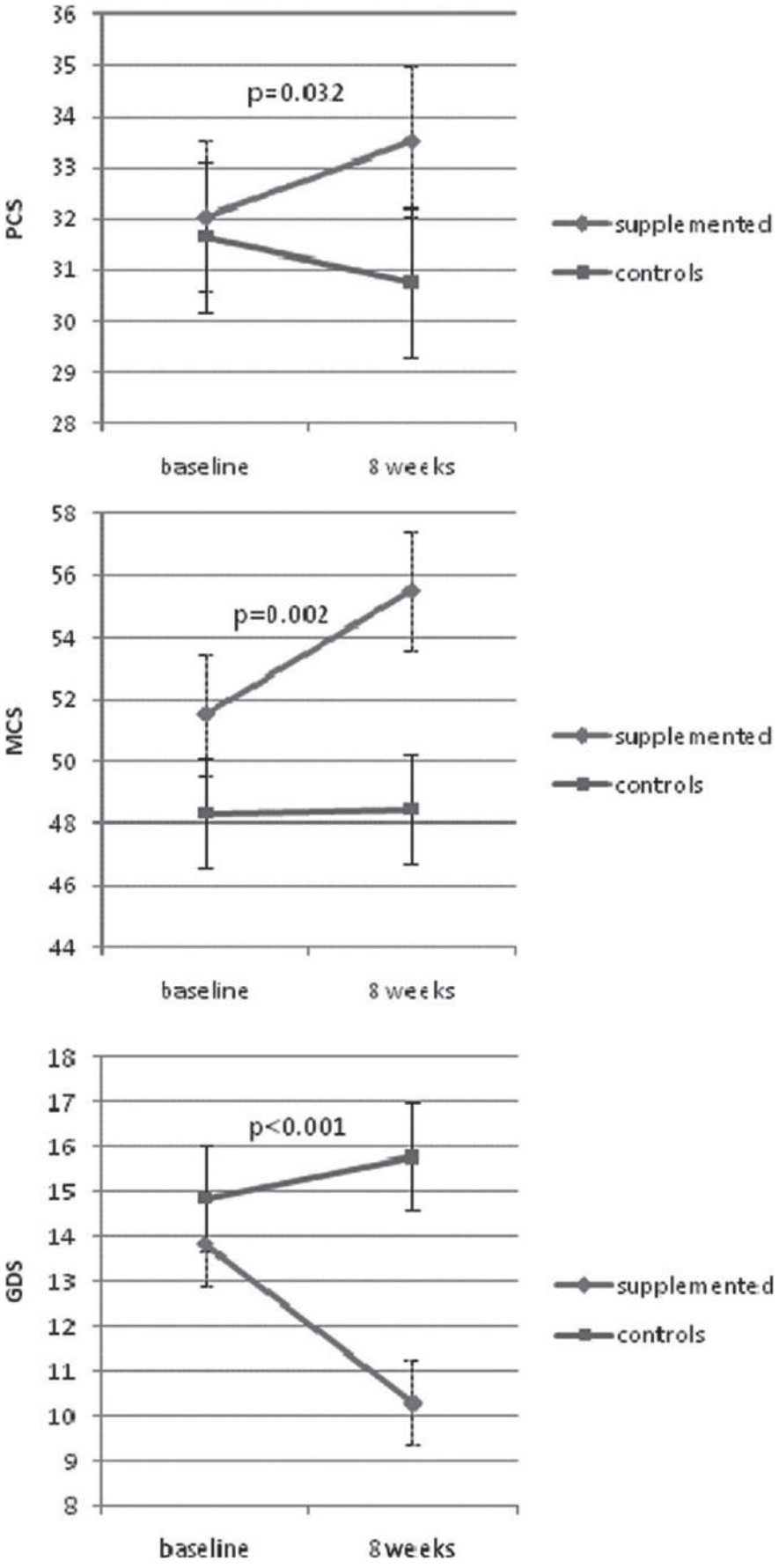

Fig. 2. Trend over time of PCS (Physical Component Score), MCS (Mental Component Score) of QoL SF-36 test and GDS (Geriatric Depression Scale) in supplemented patients and controls.

Table 4
Nutritional intakes of experimental and control patients at beginning of the study and after 8 weeks.

	Control group		EAAs supplemented group		*p* value
	baseline	8 weeks	baseline	8 weeks	
Daily nutritional intakes					
Energy (Kcal/day)	1920 ± 350	1800 ± 273	1550 ± 215	1668 ± 339	ns
Proteins (g/day)	59 ± 8	60 ± 9	50.1 ± 12	55 ± 11 [a]	ns
Fat (g/day)	54 ± 12	55 ± 11	46 ± 9	53 ± 14	ns
Carbohydrates (g/day)	225 ± 4	220 ± 5	204 ± 3	219 ± 4	ns

Data are expressed as mean ± standard deviation (SD).
Statistical analysis: Anova test; control group vs EAAs supplemented group.
ns: not significant.
[a] the figure included nitrogen of supplemented EAAs.

muscle function (handgrip), but improved more in EAA than in the placebo group (interaction $p = 0.001$) (Table 3).

Baseline performance on daily life activities was unchanged over time in controls but improved in patients on EAAs (interaction $p = 0.04$).No change was observed over time for cognition (MMSE) either for placebo-or EAA patients.

Placebo and EAA patients reduced and respectively improved their quality of life as indicated by MCS and PCS components (interaction = 0.02 and respectively $p = 0.032$) (Fig. 2).

Plasma insulin, peripheral tissue insulin sensitivity (HOMA model) and glucose concentration remained virtually unchanged over time in both groups. Plasma Trp ratio tended to be lower in controls and higher in patients on EAAs (interaction $p = 0.05$) suggesting a preferential entry of tryptophan into brain in the latter group.

4. Discussion

The study indicates that supplemented EAAs to elderly patients may improve depressive symptoms and physical performance and potentiates the retrieval of QoL, muscle strength and nutritional status. The GDS score of the subjects studied indicates that they were suffering from moderate depression, which is widespread in the nursing home population[26].

Improvement of depression is of great clinical significance as depressive symptoms is associated with a number of adverse conditions[4] including increased cardiovascular risk, silent cerebral infarctions, white-matter hyper intensities, amplified immune response, falls, unintentional weight loss, decreased muscle strength and frailty, poor psychosocial adjustment after a somatic event.

In this study, reduced depression probably contributed to the gain in ADL since the severity of depression risk predicts physical recovery in elderly patients with hip fractures,[6] 34% of the study patients.

The ADL score of the subjects studied are a typical score among institutionalized elderly[27]

In respect to improving depression, EAAs might act by both direct and indirect means. Directly, EAA may have increased brain serotonin synthesis as suggested by higher Trp ratio in treated patients than in placebo ones. Thus t he study seems to suggest that patient mood improvement was more sensitive to serotoninergic pathway than to other neurotransmitter pathways, including norepinephrine one.

In this study we can not explain the higher Trp ratio in EAA-than in control group. We postulate that the trend towards higher improvement in insulin tissue sensitivity observed in treated group could have favored the increase in both plasma Trp and Trp ratio. Indeed peripheral tissue amelioration of insulin sensitivity favors the entry of amino acids into the muscles, but muscle uptake of BCAAs and other amino acids is proportionally higher than that of Trp[28]. Consequently plasma Trp concentration increases relatively to other amino acids. In this way Trp ratio results increased.

EAAs may indirectly relieve depression by improving patient nutritional status as indicated by the gain in MNA score. This is in line with previous studies documenting the positive effect of nutritional supplementation on depression levels in hospitalized older patients [7] as well as in undernourished community-living frail elderly people. [8]

EAAs can improve nutritional status by both inducing protein anabolism[29], independent of insulin[30], and boosting aerobic metabolism, essential for protein synthesis. Anabolic process is suggested by increases in visceral protein synthesis (serum albumin and prealbumin concentrations) and muscle strength. This occurs with plasma insulin concentration and insulin sensitivity of peripheral tissue similar between the two groups. EAAs can also increase protein synthesis by favoring aerobic energy formation, essential for protein synthesis.

Improvements in nutritional status in this study agrees with other investigations that used the same EAA formula, with the same dose, in individuals suffering from chronic heart failure [9] and severe chronic obstructive pulmonary disease.[31] Like reduced depression, improvements in nutritional status and muscle function may have contributed to increase ADL in treated patients.

This study shows that all patients, independent of their randomized allocation, improved the subjective view of their own health state (HRQoL). This is probably an effect of better care in specially organized settings. However, the improved quality of life was more marked in treated than in non-treated patients. This is not surprising given the results of the study. Indeed, HRQoL is linked to nutritional status, [3,14] physical function, decreased depression.[32] Improvement in QoL was probably not influenced by cognition as the two groups of patients had similar (normal) cognitive functions.

The study offers some practical considerations. Eight grams a day of EAA formula used in the study provide 2.5 g of leucine, the most important amino acid for protein synthesis. This is the amount of leucine content in 160 g of cow lean meat. EAA supplementation could be useful for those individuals who do not or can not eat protein-rich foods.

It is of note that EAAs may be superior than to giving high-protein diets to increase muscle mass and strength and protein synthesis[33].

The amount of leucine provided by 8 g EAA formula should not be underestimated as it represent more than 30% of measured daily leucine oxidation (8g/day)[34].

As the effects of EAAs on protein synthesis seem to lost between 3 h[35] and 6 h[36], the absence of measured plasma amino acid profiles after EAA ingestion might be a limitation of the study.

Future investigation addresses the effect of EAAs on catabolism of contractile fibre proteins[35] by measuring plasma level of 3

methylhistidine. This could better explain the improvement in muscle strength observed in subjects.

In conclusion the study indicates that EAAs supplementation can meet a number of important contributory factors to improve quality of life. The value of HRQoL is important not only for patients, obviously, but also for clinical practice because patients have better treatment compliance, are more satisfied with the consultation and report less symptoms.[37]

Therefore, this study indicates the efficacy in elderly institutionalized elderly patients of supplemented essential amino acids in improving a vast array of determinants of quality of life such as nutritional status, muscle function, physical performance, depression.

Statement of authorship

None of the authors had a financial or personal interest in any company or organization sponsoring this study.

Conflict of interest

All authors disclose any financial and personal relationships with other people or organisations that could inappropriately influence this work.

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MR and RA designed research; MR, NA and AO conducted research; PI provided essential materials; FB performed statistical analysis; MR, EP and RA wrote paper; MR, AO, RA, FB, EP, NA had primary responsibility for final content. FSD helped the authors to discuss the study.

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