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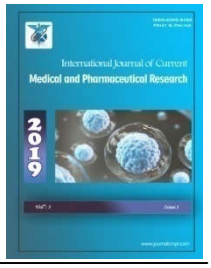

THE IMAPCTS OF USING MODULAR PROTEIN FORMULAS IN CRITICALLY ILL PATIENTS REGARDING ALBUMIN LEVEL

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ABSTRACT

Objectives: Physiologically, most critically ill patients are under stress conditions from a variety of insults, which are ultimately lean body wasting and hypoalbuminemia. The aim of this study is to evaluate the clinical impacts of using modular protein formulas (MPFs)to increase protein provision in critically ill patients who are used standard enteral nutritional formulas (ENFs) in terms of average serum albumin level during first week of intensive care unit (ICU) admission (ALB avg) in survivor group (Group I) and nonsurvivors group (Group II).

Methods: We performed a retrospective analysis of patients admitted to the adult ICU between April 2017 and January 2019 Patients were excluded if they discharged from ICU or died before completed 1 week of ICU admission.All patient's continuous variables were expressed as mean± SD by using the independent samples T-test or as numbers with percentages by using $\chi 2$ test.

Results: The mean overall age was 56.92±9.55 years and 50 subjects (66.66%) were male. The overall 28-day ICU mortality rate was 22.67% (17 patients). Although there were insignificant nutritional inputs difference between survivors and nonsurvivors, the ALB avg was significantly higher in survivors than in nonsurvivors (3.93±0.49 g/dl vs 2.73±0.89 g/dl) with mean difference of +1.08±0.43 g/dl.

Conclusion: We demonstrate the importance of provision protein to fill the protein gap deficit that are highly expected in critically ill patients who are taking standard ENFs.MPFs are effective to increase or at least to stabilize serum albumin level in hypercatabolic critically ill patients which ultimately may improve survival rate.

INTRODUCTION

Physiologically, most critically ill patients are under stress conditions from a variety of insults, which are ultimately caused wasting syndromes.[1-2] Kwashiorkor is the most commonly wasting syndrome occurred in hospitalized patients with a major cause of high treatment cost, morbidity, and mortality.[3]Kwashiorkor is primarily characterized by lean body wasting, excessive protein breakdown, and hypoalbuminenia due to protein and albumin hypercatabolism to sustain life as possible.[4-7]Hypoalbuminemia is a negative readily and affordable attained prognosticator and can predict morbidity and mortality among critically ill patients.[8-11]The aim of this study is to evaluate the clinical impacts of using available MPFs either PROSource®TF or Whey Protein 100% Powder to increase protein provision in critically ill patients who are used standard ENFs in terms of ALB_{avg}.

MATERIAL AND METHODS

This was a single-center observational retrospective study conducted in the department of adult ICU of King Hussein Medical Center (KHMC) at Royal Medical Services (RMS) in Jordan. This study was approved by our Institutional Review Board (IRB), and a requirement for consent was waived owing to its retrospective design. This study included a cohort of critically ill patients admitted to our adult ICU via the emergency department (ED) or via other hospital wards with any medicalor surgical problem. Flow chart of critically ill patient's selection and data collectionprocess is fully illustrated in Figure 1.

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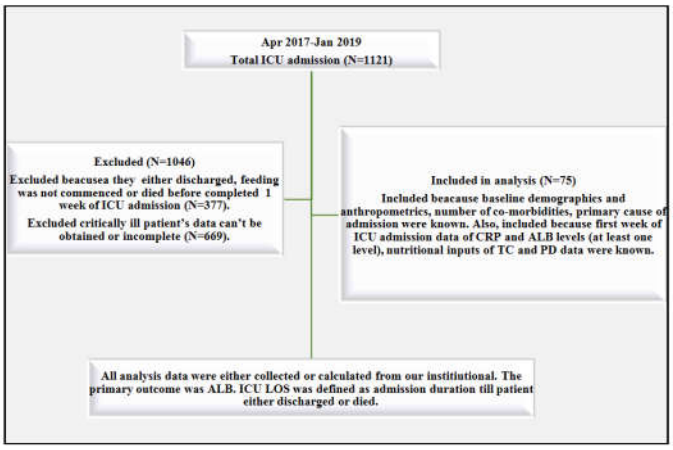

Fig 1 Flow chart of critically ill patient's selection and data collection process.
Apr: April. CRP: C-reactive protein. PD: Protein density.
Jan: January. LOS: Length of stayALB: Albumin.
ICU: Intensive Care Unit TC: Total calorie.

Statisticalanalyses were performed using IBM SPSS ver. 25 (IBM Corp., Armonk, NY, USA) and P-values ≤0.05 were considered statistically significant.

RESULTS

The mean overall age was 56.92±9.55 years and 50subjects (66.66%) were male. The overall 28-day ICU mortality rate was 22.67%(17 patients).Mortality was significantly higher in medical than surgical critically ill patients (88.23% vs 56.89%, respectively). Also, baseline pre-ICU admission days, ICU stay days, overall hospital stay day, and number of co-morbidities (>1) were also significantly higher in nonsurvivors than survivors (8.88±3.52days, 15.82±3.86 days, 24.71±0.77 days, and 65.63%vs 2.81±1.42 days, 9.81±1.42 days, 12.62±2.84 days, and 48.28%, respectively).

Table 1 Baseline and follow-up comparison data of the study's critically ill patients

Variables		Total (N=75)	Survivors (N=58)	Nonsurvivors (N=17)	P-Value
Age (Yrs)		56.92±9.55	56.33±9.22	58.94±10.64	0.324NS
Gender	Male		50 (66.66%)	12 (70.59%)	0.004S
	Female		25 (33.33%)	5 (29.41%)	
Day(s) Pre-ICU admission (day(s))		4.19±3.28	2.81±1.42	8.88±3.52	0.000S
ICU Stay $day_{(s)}$($Day_{(s)}$)		11.17±3.35	9.81±1.42	15.82±3.86	0.000S
Hospital Stay day(s)		15.36±5.68	12.62±2.84	24.71±0.77	0.000S
Number of comorbidities	0, 1	34 (45.33%)	30 (51.72%)	4 (34.38%)	0.000 S
	2 , 3, 4+	41 (54.66%))	28 (48.28%)	13 (65.63%)	
Admission class	Medical	48 (64.00%)	33 (56.89%)	15 (88.23%)	0.000 S
	Surgical	27 (36.00%)	25 (43.10%)	2 (11.76%)	
BW_1 (Kg)		70.73±8.66	71.74±8.11	67.28±9.81	0.061NS
BMI_1 (Kg/m²)		24.33±3.66	24.64±3.27	23.30±4.70	0.187NS
ALB_1 (g/dl)		2.58±0.14	2.61±0.13	2.49±0.11	0.001 S
ALB_{avg}(g/dl)		3.66±0.79	3.93±0.49	2.73±0.89	0.000 S
Δ ALB (g/dl)		+1.08±0.65	+1.32±0.36	+0.24±0.79	0.000 S
ALB Diff			+1.08±0.43		
CRP_{Avg} (mg/dl)		38.43±20.34	33.15±16.77	56.44±21.57	0.000 S
CRP: ALB $Ratio_{avg}$ (X: 1)		15.31±8.87	13.05±7.27	23.03±9.71	0.000 S
ENF Vol_{avg} (ml/day)		1314.18±361.44	1317.01±374.95	1304.49±321.33	0.901 NS
MPF Vol_{avg}(ml/day)		415.83±368.99	428.74±377.60	371.79±345.13	0.579 NS
TC $Input_{avg}$(Cal/day)		1932.19±492.27	1916.82±515.83	1984.63±411.19	0.621NS
TC $Input_{avg}$(Cal/kg/day)		28.46±6.83	28.05±7.09	29.88±5.82	0.332NS
∑ g PRO $Input_{avg}$ (g/day)		110.79±56.96	114.29±58.89	98.88±49.54	0.330NS
PD $Input_{avg}$(g/100Cal/day)		5.41±1.66	5.59±1.65	4.77±1.59	0.072NS
% NNC_TC		16.63%±6.04%	16.08%±5.62%	18.51%±7.17%	0.145NS
Overall 28-day ICU Survival			58 (77.33%)		0.000 S
Overall 28-day ICU Mortality			17 (22.67%)		

Values are presented as mean±standard deviation by using independent T-test in case of comparison between groups or by using dependent T-test in case of comparison within group or number (%) by using Chi square test.

Yrs: Years.
Kg: Kilogram.
m: Meter.
BW_1: Actual body weight at admission.
BMI_1: Body mass index at admission.
ALB: Albumin level.
CRP: C-reactive protein.
CRP:ALB ratio: C-reactive protein to albumin level ratio.
TC: Total calorie.
NNC: Non-nutritional calorie from maintenance dextrose saline fluids.
1: Baseline at admission.
Avg: average values during first week of ICU admission.
ICU: Intensive care unit.
S: Significant (P-Value <0.05).
NS: Nonsignificant (P-Value >0.05).
N: Number of study's critically ill patients.
VFDs: Ventilator free days.
ENFs: Enteral nutritional formulas (Ensure® and RESource®Optimum in our study).
MPFs: Modular protein formulas (PROSource®TF or Whey protein powder in our study).
PRO: protein.
PD: Protein density in g per 100 Cal.
Δ: Changes occurred after intervention.

All patient's continuous variables was expressed as mean± standard deviation by using the independent samples T-test between groups and dependent T-test within group. Categorical and ordinal variables was expressed as numbers with percentages by using $\chi 2$ test. Analysis values were compared for the two tested groups (survivors vs nonsurvivors).

Although there were insignificant nutritional inputs difference between survivors and nonsurvivors regarding ENF and MPF vol_{avg}, TC_{avg}, PD_{avg}, and percentage of non-nutritional calories from total calories input (% NNC_TC), the ALB_{avg} was significantly higher in survivors than in nonsurvivors (3.93±0.49 g/dl vs 2.73±0.89 g/dl) with mean difference of +1.08±0.43 g/dl. Demographics, admission co-morbidities and class, anthropometrics, and follow-up comparison data of the study's critically ill patients are fully summarized in Table 1.

DISCUSSION

This study included mechanically and non-mechanically ventilated critically ill patients who were received standard ENFs with average volume of 1314.18±361.44 ml/day. Either Ensure® (67%) or RESource®Optimum (33%) were used as standard ENFs in our study. According to our knowledge; this is the first study addressed the positive albumin impacts of MPFs when added as protein supplemental to the standard ENFs in order to increase the provision of protein in these hypercatabolic patients. On average, standard ENFs have PD and a caloric density of 3.5 g /100 Cal and 100 Cal/dl, respectively. So, if we want to cover the average protein requirement of 100 g/day, we must provide about 2800 ml/day (2800 Cal/day) which absolutely will lead to increased risk of fluid overload accompanied with overfeeding in these hypoalbumenic patients. Mathematically, the lowest PD required in critically ill patients is 5 g/100 Cal taking into consideration the average calorie and protein requirements are 2000 Cal/day and 100 g/day. After careful analysis of the data, ALB was significantly increased by +1.32±0.36 g/dl in survivors in compared with only +0.24±0.79 g/dl in nonsurvivorsdespite the insignificant differences between survivors and nonsurvivors ENFs and MPFs volume inputs. Our explanation to this significantly differences in ALB levels is the strong correlation between C - reactive protein (CRP) and ALB.[12-16]ALB catabolism and escaping rate from the intravascular compartment are directly related to the CRP level while the ALB synthesis rate is inversely related to the CRP level. In our study, CRP and CRP: ALB ratio were significantly higher in nonsurvivors than survivors (56.44±21.57 mg/dl and 23.03±9.71 vs 33.15±16.77 mg/dl and 13.05±7.27).This study demonstrates the importance of provision protein to fill the protein gap deficit that are highly expected in critically ill patients who are taking standard ENFs which already have a PD lower than 4 g/100 Cal.

In summary, MPFs like PROSource®TF® TF or reconstituted WP powder are effective to increase or at least to stabilize serum albumin level in critically ill patients who are required a high protein density to combat for hypercatabolic state which ultimately increase the mortality rate in critically ill patients who are taking standard protein density formulas. This study is limited by its retrospective design, using single-center data, including only ICU patients. Nonetheless, our center isan experienced and high-volume unit, so our data may be useful in other centers. A larger, multisite, and prospective study is needed to control for multiple confounders.

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