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Comparison of the effects of continuous *versus* intermittent enteral feeding on plasma leptin and ghrelin levels in Intensive Care Units

Comparação do efeito da alimentação enteral contínua com o efeito da alimentação intermitente nos níveis plasmáticos de leptina e grelina em Unidades de Terapia Intensiva

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ABSTRACT

Objective

The aim of this prospective randomized trial is to verify whether there is an association between the methods of administration of enteral nutrition and the leptin and ghrelin hormones, which have a major role in the regulation of energy metabolism.

Methods

This study enrolled 38 enteral-fed patients aged 18 to 85 in the Intensive Care Unit. The patients were prospectively randomized to receive either continuous infusion (n=19) or intermittent feeding (n=18) of enteral

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nutrition. In addition to routine biochemical assays, blood samples were taken from the patients for leptin and ghrelin analyses on the 1th, 7th, and 14th days of enteral nutrition.

Results

There was no statistically significant difference between the groups regarding descriptive statistics and categorical variables such as underlying diseases, complications, steroid use and others (p>0.05). The decrease in the number of white blood cells and in creatinine and C-reactive protein levels over time were statistically significant (p=0.010, p=0.026, p<0.001 respectively). There was no statistically significant difference between the groups with respect to leptin and ghrelin levels (p=0.982 and p=0.054). Leptin levels did not change over time; however, the ghrelin levels of both groups were significantly higher on the 7th and 14th days than on the first day of analysis (p=0.003).

Conclusion

This study revealed that both continuous and intermittent enteral nutrition feeding regimens were well tolerated in Intensive Care Unit patients showing minor complications. The method of administration of enteral nutrition alone did not affect the leptin and ghrelin levels. Randomized controlled large cohort trials are needed to to compare intermittent and continuous enteral nutrition to determine which one is more adaptable to diurnal patterns of secretion metabolic hormones.

Keywords: Energy metabolism. Enteral nutrition. Ghrelin. Leptin.

RESUMO

Objetivo

Este ensaio aleatório prospectivo tem por objetivo verificar se existe uma associação entre o programa de administração de nutrição enteral e os hormonios leptina e grelina, os quais funcionam no metabolismo energético.

Métodos

Este estudo incluiu 38 pacientes de Unidades de Terapia Intensiva, com idades entre os 18 e os 85 anos, que receberam nutrição enteral. Os pacientes foram escolhidos aleatoriamente para receberem nutrição enteral utilizando infusão contínua (n=19) ou intermitente (n=18). Além de exames bioquímicos de rotina, foram colhidas amostras de sangue dos pacientes para análises dos níveis de leptina e grelina no 1º, 7º e 14º dias de nutrição enteral.

Resultados

Não houve diferença estatística significante entre os grupos em relação a dados descritivos e variáveis categóricas tais como doenças subjacentes, complicações, utilização de esteroides e outros (p>0,05). A diminuição no número de leucócitos e nos níveis de creatinina e proteína C-reativa com o tempo foi estatisticamente significativa (p=0,010, p=0,026, p<0,001, respetivamente). Não existiu diferença com significância estatística entre os grupos em relação aos níveis de leptina e grelina (p=0,982 e p=0,054). Embora os níveis de leptina não mudaram com o tempo, os níveis de grelina de ambos os grupos foram significativamente superiores no 7° e 14° dias quando comparados aos verificados na análise do primeiro dia (p=0,003).

Conclusão

Este estudo revelou que os programas de nutrição enteral contínua e intermitente foram bem tolerados com pequenas complicações apresentadas pelos pacientes em Unidades de Terapia Intensiva. O padrão de administração de nutrição enteral por si só não afetou os níveis de leptina e grelina. Estudos controlados aleatórios em coortes maiores são necessários para verificar qual programa de administração de nutrição enteral, intermitente ou a contínuo, é mais adaptável ao padrão de secreção diurno de hormônios metabólicos.

Palavras-chave: *Metabolismo energético. Nutrição enteral. Grulina. Leptina.*

INTRODUCTION

Leptin and ghrelin are two hormones which play an important role in energy metabolism. Leptin, known as the satiety hormone, is released mainly from adipose tissue [1]. Its basic role in the body is to regulate nutritional intake through a negative feedback loop [2]. Ghrelin is

mainly produced by the stomach and plays a role in many metabolic events in the body [3]. Plasma ghrelin levels increase before meals and decrease after eating [4]. The effects of leptin and gherlin on energy homeostasis, neuroendocrine and immune functions, glucose, and lipid metabolism are known, but there is little information about the relationship between these hormones with feeding in Intensive Care Units (ICU).

Leptin and ghrelin, like some other Gastrointestinal System (GIS) hormones, are secreted in a diurnal pattern. However, secretion may be affected by situations such as presence of nutrients in the intestinal lumen and low gastric pH. It is known that continuous enteral feeding may disrupt this physiology and the diurnal pattern of secretion of some hormones [5].

Our hypothesis is that the method of administration of enteral nutrition will affect plasma leptin and ghrelin levels. In order to test this hypothesis, this study verified whether the intermittent or continuous administration of enteral feeding had an effect on plasma leptin and ghrelin levels.

METHODS

This prospective randomized study was approved by Ethics Committee of the Ondokuz Mayıs University (2013/475), and it was registered at ClinicalTrials.gov (NCT02282501) and conducted in accordance with the Helsinki Declaration. The present study was carried out at the Ordu University Education and Research Hospital, secondary Medical ICU, from August 2014 to October 2015. It included patients with dysphagia, aged from 18 to 85 years, who would start receiving enteral nutrition. Exclusion criteria were patients with contraindications for enteral nutrition, irreversible coma, morbid obesity, advanced renal and liver failure, multiple trauma, burns, and serious or severe sepsis. Some patients were subsequently removed from the study due to monitoring duration of less than fourteen days (because of death or discharge), use of corticosteroid or immunosuppressant medication, massive blood transfusion, development of severe sepsis or multiple organ failure, lack of tolerance of enteral nutrition or not reaching the expected calorie content within 3 days, blood sugar >200mg.dL^{-1} in spite of insulin treatment, and if they underwent an open gastrostomy or had a jejunostomy history.

All patients included in the study and/or their relatives signed the Informed Consent Form. After anamnesis and physical examination, demographic data were collected, and Sequential Organ Failure Assessment, Acute Physiology and Chronic Health Evaluation II, and Glasgow Coma Score scores were recorded for the patients. All patients had a 12-14 Fr feeding tube inserted through the nasal pathway, and gastric insertion was confirmed radiologically and clinically. Patients were randomly allocated to two groups using a computer generated sequence of numbers and a sealed envelope technique. Group 1 (n=19) patients received enteral feeding of 4-hour infusions with 1 hour break during 24 hours. Group 2 (n=19) patients were administered enteral feeding of at least 30 minutes 6-8 times within a 24 hour period and were not fed for 6 hours after midnight.

The required calorie amount for the patients was calculated using the Harris-Benedict equation. For enteral nutrition, a standard commercial feeding solution (Jevity 1kcal.mL^{-1}, Abbott Nutrition International, Istanbul, Turkey) was administered using a feeding pump (JYB-500, JYM MedTechCo Ltd, Changsha, China) and a feeding bag (OpMask, Erenler MedCo Ltd, Istanbul, Turkey). In Group 1, enteral feeding started at the rate of 20mL.h^{-1}, which increased by 20mL every 6-8 hours. In Group 2, feeding was administered 6 times per day of 50mL, which increased by 50-100mL. In both groups the nasogastric tube was left to free drainage for 30 minutes at 4-6 hour intervals, and gastric residual volume was monitored. When the gastric residual was greater than 250mL, the

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infusion volume was reduced and prokinetic agents were used, if necessary.

During feeding, the head of the bed was raised to an angle of 30-45°, and the solutions were administered at room temperature; afterwards, the tube was flushed with 20-30mL of tap water. All patients received stomach protector medication (Ranitidine 50mg, Ulcuran amp, Yavuz *İlaç*, Istanbul, Turkey or pantoprazole 40mg, Pantpas flakon, *Nycomedİlaç*, Istanbul-Turkey) by IV administration. Intubated patients were sedated to achieve 3-4 values on Ramsey Sedation Score for compliance with mechanical ventilation. During the study, patients were monitored for signs of gastrointestinal intolerance (vomiting, diarrhea, etc.), and developing complications were recorded. Patients' daily basal fluid requirements were calculated according to with body weight, as recommended by Holliday & Segar [6]. The daily fluid requirements that were not met with feeding solution administered were supplemented with an IV balanced electrolyte solution based on vital function parameters (mean arterial pressure, pulse, hourly urine output, central venous pressure).

Patients' hemogram was recorded daily; urea and creatinine levels were measured daily, and total bilirubin, triglyceride, total protein, cholesterol, activated partial throboplastin time, albumin, prealbumin, and C-reactive protein levels measured twice a week. For the measurement of leptin and ghrelin levels, venous blood samples were taken on the 1st, 7th, and 14th day (T0, T1, and T2) between 6-8 am in 10mL-flat bottom tubes. Since peptides in cells are easily disintegrated by protease, to accurately measure serum ghrelin amounts, approximately 20-30µL of the protease inhibitor aprotinin were added per each mL of blood to the tubes. Blood samples were centrifuged for 10 minutes at 2000xg, placed in sterile eppendorfs, and stored at -80°C in a freezer until analysis. Serum was allowed to thaw, and the tubes were inverted several times for homogenization before analysis.

Serum leptin and ghrelin levels were measured using the Enzyme-Linked Immunosorbent Assay (ELISA, BioTek ELX800 reader, BioTek ELX50 washer, Winooski, Vermont, United States). Quantitative determination of serum leptin was performed by sandwich enzyme immunoassay (Leptin-Sandwich-ELISA, EIA-2395, DRG Instruments GmbH, Marburg, Germany), and serum ghrelin was measured using the double-antibody sandwich ELISA (Human Ghrelin ELISA Kit, DZE201120973, Sunredbio, Shanghai, China), according to the manufacturer's instructions.

Power analysis and statistical analysis

Based on a study on the effect of bolus tube feeding on leptin and ghrelin concentration in healthy volunteers [7], power analysis was carried out using with the Minitab 13.0 statistical software (State College, Pennsylvania, United States), at 95% confidence interval, with 80% power and equal number of patients (17) in each group. Considering participant dropout, the groups included 19 patients.

Analysis of variance was also carried out, and the student's *t*-test, Kolmogorov-Smirnov test, and Levene's test were used; normality and homogeneity of variance were checked. For comparison of descriptive properties of the groups, the continuous variables were analyzed using the student's *t*-test, and ordinal variables were analyzed using the Mann-Whitney U test. The Chi-square test was used to compare the categorical data between the groups. Two-way repeated measures Analysis of Variance (ANOVA) was used to determine the effects of groups, period, and their interactions on the blood parameters. Means were compared using the Bonferroni honestly significant difference test, and the results were presented using letters. The alpha level was set at 5%. All statistical analyses were performed using Statistical Package for the Social Sciences (SPSS Inc., Chicago, Illinois, United States) statistics, version 23.

RESULTS

Data of a total of 37 patients were assessed (Figure 1). Descriptive statistics for the patients included in the study and the comparison of variables between the groups are given in Table 1. As can be seen from Table 1, the differences between the feeding groups are not statistically significant for all variables ($p>0.05$).

The frequency distribution of categorical variables such as sex, underlying disease, and complications for the 37 patients investigated, and the comparison of this frequency distribution

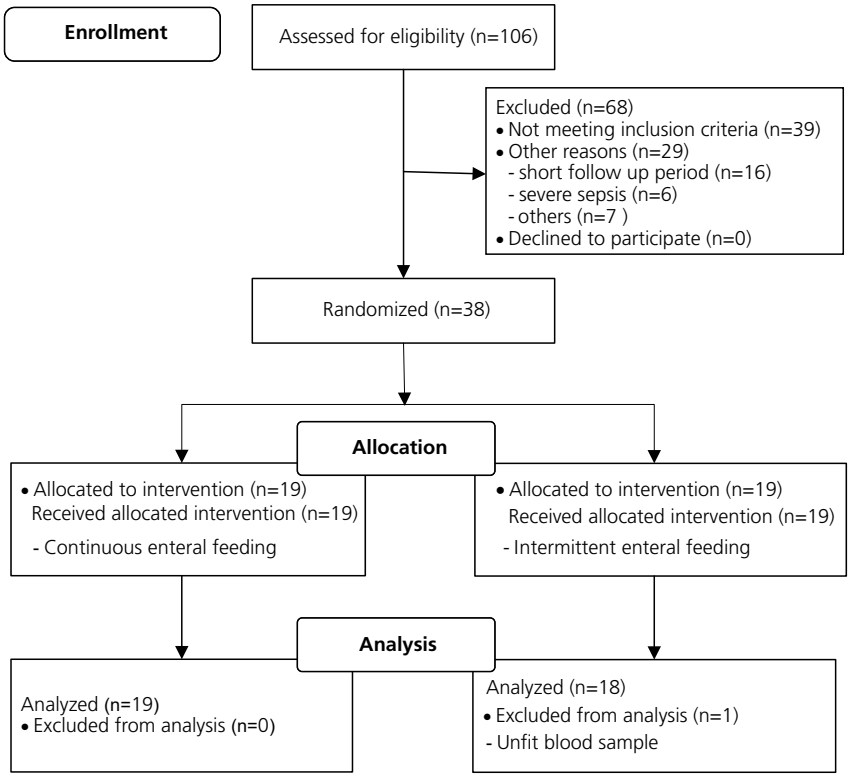

Figure 1. Flow diagram of the randomized trial.

Table 1. Descriptive statistics and results of *t*-test/Mann-Whitney U test. Ordu, Turkey (2014-2015).

Parameters	Continuous feeding (n=19)			Intermittent feeding (n=18)			*p*-value
	Mean	SD	Median	Mean	SD	Median	
Age (year)	75.74	13.15	80	77.83	8.76	80.0	0.574^{NS}
Apache II	22.74	4.78	23	23.61	3.05	23.5	0.242^{NS}
GCS	9.68	2.21	10	9.17	1.50	9.0	0.533^{NS}
SOFA	4.89	1.79	5	5.39	1.24	5.0	0.323^{NS}
BMI (kg/m^2)	25.47	3.02	26	23.83	3.01	22.5	0.108^{NS}
Calculating calories (kcal)	1731.60	194.51	1700	1622.20	296.16	1700.0	0.191^{NS}
Days of entubation	9.05	6.18	10	8.83	6.49	11.5	0.915^{NS}

Note: NS: Statistically Not Significant (according to *t*-test, $p>0.05$ and according to Mann-Whitney U test, $p>0.05$).

Apache: Acute Physiology and Chronic Health Evaluation; GCS: Glasgow Coma Scale; SOFA: Sequential Organ Failure Assesment; BMI: Body Mass Index; SD: Standard Deviation.

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between the groups are given in Table 2. Table 2 shows that the frequency distributions are not dependent on the feeding group ($p>0.05$) for all variables. In the continuous enteral nutrition group, 2 patients (10.2%) had diarrhea, and in the intermittent enteral nutrition group, 1 patient (5.5%) had diarrhea and 2 (11.1%) had vomiting. There was no statistically significant difference between the groups in terms of GIS-related complications ($p>0.05$).

The laboratory parameters and time-based statistics are given in Table 3. Table 3 also shows the differences in these variables between the groups, according to time and the two-way analysis of variance, evaluating the association between these factors and the Bonferroni *post-hoc* test results (if necessary). As shown in Table 3, the differences between the groups with respect to the change in the hematologic and biochemical blood parameters during the time periods were not statistically significant ($p>0.05$). Whereas, the differences in White Blood Cell (WBC), platelet, creatinine, total bilirubin, C-Reactive Protein (CRP), and ghrelin parameters were statistically significant over time ($p<0.01$, $p<0.01$, $p<0.05$, $p<0.05$, 0.001, $p<0.01$, respectively), the differences in the group means were not statistically significant ($p>0.05$). As for the other variables, both differences in time and group means were not statistically significant ($p>0.05$). In other words, the means did not vary between the groups or at different times.

DISCUSSION

In the present study investigating the effects of continuous and intermittent enteral nutrition on leptin and ghrelin levels, in terms of morning plasma leptin and ghrelin levels, there was no statistically significant difference between continuous and intermittent enteral nutrition feeding regimens.

Table 2. Frequency distribution and results of Chi-square test for categorical variables based on the groups evaluated. Ordu, Turkey (2014-2015).

Parameters	Continuous feeding		Intermittent feeding		*p*-value
	n	%	n	%	
Outcome					
Inpatients	7	36.8	6	33.3	
Discharged	4	21.1	5	27.8	0892
Exitus	8	42.1	7	38.9	
Respiratory type					
Spontaneous	4	21.1	5	27.8	
Mechanical ventilation	8	42.1	7	38.9	0.892
Spontaneous + MV	7	36.8	6	33.3	
Patient acceptance					
Emergency service	9	47.4	11	61.1	
In-hospital	7	36.8	6	33.3	0.839
Other Intensive Care Unit	2	10.5	1	5.6	
Other hospital	1	5.3	0	0.0	
Underlying diseases					
Respiratory disease	7	36.8	7	38.9	
Cardiovascular disease	1	5.3	2	11.1	
Neurologic disease	6	31.6	5	27.8	0.922
Gastrointestinal disease	2	10.5	1	5.6	
Urologic disease	2	10.5	1	5.6	
Other	1	5.3	2	11.1	

Note: MV: Mechanical Ventilation.

Known as the satiety hormone, leptin is mainly synthesized in adipose tissue, and low levels have been detected in the placenta, gastric epithelium, skeletal muscle, pituitary, and breast

Table 3. Descriptive statistics and results of Analyse of Variance (ANOVA) for blood parameters. Ordu, Turkey (2014-2015).

Parameter	Period	Continuous feeding (n=19)			Intermittent feeding (n=18)			Grand Mean (n=37)		
		Mean	SEM	SD	Mean	SEM	SD	Mean	±	SEM
WBC x10.e3.uL^{-1}	1	10.842	0.842	3.671	11.389	1.329	5.638	11.108	±	0.768AB
	2	11.316	0.905	3.945	12.167	1.294	5.491	11.730	±	0.775A
	3	9.526	1.135	4.948	9.833	1.532	6.501	9.676	±	0.933B
	G Mean	10.561±0.559			11.130±0.798					
	p-value	Group: 0.704^{NS}; Time: 0.010**; GroupXPeriod Int: 0.922^{NS}								
APTT sec	1	31.595	1.708	7.447	28.678	0.924	3.918	30.176	±	1.002
	2	34.405	2.019	8.802	30.139	1.266	5.372	32.330	±	1.242
	3	33.163	1.437	6.266	31.533	1.866	7.915	32.370	±	1.161
	G Mean	33.054±0.997			30.117±0.813					
	p-value	Group: 0.072^{NS}; Time: 0.201^{NS}; GroupXPeriod Int: 0.638^{NS}								
Albumin g.dL^{-1}	1	2.782	0.112	0.487	2.733	0.080	0.340	2.758	±	0.069
	2	2.742	0.074	0.322	2.628	0.063	0.265	2.687	±	0.049
	3	2.826	0.103	0.450	2.828	0.072	0.306	2.827	±	0.063
	G Mean	2.783±0.056			2.730±0.042					
	p-value	Group: 0.527^{NS}; Time: 0.190^{NS}; GroupXPeriod Int: 0.754^{NS}								
CRP mg.dL^{-1}	1	8.530	1.298	5.657	8.934	1.096	4.649	8.727	±	0.842A
	2	6.688	0.786	3.427	6.236	0.787	3.340	6.468	±	0.550B
	3	5.763	0.467	2.035	5.511	0.710	3.0115	5.641	±	0.415B
	G Mean	6.994±0.542			6.894±0.538					
	p-value	Group: 0.914^{NS}; Time: 0.000***; GroupXPeriod Int: 0.842^{NS}								
Prealbumin mg.dL^{-1}	1	9.790	0.812	3.537	9.944	0.834	3.539	9.865	±	0.574
	2	11.053	1.02448	4.466	11.389	0.682	2.893	11.216	±	0.614
	3	10.632	0.6269	2.733	11.444	0.776	3.294	11.027	±	0.494
	G Mean	10.491±0.480			10.926±0.445					
	p-value	Group: 0.613^{NS}; Time: 0.087^{NS}; GroupXPeriod Int: 0.874^{NS}								
Leptin ng.mL^{-1}	1	4.905	0.951	4.143	4.669	0.540	2.28875	4.790	±	0.547
	2	5.311	1.060	4.618	5.194	0.795	3.37438	5.254	±	0.658
	3	5.227	0.964	4.201	4.979	0.927	3.93284	5.107	±	0.661
	G Mean	5.148±0.563			4.947±0.438					
	p-value	Group: 0.867^{NS}; Time: 0.472^{NS}; GroupXPeriod Int: 0.982^{NS}								
Ghrelin pg.mL^{-1}	1	2595.890	366.076	1595.690	2635.560	318.488	1351.231	2615.190	±	240.254B
	2	2946.320	535.376	2333.648	4481.670	577.049	2448.210	3693.240	±	407.981A
	3	2817.890	417.489	1819.794	4073.440	511.130	2168.541	3428.700	±	340.160A
	G Mean	2787.702±253.000			3730.222±294.000					
	p-value	Group: 0.089^{NS}; Time: 0.003**; GroupXPeriod Int: 0.054^{NS}								

Note: NS: Statistically Not Significant (according to *t*-test, $p>0.05$); *Statistically significant (according to ANOVA, $p<0.05$); **Statistically significant (according to ANOVA, $p<0.01$); ***Statistically significant (according to ANOVA, $p<0.001$) means that do not share a common uppercase letter are significantly different (according to Bonferroni test, $p<0.05$).

SEM: Standard Error Mean; SD: Standard Deviation; WBC: White Blood Cell; APTT: Activated Partial Thromboplastin Time; CRP: C-Reactive Protein.

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glands, and its receptors can be found in the hypothalamus [1]. The main role of leptin in the body is a negative feedback signal regulating food intake and energy metabolism. It is thought to have a role in many physiological situations such as reproduction, hematopoiesis, gastrointestinal functions, angiogenesis, sympathetic nervous system regulation, determination of bone density and thermogenesis [8]. Glucose, fatty acids, sympathetic nervous system, insulin, glycocorticoids, growth hormones, and catecholamine play a role in the synthesis and release of leptin. Leptin is released in a pulsatile and diurnal pattern. Serum leptin levels begin to increase after lunch, and its peak occurs in the middle of the night, reducing to lowest levels in the early morning hours [9]. The amount of fat is a major determinant of leptin levels in the body. There is a correlation between obesity, diabetes *Mellitus*, and especially fasting serum insulin levels and serum leptin levels [1].

In this study, there was no statistically significant difference between morning leptin levels in patients administered continuous and intermittent enteral nutrition. In the group that received intermittent feedings, blood samples were taken after 6 hours of fasting; therefore, it was expected that leptin levels would be lower than those of patients receiving continuous enteral nutrition. Since insulin increases in response to feeding causing leptin production, the decrease in insulin levels during fasting, causes a decrease in leptin concentrations [10]. There are studies that have demonstrated that feeding does not have a major effect on leptin concentration. Although Schoeller *et al.* [11] argued that feeding pattern is a physiological factor affecting the diurnal rhythm of leptin levels, these authors found no evidence of a signal for leptin level regulation.

Ghrelin is an adipogenic peptide mainly produced in the stomach. The effects of ghrelin on the body include the stimulation of growth hormone release, feeding behavior, carbohydrate and energy balance, gastric motility and gastric acid secretion, cell proliferation, and endocrine and exocrine functions of the pancreas [3]. Ghrelin secretion by the stomach is largely linked to nutritional status. Ghrelin levels increase in the preprandial period and decrease in the postprandial period. Additionally, ghrelin levels are subject to diurnal variations and are affected by age, sex, body mass index, growth hormone, glucose, and insulin [12].

The level of ghrelin is controlled by body weight in the long term. Ghrelin levels increase with weight loss and decrease with weight gain. Studies of obese individuals have reported an inverse correlation between insulin resistance and hyperinsulinemia with ghrelin concentration [3,13]. Increased plasma levels of ghrelin due to fasting have been reported to reduce after eating, especially foods rich in sugar and fat [14].

It has been shown that continuous enteral nutrition does not reduce appetite and nutrition intake [15]. A study of 6 healthy volunteers with bolus enteral nutrition reported that food intake and ghrelin concentrations in circulation were suppressed [7]. In this study, a positive correlation was found between daily food intake and ghrelin concentration, but a negative correlation was found with leptin, insulin, glucose, and glucagon during bolus feeding. In the present study, in the intermittent enteral nutrition group, morning plasma ghrelin levels of patients were higher than those of patients in the continuous enteral nutrition group. Although this difference was not statistically significant, it was at the limit of significance (p=0.054).

In the literature, continuous or intermittent enteral nutrition administration has been shown to be reliable and well tolerated by patients [16,17]. Continuous administration provides infusion at the rate of 50-125mL^{-1} over 24 hours using a volumetric pump. This method has proved to have fewer gastrointestinal side effects [18]. Intermittent enteral nutrition feeding regimen appears to have some advantages, such as postabsorbative situation, habitual hormone release pattern, and allowing feedback mechanisms [5].

In a new review comparing continuous and intermittent enteral nutrition in the ICU in terms of nutritional status, patient tolerance and complications, the authors reported insufficient evidence to support one method over the other [19]. Another study comparing continuous and bolus enteral nutrition in the ICU reported that there was no significant difference between the groups in terms of occurrence of aspiration, high gastric residual volume, vomiting, and diarrhea [16].

The most common GIS complications of enteral nutrition are nausea and vomiting, high gastric residual volume, diarrhea, and constipation. Due to this type of complications, patients receiving enteral nutrition do not to reach targeted values. Another concern related to high gastric residual volume is the risk of aspiration. A study comparing intermittent and continuous enteral nutrition in the ICU found diarrhea and vomiting rates of 20% and 5%, respectively, in continuously fed patients; these rates were reported as 15% and 20% in the intermittent group [20]. Another study comparing continuous and bolus enteral nutrition in critical patients did not identify differences in terms of complications (the complication rate for diarrhea and vomiting was 14%) [21]. In the present study, GIS complication rates were similar to those reported in the literature, and there was no statistical difference between the groups.

The main limitation of this study is the multiple situations that are expected to affect leptin and ghrelin levels in the ICU. For example, it is reported that leptin levels increase during inflammatory events [22]. Again, similarly, changes in leptin levels are expected with sepsis [23]. In our study, CRP and WBC levels showed a statistically significant decrease in the 3rd measurement, and there was no difference between the groups. However, nothing can be said in terms of inflammation degree. Another limitation may be related to the evaluation of sufficient nutrition of patients. Due to the relatively short duration of the present study and that no significant changes were expected, anthropometric measurements such as mid-upper arm circumference and triceps skin fold thickness were not performed. However, measuring patient weight in the ICU may have been valuable. In this study, there was no significant difference in the serum prealbumin levels, which was used to monitor nutritional sufficiency. Prealbumin is a sensitive test to evaluate nutritional status. The half-life of prealbumin is 2-3 days, and it is known to be a more sensitive marker for acute changes when compared to albumin [24].

The present study revealed that both continuous and intermittent enteral nutrition feeding regimens were well tolerated in ICU patients showing minor complications. The method of administration of enteral nutrition alone did not affect the plasma leptin and ghrelin levels. Randomized controlled large cohort trials are needed to compare intermittent and continuous enteral nutrition to determine which one is more adaptable to diurnal patterns of secretion metabolic hormones.

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CONTRIBUTORS

All authors contributed equally to all stages of conception and design of this study.

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