The Enteral Nutrition as Factor Affecting Duration of Mechanical Ventilation in Critically Ill Patients

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Abstract: **Background**: A growing body of evidence suggest \s that higher fat content diet may be more beneficial for ventilator-dependent patients. Therefore, the aim of the present prospective study was to assess whether the high-fat low-carbohydrate diet has an advantage role over the usual enteral nutrition (EN) diet. **Methods**: The study was conducted on 40 patients with repertory failure who were admitted to the critical care unit of Benha University and required mechanical ventilation. Patients were divided into two groups: group A which received the usual high-fat low-carbohydrate diet; and group B which received ready regular EN. The statistical analysis was conducted using SPSS version 21. **Results**: Twenty patients were included in group A and similar number of patients were included in group B. The mean mechanical ventilation duration in group A was 8.5 ± 4.7 days and in group B 4.4 ± 1.6 days, the difference between both group was statistically significant (p <0.001). Similarly, there was a statistically significant difference between the two groups regarding the mean of the length of stay in ICU (group A = 10.6 ± 3.7 days, and group B = 6.1 ±1.2 days; p <0.001). Almost 30% of patients in the group A and B complicated with diarrhea. There is no significant statistical difference between the two groups regarding any of the observed complications. **Conclusions**: In conclusion, high fat, low carbohydrates diet seems to be associated with shorter duration of mechanical ventilation and length of hospital stay compared to usual PN.

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1. Introduction:

Adequate nutrition is an important prognostic factor in critically ill patients and (post CABG), the current body of evidence shows that malnutrition is associated with increased risk of mortality in this type of patients[1]. Despite this, the prevalence of malnutrition, including marked reduction in essential micronutrients and body mass, was reported to be as high as 40% in in critically ill patients admitted to the intensive care units (ICUs)[2]; the incidence of malnutrition was reported to be even higher among patients with longer hospital stay[3]. This high risk of malnutrition among critically ill patients (post CABG) can be subsequently associated with higher rate of complications, especially infectious diseases, and longer hospital stay with more days of mechanical ventilation[4]. Therefore, nutritional support is an essential element during the management of ICU patients who admitted with malnutrition or at increased risk of malnutrition during their hospital stay[5].

Parentral nutrition (PN) is the standard nutritional support for critically ill patients with non-functioning gastro-intestinal tract[6]. However, the optimal use of PN in ICU setting is still a subject of controversy within the published literature; PN was reported to be associated with increased risk of infectious and metabolic complications, and improper preservation of gut functional barriers[7]. Over the past 30 years, enteral nutrition (EN) has emerged as the favourable nutritional support technique in malnourished patients with functioning gut system[5]. EN was reported to significantly reduce mortality, infectious complications, number of days with mechanical ventilation, and length of hospital stay[8]. Moreover, previous systematic reviews and meta-analyzes reported that EN is superior to PN in terms of mortality rate and complications among critically ill patients[9,10]. Thus, the current body of evidence recommended the use of EN, as in patients in the ICU who have a functional gastrointestinal tract[11].

On the other hand, patients admitted to ICU with respiratory failure are usually suffered from hypercapnia; moreover, enteral formulas which contain varying levels of carbohydrates was reported to significantly increased carbon dioxide (CO_2)

level[12]. This high level of CO2 can compromise the weaning of the mechanically ventilated patients and increase the duration of the ventilation[13]. In contrary, higher fat content diet may be more beneficial for ventilator-dependent patients; fat produces less metabolic CO2 than carbohydrates and in return may ameliorate the hypercapnic condition of respiratory failure patients[14].

Therefore, the aim of the present prospective study was to evaluate the effect of EN on duration of mechanical ventilation in patient with respiratory failure admitted to ICU, and to assess whether the high-fat low-carbohydrate diet has an advantage role over the usual EN diet.

2. Material and Methods:

We followed the Strengthening The Reporting of OB servational Studies in Epidemiology (STROBE) guidelines during the preparation of the present study[15]. The study gained the approval of the local ethics and research committee of Benha University.

I. Study Design and Setting

The present prospective study was carried from April 2017 to March 2018. The study was conducted on 40 patients with repertory failure and (post CABG) patients, who were admitted to the critical care unit of Benha University and required mechanical ventilation. Patients were divided into two groups: group A which received the standard iso caloric feeding; and group B which received iso caloric high fat, low carbohydrate feeding.

II. Inclusion and Exclusion Criteria

Adults patients with respiratory failure were included if they required hospital stay and mechanical ventilation for more than 24 hours. Patients were excluded if they received PN or had conditions that result in a life expectancy shorter than 48 h.

III. Data collection

The following demographic and clinical data were collected from every participants: history, clinical examination, anthropometric measures, Glasgow Coma Scale (GCS), Acute Physiology and Chronic Health Evaluation II (APACHE II) score, Sequential Organ Failure Assessment (SOFA) score, serum electrolytes, serum glucose level, liver function tests (serum aspartate aminotransferase, alanine aminotransferase, γ-glutamyl transferase, alkaline phosphatase, total and direct bilirubin levels), kidney function tests (blood urea nitrogen, creatinine), duration of mechanical ventilation, length of hospital stay, and complications.

The primary outcome measures in the present study were the duration of mechanical ventilation and length of hospital stay. Secondary outcome measures included complications during feeding and biochemical parameters.

IV. Nutritional Support

Patients received either a high fat, low carbohydrate feed or a standard enteral feed. The dosage prescribed was 1.5 times basal metabolic rate calculated from the tables of Harris and Benedict and was kept constant during the study.

The EN was given through a nasogastric tube by continuous flow for 24 h per day using a Flexiflo II enteral feeding pump. As high fat, low carbohydrate enteral feed, a diet consisting of 16.7~ protein, 55.2% fat and 28.1% carbohydrates, was used. As standard enteral nutrition, a diet consisting of 16.7% protein, 30% fat and 53.3% carbohydrates, was used.

V. Statistical Analysis

The collected data were summarized in terms of mean ± Standard Deviation (SD) and range (minimum - maximum) for quantitative data and frequency and percentage for qualitative data. Comparisons between the different study groups were carried out using the Chi-square test ($\chi 2$) and the Fisher Exact Test to compare proportions as appropriate, the Independent t-test (t) was used to detect difference between parametric quantitative data, while the Mann-Whitney U test was used to compare non-parametric data. Pearson's Correlation coefficient was used to test for the correlation between mechanical ventilation duration and length of stay in the ICU with the studied variables. A P value <0.05 was considered statistically significant. The statistical analysis was conducted using SPSS version 21.

3. Results:

The mean mechanical ventilation duration in group A was 8.5 ± 4.7days and in group B 4.4 ± 1.6 days, the difference between both group was statistically significant (p <0.001; **Figure 1**).

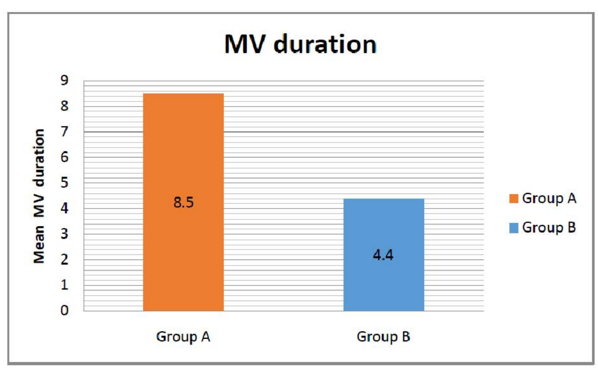

Figure 1. The mean mechanical ventilation duration in group A was 8.5 ± 4.7days and in group B 4.4 ± 1.6 days, the difference between both group was statistically significant (p <0.001)

Twenty patients were included in group A and similar number of patients were included in group B. The mean age in group A was 58.5 ±9.94 years, while the mean age in group B was 57.35±7.66 years. Almost half of the included patients were smokers, hypertensive, and diabetic. Only 4 patients (20%) in group A and 3 patients (15%) in group B had interstitial pulmonary fibrosis (IPF). The mean BMI in group A was 35.5 ±11.5 and 38.7 ± 10.5 in group B. There was no statistically significant difference between both groups in any of the demographic characteristics or vital signs (p >0.05). Moreover, there was no significant difference between the two groups in terms of GCS, APACHE II score, or SOFA score (p =0.16, 0.54, and 0.13, respectively). Notably, the serum potassium, phosphorus, and magnesium levels were significantly higher in group B than group A (p <0.001), however, there was no significant difference between the two groups in terms of the other laboratory findings (**Table 1**).

Table 1. The serum potassium, phosphorus, and magnesium levels were significantly higher in group B than group A (p <0.001), however, there was no significant difference between the two groups in terms of the other laboratory findings

Variable		Group A (n =20)	Group B (n =20)	Test
Serum K^+	**Mean ±SD**	3.4 ± 0.5	4.2 ± 0.5	Independent t- test
	Minimum-Maximum	2.5 - 4.9	3.5 - 5.5	**P <0.001 (HS)**
Serum Na^+	**Mean ±SD**	136.4 ±7.4	135.7 ± 4.3	Mann-Whitney U test
	Minimum-Maximum	127 -155	130 - 143	P =0.93 (NS)
Serum Phosphorus	**Mean ±SD**	2.9 ± 0.6	3.8 ± 0.6	Independent t- test
	Minimum-Maximum	2 - 4.1	3 - 5.5	**P < 0.001 (HS)**
Serum Mg^+	**Mean ±SD**	1.6 ± 0.3	2.1 ± 0.2	Independent t- test
	Minimum-Maximum	1 - 2.1	1.7 - 2.5	**P < 0.001 (HS)**
Serum Creatinine	**Mean ±SD**	1.7± 1.7	1.4 ± 0.4	Mann-Whitney U test
	Minimum-Maximum	0.6 - 9	0.8 - 2.2	P =0.54 (NS)
Serum Urea	**Mean ±SD**	61.9 ± 36.5	62.6 ± 19.2	Mann-Whitney U test
	Minimum-Maximum	19 -152	36 -95	P =0.46 (NS)
AST	**Mean ±SD**	46.6 ± 37.3	43.3 ± 20.7	Mann-Whitney U test
	Minimum-Maximum	15 - 190	12 - 92	P =0.75 (NS)
ALT	**Mean ±SD**	44.7 ±22.9	42.4 ± 18.3	Mann-Whitney U test
	Minimum-Maximum	15 - 110	10 - 86	P =0.73 (NS)
Serum Albumin	**Mean ±SD**	3 ± 0.5	3.6 ± 0.3	Independent t- test
	Minimum-Maximum	2.2 - 4.2	2.9 - 4.2	**P < 0.001 (HS)**
Serum Bilirubin	**Mean ±SD**	1.1 ± 0.5	1.2 ± 0.3	Independent t- test
	Minimum-Maximum	0.5 - 2.5	0.7 - 2	P = 0.24 (NS)
HB	**Mean ±SD**	12.4 ± 2.6	11.4 ± 1.6	Independent t- test
	Minimum-Maximum	8 - 16	8.3 - 14.2	P = 0.14 (NS)
HCT	**Mean ±SD**	37.8 ± 7.8	36.1 ± 7.5	Mann-Whitney U test
	Minimum-Maximum	23 - 55	22 - 52	P =0.36 (NS)
PLT	**Mean ±SD**	233.4 ± 105.7	221 ± 74	Mann-Whitney U test
	Minimum-Maximum	90 - 433	100 - 400	P = 0.93 (NS)
TLC	**Mean ±SD**	15.1 ± 5.9	14.1 ± 8.2	Independent t- test
	Minimum-Maximum	5 - 26	4 - 32	P = 0.65 (NS)

Similarly, there was a statistically significant difference between the two groups regarding the mean of the length of stay in ICU (group A = 10.6 ± 3.7 days, and group B = 6.1 ±1.2 days; p <0.001; **Figure 2**).

Table 2. At the time of weaning, there was statistically significant difference between both groups in terms of RR, average TV, PEEP, and PIP

Variable		Group A (n =20)	Group B (n =20)	Test
RSBI	**Mean ±SD**	88.8 ± 21.7	61.8 ± 18.5	Mann-Whitney U test
	Minimum-Maximum	44 - 133	36 - 100	**P <0.001 (HS)**
TV	**Mean ±SD**	499 ± 35.4	499.5 ± 37.2	Mann-Whitney U test
	Minimum-Maximum	450 - 550	450 - 550	P =0.98 (NS)
RR	**Mean ±SD**	27 ± 3	26 ± 3	Independent t- test
	Minimum-Maximum	22 - 32	20 - 30	P = 0.15 (NS)
PEEP	**Mean ±SD**	5.8 ± 0.8	5.7 ± 0.7	Independent t- test
	Minimum-Maximum	5 -7	5- 7	P = 0.84 (NS)
PPLAT	**Mean ±SD**	27.3 ± 5.2	19.7 ± 2.7	Independent t- test
	Minimum-Maximum	12 - 35	14 - 23	**P < 0.001 (HS)**
PPLT	**Mean ±SD**	23.6 ± 3.9	23.7 ± 3.1	Independent t- test
	Minimum-Maximum	18 -32	20 -29	P = 0.96 (NS)
PF ratio (pao2/fIo2)	**Mean ±SD**	184.5 ±57.1	222.1 ± 30.4	**Mann-Whitney U test**
	Minimum-Maximum	109 - 300	164 - 280	**P =0.02(SS)**
Compliance	**Mean ±SD**	27.8 ± 9.1	37.7 ± 6.6	**Independent t- test**
	Minimum-Maximum	16 - 42	23 - 45	**P < 0.001 (HS)**
Resistance	**Mean ±SD**	10 ± 1.5	10 ± 2	Independent t- test
	Minimum-Maximum	7 - 13	7 - 14	P = 0.93 (NS)

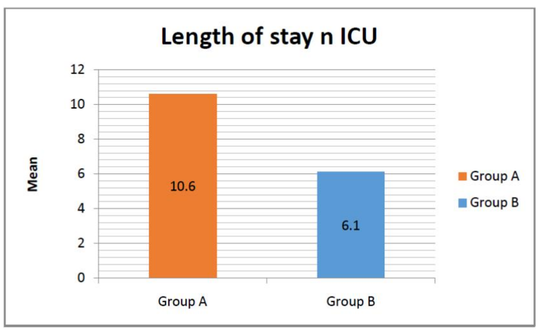

Figure 2. There was a statistically significant difference between the two groups regarding the mean of the length of stay in ICU (group A = 10.6 ± 3.7 days, and group B = 6.1 ±1.2 days; p <0.001)

At the baseline, the following mechanical ventilation parameters were significantly different between both groups: rapid shallow breathing index (RSBI), plateau pressure (PPLAT), PF ratio (pao2/fIo2) and compliance during the hospital stay (p< 0.001). Meanwhile there was no significant difference between the two group in tidal volume (TV), respiratory rate (RR), positive end expiratory pressure (PEEP), peak pressure (PP), and resistance. At the time of weaning, there was statistically significant difference between both groups in terms of RR, average TV, PEEP, and PIP (**Table 2**).

Almost 30% of patients in the group A and B complicated with diarrhea. Thirty-five percent of patients in group A complicated with vomiting compared to 25% in group B. There is no significant statistical difference between the two groups regarding any of the observed complications (**Table 3**).

Table 3. Thirty-five percent of patients in group A complicated with vomiting compared to 25% in group B. There is no significant statistical difference between the two groups regarding any of the observed complications

Variable (no.=40)		Group A (no.=20)		Group B (no.=20)		Test
		No.	%	No.	%	
Complications	No Complications	5	25	9	45	Fisher's Exact test P=0.13 (NS)
	Vomiting	7	35	5	25	
	Diarrhea	6	30	6	30	
	Vomiting & Diarrhea	2	10	0	0	

Interestingly, there was a statistically significant negative association between serum magnesium and length of stay in ICU in group A (r =-0.46, p value <0.05). In addition, a statistically significant negative association between serum magnesium and duration of mechanical ventilation was also detected in group A and B (r =-0.65 and -0.60, respectively).

4. Discussion:

A growing body of evidence has suggested that higher fat content diet may be more beneficial for ventilator-dependent patients; fat produces less metabolic CO2 than carbohydrates and in return may ameliorate the hypercapnic condition of respiratory failure patients[14]. Therefore, in the present prospective study, we evaluated the effect of EN on duration of mechanical ventilation and the beneficial role of high-fat low-carbohydrate diet among 40 patient with respiratory failure admitted to ICU and required mechanical ventilation.

The duration of mechanical ventilation is one of the important prognostic factors during ICU admission, previous reports have shown that prolonged mechanical ventilation is associated with adverse clinical outcomes, including pneumonia and lung injuries[16]. Moreover, prolonged mechanical ventilation leads to high health care expenditures and high total cost illness[17]. In critically ill patients, weaning from ventilatory assistance is a key survival factor[18]. Therefore, assessing the duration of mechanical ventilation is important during the evaluation of efficacy of the EN in critically ill patients.

In addition, the beneficial role of high-fat diet on CO2 level may significantly reduce the number of days needed for mechanical ventilation. In the present study, patients with high-fat low carbohydrates diet showed a statistically significant shorter duration of mechanical ventilation than patients with usual diet (4.4 ± 1.6 vs. 8.5 ±4.7, respectively; p value is < 0.001). Moreover, the length of hospital stay was significantly shorter in high-fat diet compared to standard diet patients (6.1 ±1.2 vs. 10.6 ± 3.7, respectively; p <0.001).

In concordance with our findings, **Faramawy and colleagues** compared the effect of a high fat, low carbohydrate EN to a standard iso-caloric diet among 100 patients with type II respiratory failure secondary to pulmonary disease requiring mechanical ventilation. The results showed a statistically significant difference (p < 0.001) between both groups as regards duration of mechanical ventilation, patients with high-fat diet spent about 62 hours less than those receiving the iso-caloric standard feed[13]. Similarly, **Al-Saady and colleagues** conducted a randomized controlled study on 20 patients with acute respiratory failure requiring artificial ventilation in order to compare high fat, low carbohydrate EN with a standard iso-caloric EN. The authors reported that the time spent on artificial ventilation from the commencement of feeding to successful weaning was 42O7o less in the high fat feed group (86.1 ±17.8 h) compared to the standard feed group (148.7 ±36.7 h) [19].

In addition, **Van den Berg and colleagues** performed a prospective, randomized controlled study on 32 ventilator-dependent patients with a prospect of weaning from mechanical ventilation. The median time of the study amounted to 4 days in the high fat, low carbohydrate feeding group against 6 days in the standard nutrition group: a difference which was statistically significance[14]. **Gottschlich 1990** reported statically significant reductions in length of stay (P <0.02) with low fat enteral feeds as well[20].

In contrary to our findings, **Garrel and colleagues** compared high-fat, low carbohydrates EN to high-carbohydrate, high-protein, low-fat among 37 patients requiring mechanical ventilation. There were no statistically significant differences between both groups in terms of duration of mechanical ventilation and length of hospital stay[21]. The difference between our findings and **Garrel and colleagues** can be explained by the different type of study population. **Garrel and colleagues** included patients with 10% or greater total body surface area burns in the immediate post-burn period.

Notably, there was a statistically significant negative association between serum magnesium and length of stay in ICU in standard diet group (r =-0.46, p value <0.05). In addition, a statistically significant negative association between serum magnesium and duration of mechanical ventilation was also detected in both study groups (r =-0.65 and -0.60, respectively). Previous reports have shown that the change in serum potassium level during ICU stay is associated with the need for mechanical ventilation; and that monitoring of the serum potassium levels may be a good prognostic factor for the requirement of mechanical ventilation[23]. Similarly, serum phosphorus level was suggested as a predictor of the need to mechanical ventilation in critically ill patients, **Talakoub and colleagues** reported that hypophosphatemia may increase the need to mechanical ventilation. Therefore, monitoring serum phosphorus level is a good prognostic factor to predict the need to ventilation[24].

Both serum magnesium and serum albumin were reported as a predictor of morbidity or mortality in critically ill patients, patients with hypomagnesemia and hypoalbuminemia were reported to suffer from longer hospital stay and worse survival rates than patients with normal values[25,26].

With regard to EN-associated complications, almost 30% of patients in both groups complicated with diarrhea. There was no significant statistical difference between the two groups regarding any of the observed complications. When a patient is artificially fed by nasogastric tube several problems can present: gastrointestinal (diarrhea, constipation, nausea and vomiting); tube‐related (nasal ulcers, tube clogging and tube dislodgement); respiratory (pulmonary aspiration); and metabolic (hyperglycaemia, hyper or dehydration, electrolytic alterations)[27].

We acknowledge that the present study has a number of Limitations. The sample size in the present study was relatively smaller than previous reports, which may affect the generalizability of our findings. Moreover, we did not assess the arterial CO2 pressure, an important proxy for the efficacy of high fat, low carbohydrates diet.

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