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Biochemical and nutritional profile of patients with exclusive enteral nutrition during hospitalization

Perfil bioquímico y nutricional de pacientes con nutrición enteral exclusiva durante hospitalización

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RESUMEN

Introducción: La terapia de nutrición enteral (TNE) tiene la finalidad de recuperar el estado nutricional de los pacientes.

Objectivo: Se evaluó el perfil bioquímico y nutricional de pacientes hospitalizados con nutrición enteral exclusiva.

Métodos: Estudio longitudinal, con muestra compuesta por 42 adultos y ancianos hospitalizados, con TNE exclusiva, por lo menos siete días. Los pacientes fueron sometidos a evaluación nutricional, antropométrica (Índice de Masa Corporal, área muscular del brazo corregida y circunferencia del brazo) y bioquímica como albúmina, proteína C-reactiva, vitamina C, hierro zinc y cobre sérico.

Resultados y Discusión: Se observó que los parámetros antropométricos como el peso, IMC, área y circunferencia muscular del brazo aumentaron durante el tiempo de internación solo en los ancianos (P= 0.016; P=0.018; P = 0.021; P = 0.020). El porcentaje de adecuación de energía, proteica y micronutrientes como vitamina C, hierro, zinc y cobre fueron adecuados durante el tiempo de internación para ambos grupos de edad, de acuerdo con las necesidades medias estimadas. Los niveles séricos de estos micronutrientes se mantuvieron dentro de los valores normales para ambos grupos de edad, a excepción del zinc, que disminuyó durante la hospitalización en ancianos. Esto puede asociarse a la mayor necesidad de este mineral en este grupo de edad o a un deterioro en su absorción.

Conclusión: La TNE influye en el aumento de peso y la masa muscular en ancianos y, apesar de la administración adecuada de micronutrientes, se observó un deterioro en la absorción de zinc. Por lo tanto, el monitoreo de la nutrición enteral es esencial para evitar el empeoramiento del estado nutricional durante la hospitalización.

PALABRAS CLAVES

Evaluación nutricional; Desnutrición; Absorción; Micronutrientes; Deficiencia de proteína.

ABSTRACT

Background: Enteral nutrition therapy (ENT) is intended to restore the nutritional status of patients.

Objective: The objective of this study was to evaluate the biochemical and nutritional profile of hospitalized patients with exclusive enteral nutrition.

Methods: It is a longitudinal study, with a sample of 42 hospitalized young and elder adults, with exclusive ENT, for at least seven days. The patients were submitted to nutritional, anthropometric (Body Mass Index, corrected arm muscle area

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and arm muscle circumference) and biochemical evaluation as albumin, hemoglobin, C-reactive protein, vitamin C, Iron, Zinc and Copper serum.

Results and Discussion: It was observed that anthropometric parameters such as weight, BMI, muscle area and circumference increased during hospitalization time only in the elderly (P= 0.016; P=0.018; P = 0.021; P = 0.020). The percentage of adequacy in energy, protein and micronutrients with vitamin C, iron, zinc and copper were adequate during hospitalization for both age groups, according to the estimated average needs. Serum levels of these micronutrients were within normal values for both age groups, with the exception of zinc, which decreased during hospitalization in the elderly. This may be associated with the greater need for this mineral in this age group or with a implicate in its absorption.

Conclusion: The ENT influence the weight and muscle mass gain in hospitalized elderly patients and, although the appropriate administration of micronutrients, the absorption of zinc was affected. Therefore, monitoring of enteral nutrition is essential in order to avoid worsening nutritional status during hospitalization.

KEY WORDS

Nutritional assessment; malnutrition; Absorption; Micronutrients, Protein Deficiency.

INTRODUCTION

Accelerated aging reveals an increase in the number of hospitalized elderly people, who, due to metabolic, physiological, anatomical and psychosocial changes inherent to their age, are considered to be nutritionally vulnerable. These nutritional imbalances are known to be related to increased mortality, susceptibility to infections and reduced quality of life[1].

Several studies recognize the influence of nutritional status on the clinical evolution of these patients, in which the assessment of the nutritional status of hospitalized patients is fundamental to identify the presence of malnutrition and muscle depletion during hospitalization[2]. In this age group, anemia is frequent, with a high prevalence and is present in about 10% of individuals over 65 years of age[3].

However, malnutrition in hospitalized patients is not frequently evaluated in Brazil and its prevalence remains high[4]. Thus, the presence of malnutrition observed in hospitalized patients requires a rigorous nutritional control and should be investigated from admission to discharge, in order to identify patients with an increased risk of complications associated with nutritional status during hospitalization[5]. Malnutrition in the elderly may lead to anaemia and immune deficiency, therefore, risk factors for poor survival included decreased or decreasing serum albumin levels, increasing age or over 80 years and male gender, and malnutrition in the elderly may lead to anemia and immune deficiency[6].

In this context, the administration of enteral nutrition therapy (ENT) in a hospital environment is common, in order to meet the nutritional needs of the individuals, once the oral route is impossible. ENT aims to provide the outpatient or hospitalized patient with the quantity and quality of nutrients needed to maintain and restore nutritional status[7].

Among the micronutrients monitored in this study, the ones that act on the main consequences of malnutrition, as for example, anemia and muscle depletion were opted for, such as iron (Fe), which has a fundamental function for cellular homeostasis, mainly used for the synthesis of hemoglobin, its deficiency has consequences for the whole organism, with anemia being the most relevant disorder[8]; Copper (Cu) acting in iron homeostasis, and present as cofactor of several enzymes, in mechanisms of antioxidant protection and formation of collagen and elastin[9]; Zinc (Zn) for being a mineral with physicochemical characteristics that allow its extensive participation in the metabolism of proteins, nucleic acids, carbohydrates and lipids[10]. With a protection function, vitamin C participates in the cellular processes of oxidation and reduction, being important in the defense of the organism against infections and fundamental in the integrity of the walls of the blood vessels. It is essential for the formation of collagen fibers existing in virtually all tissues of the human body, such as the dermis, cartilage and bones[11].

Therefore, there is concern about the early initiation of ENT in the hospitalized patient, when necessary, in order to guarantee the efficiency in the adequacy of a nutritional support to increase the quality and benefits in the evolution of the critically ill patient. Thus, the present study aimed to evaluate the biochemical and nutritional profile of hospitalized patients with exclusive enteral nutrition.

METHODS

A longitudinal, prospective non-randomized study with convenience sampling. The research involved patients hospitalized during the interval from October 2016 to August 2017 in a public hospital. The study included young adults and elderly, of both genders, with exclusive enteral nutrition, for at least seven days, hospitalized for up to 72 hours in the medical clinic of the hospital. Patients with enteral nutrition associated with other forms of oral or parenteral feeding; patients with edema, sepsis, mechanical ventilation, renal failure; patients to whom performing an anthropometric evaluation would be impossible or patients in palliative care were excluded from the study.

This study was approved by the Ethics and Research Committee and is registered under the number 2.103.411. Data collection occurred after written informed consent was obtained from the patients or their guardians and consisted of

medical records with all the personal identification data of the patient, such as age, gender, clinic of hospitalization with medical diagnosis and associated diseases.

Nutritional assessment of hospitalized patients

The nutritional assessment was composed by dietary, biochemical and anthropometric parameters. For dietary assessment, data such as: energy and protein nutritional needs, daily evolution of the prescription and dietary administration with total caloric value (TCV), protein, type of diet, caloric density and infusion volume (ml/day and ml/hour) were collected daily by means of an electronic medical record, used by hospital professionals.

The assessing energy needs wad used according to the nutritional diagnosis, from 30 to 35 kcal/kg of current weight for undernourished patients; from 25 to 30 kcal/kg of current weight for eutrophic patients; 25 kcal/kg of current weight for overweight patients; and 20 to 25 kcal/kg of adjusted weight for obese patients. The protein quantity offered varied from 0.8 to 2.0 g/kg of current weight, according to the hospital protocol for each diagnosis. In both groups, the patients started at the goal rate within 72 hours.

The enteral diets available at the study hospital were normocaloric and normal protein, with a caloric density of 1.0 Kcal/ml, one of them with hydrolyzed nutrients. Also, hypercaloric diet with a caloric density of 1.2, 1.5 and 2.0 Kcal/ml, hyperproteic diet with a variation of 7.5 to 10 grams of protein per 100 ml of diet, one of them with the addition of fibers in the composition. Regarding micronutrients, enteral diets had very varied amounts of zinc, copper, vitamin C and iron, as well as other micronutrients that were not assessed in this study.

The anthropometric measures were determined by a single trained evaluator, with the aim of avoiding bias in the study. The weight, circumferences and skinfolds were checked weekly. As most patients were bedridden and unable to stand, the weight (kg) and height (m) were estimated using the criteria of Chumlea et al.[12] and Gray et al[13], respectively. The Body Mass Index (BMI, kg/m²) was measured and the criteria used for classification were WHO[14] for adults and Lipschitz[15] for the elderly, the percentage of weight loss (%WL) was classified by parameters of Blackburn and Bistrian[16].

Measurements of arm circumference (AC, cm) and calf circumference (CC, cm) were performed using an inelastic tape measure. The triceps skinfold thickness (TST, mm) and the thumb abductor muscle thickness (TAMT, mm) were determined using the scientific plicometer Cescorf® and performed in triplicate. The arm muscle circumference (AMC, cm²) was obtained by means of the TST and AC formula according to criteria suggested by Blackburn and Thornton[17]; the corrected arm muscle area (CAMA cm²) was determined using the formula with the result of AMC (cm²) also according to Blackburn and Thornton[17]; the fatty area of the arm (FAA, cm²) was determined by AC and CAMA, according to Frisancho[18].

The biochemical assessment was performed weekly, according to data recorded in medical records, by medical request, and it was composed of the interpretation of the hemogram, albumin, C-reactive protein (CRP), urea, creatinine, potassium, sodium, calcium and the capillary glycemia monitoring. In addition to these analyses, the lipid profile and determinations of vitamin C and the chemical elements Iron (Fe), Zinc (Zn) and Copper (Cu) were carried out in other laboratories. The analyses are described below:

- Lipid Profile

Samples were stored at -80 ° C. Aliquots of serum samples were used to evaluate the total cholesterol (TC) and triglycerides (TG) by colorimetric method and the high density lipoproteins (HDL) by enzymatic means. The plasma LDL-cholesterol level was defined by the Friedewald equation[19], which estimates the plasma LDL-cholesterol level by total cholesterol plasma concentrations, HDL-cholesterol and VLDL from the concentration of triglycerides.

- Iron (Fe), Zinc (Zn) and Copper (Cu)

The parameters were measured with approximately 50 µl of plasma and transferred to a teflon flask (PTFE-TFM) of a microwave radiation-assisted decomposition system (model, Multiwave 3000, Anton Paar, Austria). About 3 mL of concentrated nitric acid were added, and the flasks were sealed and inserted into the system at a heating temperature of 210°C and a maximum pressure of 30 bar. Cu, Fe and Zn were determined using an inductively coupled plasma optical emission spectrometer (ICP-OES) (model, Optima 4300DV, Perkin Elmer). The wavelengths evaluated were 324,752, 238, 204, 206, 200 nm for Cu, Fe and Zn, respectively. Results were expressed as µg/dL.

- Vitamin C

The determination of vitamin C or ascorbic acid, was performed according to Jaques-Silva et al.[20]. Plasma was precipitated with trichloroacetic acid (10%) in the ratio of 1.5/1 and centrifuged for 15 minutes at 3000 rpm. The supernatant was mixed with dinitrophenylhydrazine (DNPH), after incubation for 3 hours at 37ºC. Then 100µl of H_2SO_4 (65%) were added to stop the reaction. The ascorbic acid content was calculated using the curve of (1.5-9) mol/l of ascorbic acid and expressed as µg of ascorbic acid/ mL plasma.

Statistical analysis

The sample size calculation considered the number of hospitalizations per month, in which 95% confidence level and 5% margin of error were used. The data were analyzed with

the software Statistica 10. Statistical analysis was performed using analysis of variance with repeated measures (ANOVA). The descriptive analysis of the data was performed to demonstrate the baseline characteristics of the patients. Data were considered statistically significant when $p < 0.05$ and were presented as mean ± standard deviation or median when appropriate.

RESULTS

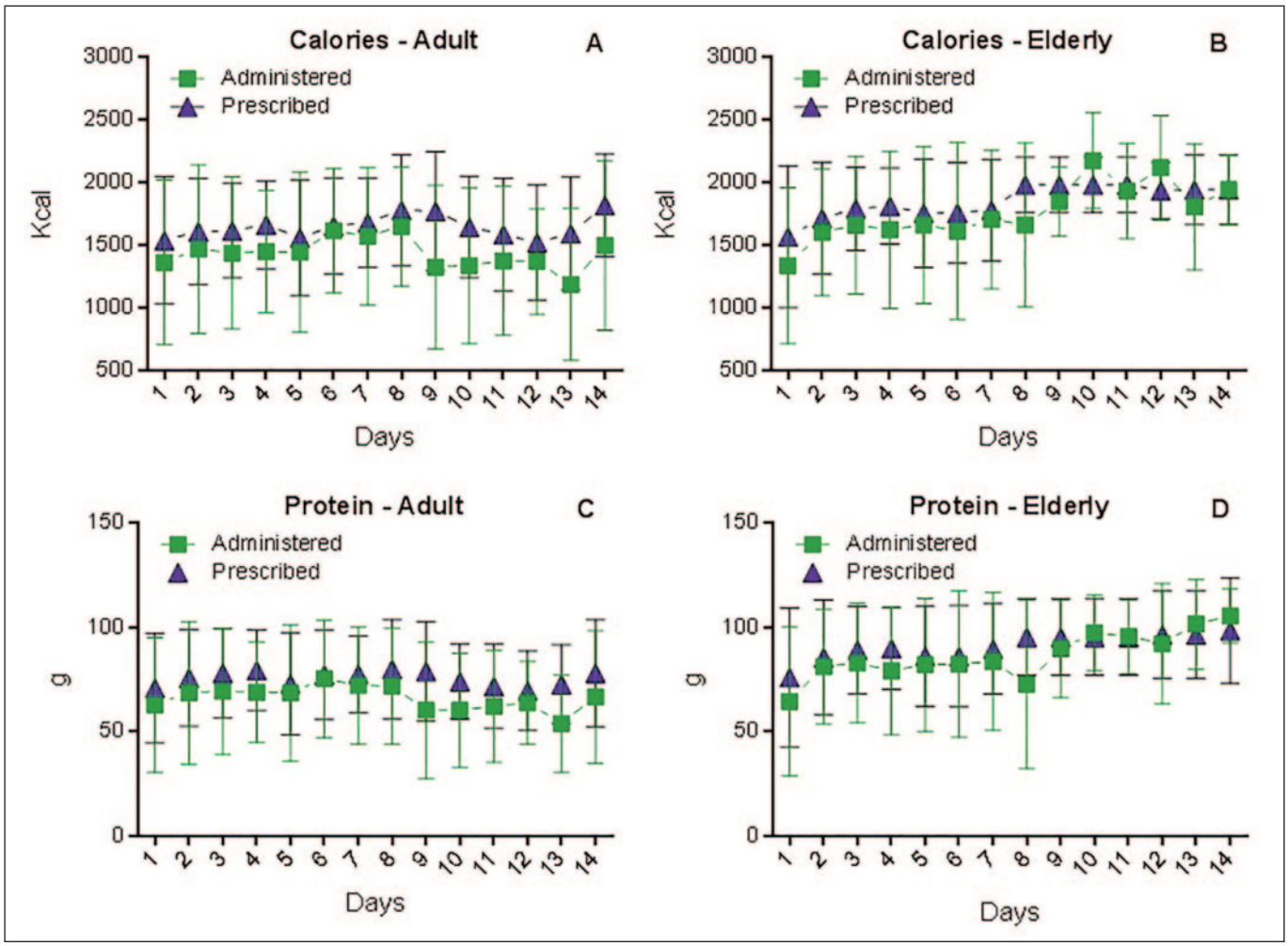
The population initially consisted of 78 patients, however, 36 had no follow-up of at least seven days and were excluded from the study. Thus, 42 individuals were included in the study, 24 adults with a mean age of 45.5 ± 10.1 years, and 18 elderly with 67.5 ± 6.5 years, of which 59.5% (n=25) were male, 40.5% (n=17) were female.

Regarding the follow-up period, all patients were followed for at least seven days (n=42). After this period, only 42% of the sample (n=18) remained hospitalized with exclusive enteral nutrition (14 days). The remaining patients were excluded from the study due to reasons such as oral feeding, hospital discharge, intensive care unit (ICU) transfer, adherence to palliative care or death. Only two patients remained with exclusive EN after two weeks (> 14 days), but due to the small number of patients, the results were not considered in the present study.

The energy and protein balance of the individuals during the time of hospitalization were analyzed and the patients were observed to receive lower amounts of calories and protein in relation to that prescribed in both age groups. However, from the 9th day onwards, it was observed that the elderly received caloric and protein amounts of ENT closer to their needs in relation to adults (Figure 1).

Although the prescribed calories and protein values fell short of the amount administered, the adequacy rate was

Figure 1. Values of prescribed calories versus administered in adults (A) in the elderly (B), prescribed protein versus administered in adults (C) in the elderly (D) in hospitalized patients during hospitalization time.



Data presented in mean ± SD.

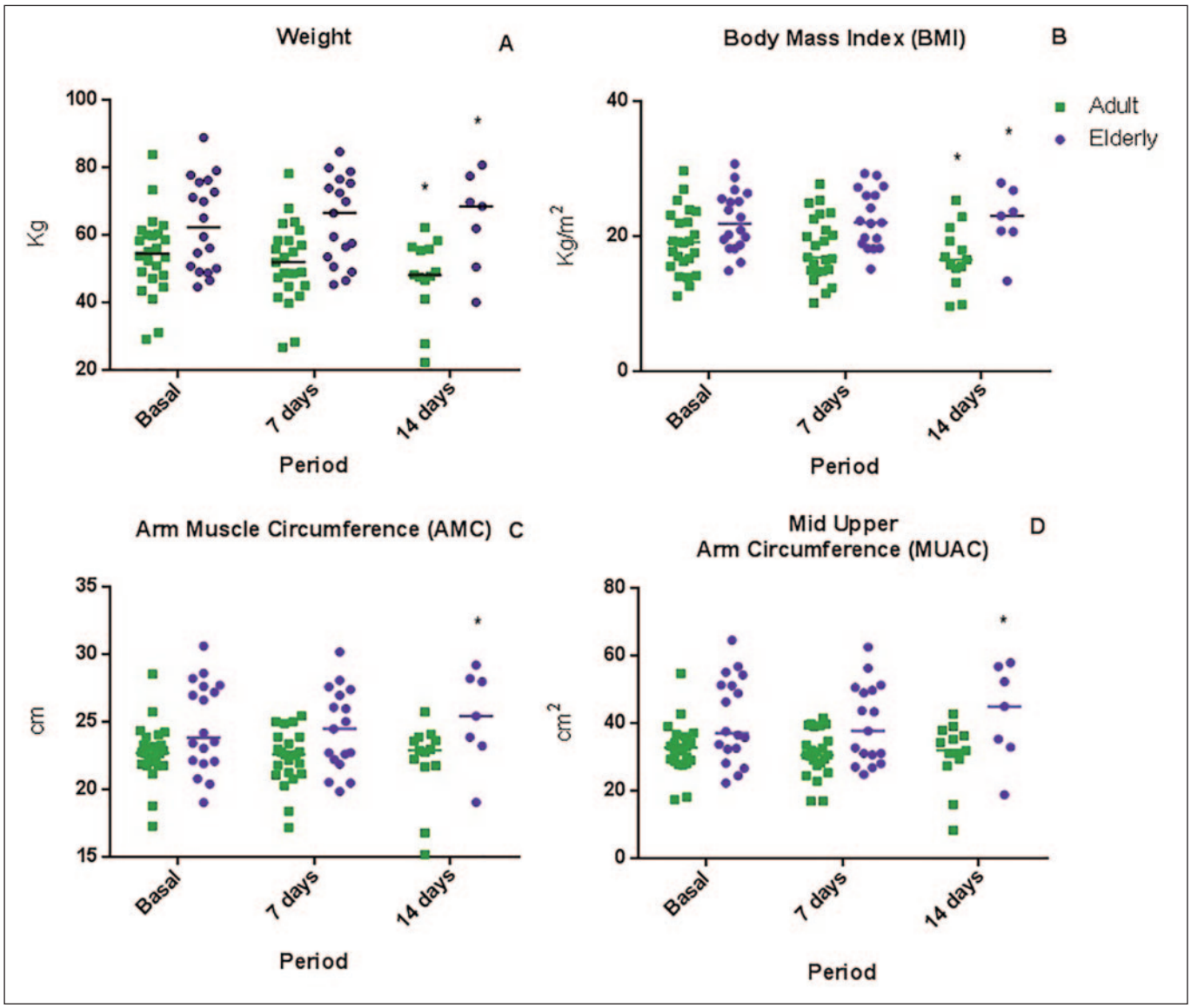
90% in the first week of monitoring for both adults and the elderly. In the second week, the adults presented reduction to 85% and in the elderly there was an increase to 95% in the adequacy percentage.

In view of these results, the anthropometric parameters were evaluated and a significant reduction of weight in adults and weight gain in the elderly in the 14 days of hospitalization were observed in relation to the baseline (comparison of groups by repeated measures - ANOVA, P= 0.016; F=7.08, Figure 2A). Consequently, BMI showed a significant difference in both ages and in the same follow-up period (P = 0.018; F= 6.73, Figure 2B). When compared, AMC and CAMA presented an increase in the elderly in the 7-day period compared to 14 days of follow-up (repeated measures - ANOVA, P = 0.021, F=6.43, Figure 2C, P = 0.020, F=6.52, Figure 2D, respectively).

Other anthropometric measures analyzed as % WL, TST, AC, CC, TMAT, FAA did not present significant differences during the follow-up time of the present study (data not shown).

According to the BMI classification in line with Lipschitz[15], the elderly patients were eutrophic at admission and remained with adequate weight during hospitalization. According to the World Health Organization[3], the

Figure 2. Anthropometric evaluation in hospitalized adults and elderly patients with exclusive enteral nutrition during hospitalization time.



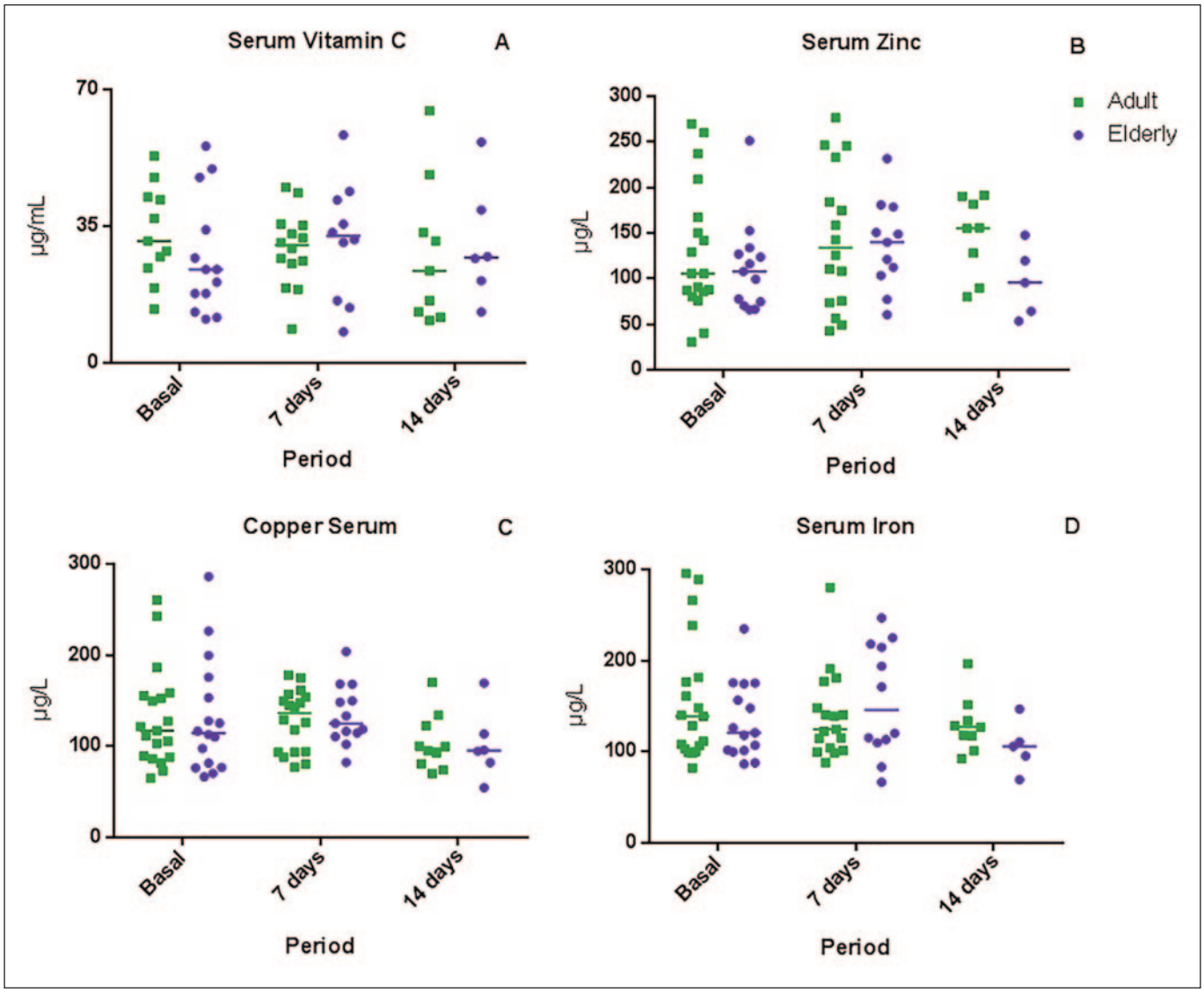
Weight (A); BMI (Body Mass Index) (B); AMC (Arm Muscle Circumference) (C); MUAC (Mid Upper Arm Circumference) (D). *P < 0.05. Analysis of variance with repeated measures (ANOVA).

majority of the adults were underweight at the time of admission and remained with the same classification according to the BMI.

Micronutrients, vitamin C, zinc, copper and iron were dietary assessed by ENT and in blood levels of the patients. It was observed that the dietary administration of these nutrients was above the values recommended by the Estimated Average Requirement -EAR[21], which corresponds to the amount of a nutrient that is estimated to meet the needs of a group of healthy individuals of the same sex and stage of life. There were no significant differences between the intake of these micronutrients during hospitalization time in adults and the elderly, although we observed that the elderly increased the intake of these micronutrients during hospitalization time and adults decreased their intake (Table 1).

Regarding the blood levels of the patients, there was a significant reduction of serum zinc in the elderly at 14 days of hospitalization (89.6± 26.8 µg/dL) in comparison to baseline (comparison of groups by repeated measures - ANOVA, P = 0.031, F=6.47, Figure 3B), although this concentration has not been below the reference levels < 70 ug/dL[22]. Serum levels of vitamin C, copper and iron did not change statistically during hospitalization in both age groups (P> 0.05, Figure 3A, C and D, respectively). In addition, the serum levels of these micronutrients remained within the reference values during the period of hospitalization.

Figure 3. Serum Vitamin C (A); Serum Zinc (B); Copper Serum (C); Serum Iron (D) of adults and elderly hospitalized during the period of hospitalization.



Analysis of variance with repeated measures (ANOVA).

Table 1. Average intake of micronutrients: vitamin C, zinc, copper and dietary iron compared to the Estimated Average Requirement (EAR) and Tolerable Upper Intake Level (UL) in adults and the elderly.

Micronutrients	Adults 1-7 days	Adults 8-14 days	EAR	Elderly 1-7 days	Elderly 8-14 days	EAR	UL
Vitamin C (mg/day)	250.1 ± 42.9	191.9 ± 43.9	§: 75 ‖: 60	128.5 ± 71.2	161.1 ± 72.8	§: 75‖: 60	2.000
Zinc (mg/day)	20.8 ± 6	17.6 ± 4	§: 9.4 ‖: 6,8	19.1 ± 7.8	22.2 ± 2.8	§: 9,4‖: 6,8	40
Copper (µg/day)	2.016,4 ± 164.4	1.770,1 ± 173.9	700	2.020,2 ± 272.6	2.560,5 ± 288.5	700	10.000
Iron (mg/day)	19.5 ± 1.6	18.0 ± 1.7	6-8.1	25.5 ± 2.9	25.8 ± 3.2	5	45

EAR: Estimated Average Requirement, UL: Tolerable Upper Intake Level. Reference values of the Institute of Medicine (2001); §: male; ‖: female. Data presented on mean ± SD.

Other biochemical parameters of the studied sample were analyzed and it was observed that serum levels of total cholesterol and HLD-c increased significantly during the period of hospitalization (repeated measures – ANOVA). Total cholesterol increased 14 days after admission in relation to baseline (P = 0.049; F=4.70) and HDL-c increased two weeks after hospitalization compared to 7 days after admission (P = 0.026; F=6.16).

Increased total cholesterol was more evident in the elderly (Figure 4A) and HDL-c had an increase in both age groups (Figure 4B). In relation to the serum albumin values (Figure 4C) and hemoglobin (Figure 4D), no statistical differences were observed (P = 0.28, F=1.21; P = 0.056, F=4.17, respectively). Based on the baseline values, in both age groups, from admission and during the follow-up period only three patients (7%) were in agreement with the reference values, above 3.5 g/dL, determining a very high prevalence of protein depletion during hospitalization, as for hemoglobin, all patients presented values below the reference parameters (< 12 g/dL for women and < 13 g/dL for men), and were considered anemic[3].

Other biochemical parameters evaluated as glycemia (mg/dL), CRP (mg/dL), urea (mg/dL), creatinine (mg/dL), sodium (mEq/L), leukocytes (mg/dL), platelets (mm), potassium (mmol/L), calcium (mg/dL) did not present significant differences (data not shown).

DISCUSSION

In the present study, dietary monitoring demonstrated caloric and protein adequacy for both age groups, between what was prescribed *versus* administered according to ENT quality indicators. The goal is to reach at least 80%, and it is more common to find studies that reveal lower adequacy percentages than those observed in the present study, due to numerous intercurrences during ENT, mainly because of gastrointestinal and mechanical complications[23,24].

Similarly to the volume of the enteral nutrition, the administration of micronutrients from the enteral diet such as zinc, iron, copper and vitamin C were higher in the elderly than in adults. However, according to EAR, the amount of these micronutrients received in both age groups was higher than recommended, although these values did not exceed the maximum daily intake level, Tolerable Upper Intake Levels (UL), according to the Institute of Medicine[21]. It should be emphasized that the EAR recommendation is for healthy population and not for populations with diseases as in the present study, since there are still no reference standards of micronutrients for this population.

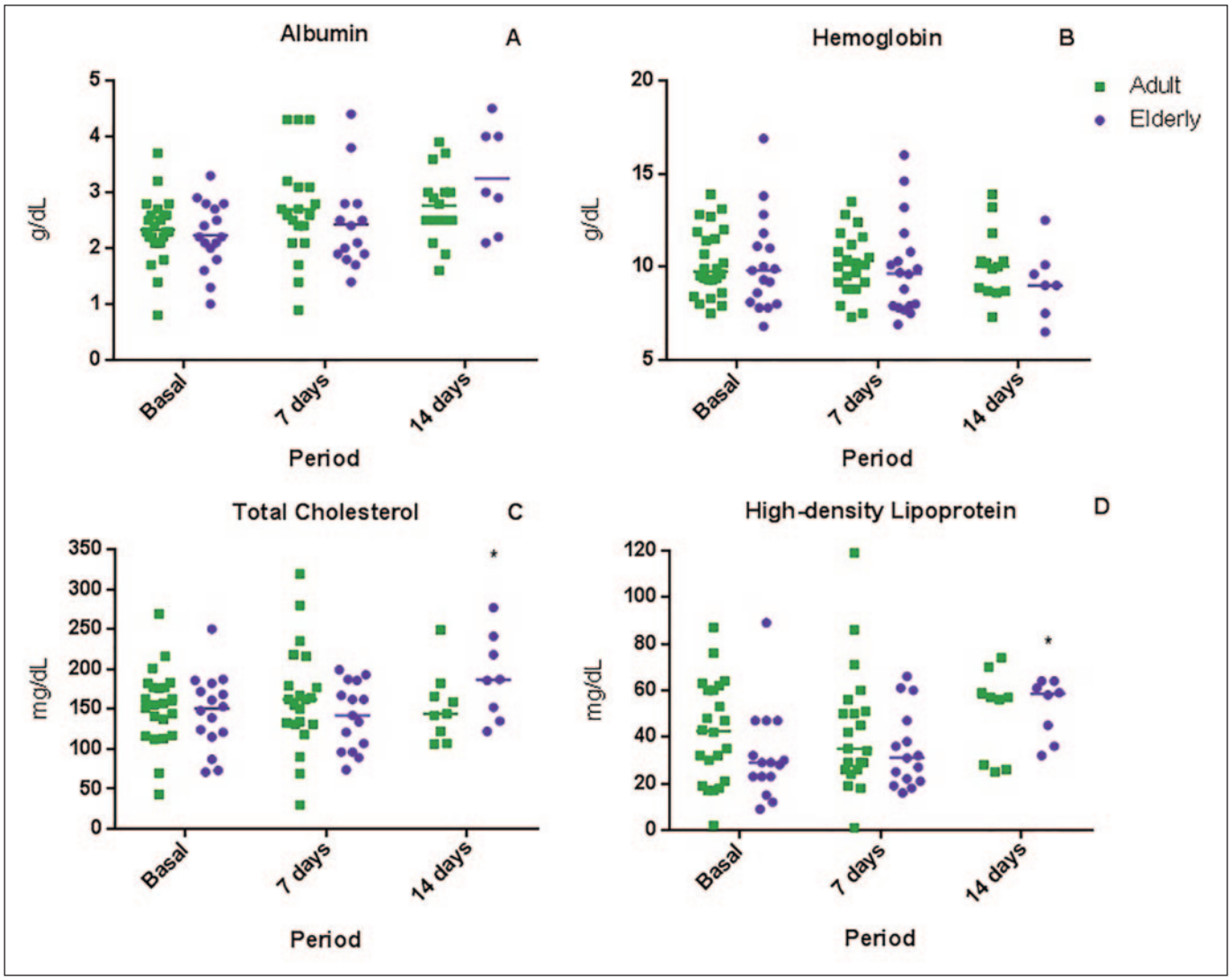
It was also possible to observe that these dietetically administered amounts did not influence the serum levels of the patients, since they did not exceed the reference limits. Except for serum zinc which presented a significant decrease in the elderly, and may be associated with the gain of muscle mass observed during the period of hospitalization. Zinc is directly related to the formation of muscle mass[25].

Changes in body composition between the different age groups were also assessed using anthropometric parameters. The results show that adults presented greater weight loss in relation to the elderly. According to the literature it was possible to observe that when patients are hospitalized with a deficit in the nutritional composition they have a greater difficulty in recovering this nutritional status[4].

This can be clearly observed in the present study, since the majority of the elderly did not have loss of weight or muscle mass during hospitalization according to BMI, CAMA and AMC, remaining well-nourished since their admission throughout the whole follow-up period, contrary to what was observed in the adults, and different from what is commonly observed in studies, which report a high prevalence of weight loss and muscle depletion in the elderly during the in-hospital period[26,27].

Data from the cross-sectional study conducted by our research group showed that the majority of adults and elderly

Figure 4. Albumin (A); Hemoglobin (B); TC (Total Colesterol) (C); HDL (*High-density Lipoprotein*) (D) of adults and elderly hospitalized during the period of hospitalization.



*P < 0.05. Analysis of variance with repeated measures (ANOVA).

patients were admitted with low weight according to BMI, besides verifying that other anthropometric parameters evaluated such as, CAMA, FAA, TAMT and AC were reduced, allowing to suggest arm muscle circumference (AMC) and corrected arm muscle area (CAMA) as good indicators of nutritional status[26]. Thus, we must highlight that ENT influenced this result, since we observed that the elderly came closer to the recommended ENT administration and in adults we observed a worsening of the nutritional status.

According to the biochemical analysis of the patients, the hemoglobin concentration during hospitalization did not change significantly, although we observed a decreased tendency during the period of follow-up of the elderly, noting that it was not possible to improve the concentration of red blood cells in the patients through EN.

Anemia was common in the present study, and it represents a public health problem with a negative prognosis for hospitalized patients[3-28]. This is a worrisome factor, because even receiving amounts higher than those recommended by EAR, hematocrit and hemoglobin levels did not improve, emphasizing the need for drug intervention measures and constant monitoring in this population.

In the present study, there was a high prevalence of protein depletion during the serum albumin monitoring period, which was also noticed in other studies, confirming a common condition in the hospital reality[28]. However, the half-life of albumin is long, approximately 15-20 days, and may not represent a good biochemical parameter of nutritional evaluation during the follow-up period of the present study, which was 14 days[29], thus being identified as a limitation in the present study.

Thus, hemoglobin and albumin were not good parameters to evaluate nutritional risk, although we observe a strong association of hemoglobin with anthropometric parameters (CC and CAMA) in other studies, however, those were cross-sectional studies (26-27). In a longitudinal study, Duarte et al.[30] found that patients hospitalized for more than 15 days had weight loss and a significant positive correlation with the reduction of hemoglobin and albumin levels. These data allow us to reflect that the analysis of the nutritional assessment of the patient during the period of hospitalization may be different from the same parameters evaluated at the moment the individual is admitted, highlighting the importance of the follow-up.

Therefore, it is clearly apparent from these results that ENT can influence the nutritional status of hospitalized patients, since we observed that during the period of hospitalization, the elderly showed an improvement in nutritional status in relation to the adults, and these patients received amounts of calories and protein closer to their needs when compared to the adults. In addition, the amount of micronutrients increased during the hospitalization of the elderly and decreased during the hospitalization of the adults, and the period of hospitalization of the elderly was shorter in comparison to the adults.

However, it should be noted that although few patients were followed up by the present study, according to the inclusion criteria, this result is still important, because it shows a strong participation of the multidisciplinary team of the hospital in the early search for the transition of the feeding route and consequently improvement of the nutritional status of the patient, aiding in the hospital discharge.

As *limitations* of this *study* it is possible to emphasize the size of the sample considered small mainly after the seven days of evaluation. The albumin parameter evaluated during 14 days of follow-up was shorter than the half-life time of approximately 15-20 days. A longer follow-up period is suggested, in order to also increase the number of patients and for the matching by place of hospitalization to be possible.

CONCLUSIONS

It can be concluded that enteral nutrition therapy influenced the weight and muscle mass gain in hospitalized elderly patients and, although the appropriate administration of micronutrients, the absorption of zinc was affected. In a country where population aging is increasing without adequate changes in living conditions, which correspond to a high rate of resources in health services, the important influence of ENT on the nutritional status has resulted in the maintenance of weight and muscle mass, resulting also in a shorter hospital stay, diminishing the occurrence of morbimortality and readmission in hospitalized patients. Therefore, monitoring of enteral nutrition is essential in order to avoid worsening nutritional status during hospitalization.

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