AN OBSERVATIONAL COMPARATIVE STUDY OF CRITICALLY ILL PATIENTS ON STANDARD FORMULA AND PEPTIDE BASED FORMULA

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Abstract : **AIM:** The aim of the study is to compare whole-protein formula (WPF) and a peptide - based formula (PEF) in terms of tolerance and nutritional outcomes in Critically ill patients.

OBJECTIVE: To observe the effect of WPF and SEF with specific outcomes of GI tolerance, length of stay of the patient and calorie deficit.

RESULTS: The results obtained illustrated that the patients of both the groups showed good tolerance towards the feed given, but 20% of the patients belonging SEF group showed diarrhea and patients belonging WPF group showed no symptoms of diarrhea. Length of stay on ventilator and in the ICU was more in patients belonging to WPF group when compared to SEF group though it was observed statistically insignificant (P-Value > 0.05) where as total length of stay in the hospital was more in patients belonging to WPF group when compared to SEF group which was observed statistically significant with **P-Value 0.001** (P-Value <0.05) when T-test was performed. Calorie & protein deficit was observed in both WPF and SEF groups due to feed disturbances.

CONCLUSION: Based on the results, it can be concluded that no significant difference was observed between both the groups except for the length of stay on ventilator , ICU length of stay, though it was observed statistically insignificant and total length of stay in hospital which was less in SEF when compared to WPF formula which was observed statistically significant.

I. INTRODUCTION

Malnutrition is a common finding in critically ill patients. Enteral nutrition is a preferred means of support for stimulating gut hormones, modulating immunity, and maintaining the barrier function of the intestinal mucosa. However, malabsorption, poor emptying, and hypoalbuminemia often occur in patients given enteral nutrition (1).

Dipeptides (2) have been reported to be more efficiently absorbed from the gastrointestinal tract than free amino acids. ICU patients(3) with poor nutritional status commonly experience immune dysfunction, weakened respiratory muscles and lowered ventilation capacity, and reduced GI tolerance . As a result, patients are at risk for a wide range of complications such as ventilator dependence; GI dysfunction with gastroesophageal reflux, esophagitis, or pulmonary aspiration and infections that can lead to sepsis, multi-organ failure, and even death. For such patients, supportive nutrition has long been used as adjunctive care

Supply of nutritional requirements is important for all patients, especially for those who cannot meet their nutritional needs normally.[4] In addition, appropriate and timely nutritional support results in reducing mortality rate in hospitalized patients.(5) Patients of Intensive Care Unit (ICU) need special medical care including nutritional care because of the complications caused by acute reaction or dysfunction of one or more body organs including the cardiovascular or respiratory systems.[6] The prevalence of malnutrition is estimated at 50% and 43% for the patients of the ICU, respectively. Besides, 15–70% of patients suffer from malnutrition on the admission to the hospitals [7].

In recent years, according to the Acute Physiology and Chronic Health Evaluation, mortality rate in ICUs is reported at 13.6–36%.[8] The high prevalence of malnutrition can be caused by the hypermetabolic state, anorexia, admission of the malnourished patients, and hospital infections[9]

Providing the calorie and macronutrients requirements, supportive formulas, and immediate and continuous nutritional assessments can prevent these disadvantages.[10,11] Moreover, consumption of dietary supplements containing multivitamins and minerals can improve the appetite.[12] Thus, anorexia as a prevalent outcome of hospitalization can be prevented to some extent and patients would receive more energy and macronutrients, subsequently.

The 2016 American Society for Parenteral and Enteral Nutrition (ASPEN)/Society of Critical Care Medicine (SCCM) Nutrition Support Guidelines for Critically Ill Adults recommend first the use of early enteral nutrition (EN) because of data demonstrating the improvement in patient outcomes such as reduction in infectious complications, in the length of mechanical ventilation, and in the overall length of hospital stay(13). Second, EN is preferred over the early use of parenteral nutrition because of earlier return of normal gut function and reduction in health care costs(14).

In the intensive care unit (ICU) setting, Peake et al reported that ~40% of patients required EN support.

The European Society for Parenteral and Enteral Nutrition guidelines also note that the clinical trial evidence for the impact of semi-elemental EN versus standard EN in ICU patients is contradictory with two trials showing a reduction in diarrhea, one showing an increase in diarrhea, and one trial showing no difference.

The European Society for Parenteral and Enteral Nutrition guidelines conclude that "As no clear cut advantage of peptide-based formula has been demonstrated in these studies and taking into account
the higher price, they concluded that the use of peptide-based
formulas should not be recommended (Grade C)."(15)

Though a standard polymeric formula (containing whole proteins and mainly long chain type of triglycerides) used as first-line EN may be adequate in a variety of clinical settings, a more specialized semi-elemental formula, containing peptides and mostly medium chain type of triglycerides, may still offer clinical benefits for some high-risk, critically ill patients.

Objectives of the study:

1)To compare the following observations in both WPF and SEF groups.
a)Length of stay on ventilator
b)Length of stay in ICU
c)Total length of stay in hospital
2)To observe the tolerance of the feed given in the study group
3)To observe the levels of Pre albumin and albumin in the study group
4)To observe the G.I symptoms towards tolerance in the study group
5)To observe the calorie and protein deficit in the study group

1.1 Population and Sample

A Observational study was performed in a Multi speciality hospital to assess the differences between WPF and PEF in critically ill patients in ICU'S with a sample size of 20(10 on standard supplements,10 on Peptide based formula) for a period of 2 months. The selection criteria included critically ill patients ,who remained in ICU for more than 72 hours, with age >18yrs and patients on RT feeds. Detailed data was collected prospectively and assessment of nutritional status (Anthropometric measurements, Biochemical parameters) was done using a pretested questionnaire to collect the day to day data of the study group. Statistical analysis was done in which percentages were calculated for some parameters(Gender, BMI, Tolerance, GI symptoms) & Student t-test was done for Total length of stay, Length of stay on ventilator, Length of stay in ICU, SOFA score, Albumin, Prealbumin, Planned calories, Received calories, Calorie deficit, Received protein, Protein deficit

1.2 Data and Sources of Data

The following detailed data was collected prospectively.

● Admission category (surgery vs. medical), primary admission diagnosis, sex, age, weight, height, comorbid diseases and Acute Physiology And Chronic Health Evaluation II (APACHE II) score [12],GCS Score.

● The daily goal calories and protein were recorded as per the dietitian's assessment, the type and amount of nutrition received for a maximum of 12 days or until death or discharge from ICU. The patients were followed while in hospital for a maximum of 12 days.

● Additional data including the length of stay in the ICU, total length of stay in the hospital were also collected for this study

● **Assessment of nutritional status - Using SGA tool:**

Only two of the following assessment tools were used.

1. **Anthropometric measurements :** Weight, height and body mass index (BMI)
2. **Biochemical tests** : Albumin, Pre albumin, Haemoglobin, sodium, potassium were assessed in the study.
● A data sheet was devised to collect the day to day data of the study group.

Statistical Analysis:

Percentages were calculated for some parameters(Gender, BMI, Tolerance, GI symptoms) & Student's t-test was done for Total length of stay, Length of stay on ventilator, Length of stay in ICU, SOFA score, Albumin, Pre albumin, Planned calories, Received calories, Calorie deficit, Received protein, Protein deficit.

1.3 Theoretical framework

A Observational study was performed to assess the differences between a whole-protein formula (WPF) and a peptide - based formula (PEF) in clinical outcomes.

Study type : Observational study.

Sample size: 20 (10 on standard supplements,10 on Peptide based formula).

Study area: Multi speciality hospitals, Hyderabad

Study period: 2 months
Target group: Critically ill patients in ICU'S.

Selection criteria:

A)Inclusion Criteria:

- Patients who remained in ICU for more than 72 hours
- Patients who were critically ill.
- Patients who were > 18 yrs of age.
- Patients on RT feeds.

B)Exclusion Criteria:

- Patients who did not remain in ICU for more than 72 hours
- Patients who were less than <18 yrs of age.
- Patients on Oral feeds.

Study flow:

- In the study conducted, patient population consisted of 20 who remained in ICU for more than 72 hours.
- Patients were divided into two groups (WPF group = 10 patients, PEF group = 10 patients).
- The patients who received peptide based enteral formula were classified as the peptide-based formula (PEF) group.
- Other patients who were fed a whole-protein formula were classified as the WPF group.
- The study patients were fed for at least 12days, with enteral formula

1.4Statistical tools and econometric models

Student t-test:

Total length of stay	Diet	N	Mean(X)	Standard error mean(S.E)	P-value(< 0.05) = Significant
	WPF	10	14.2	1.467	**0.001**
	SEF	10	6.8	1.315	
Length of stay on ventilator	WPF	10	4.44	0.729	0.492
	SEF	10	3.3	1.446	
Length of stay in ICU	WPF	10	10.9	1.509	1
	SEF	10	10.9	0.605	
SOFA score	WPF	10	9.7	1.43	0.05
	SEF	10	5.4	1.47	
Albumin	WPF	10	2.68	0.19	0.294
	SEF	10	2.28	0.313	
Pre Albumin	WPF	10	14.09	0.826	0.257
	SEF	10	16.31	1.679	
Planned calories	WPF	10	14487.4	1558.392	0.394
	SEF	10	12714	1296.821	
Received calories	WPF	10	14182	1575.322	0.357
	SEF	10	12350.5	1120.76	
Calorie Deficit	WPF	10	201.9	193.603	0.634
	SEF	10	363.5	270.435	
Planned Protein	WPF	10	611.26	64.672	0.53
	SEF	10	553.21	63.643	
Received Protein	WPF	10	601.96	64.061	0.4
	SEF	10	529.61	54.032	
Protein Deficit	WPF	10	9.3	8.654	0.508
	SEF	10	23.6	19.139	

- In the Student t-test the P-value for all the parameters was insignificant (P-Value > 0.05) except for the total length of stay with **P-Value 0.001** (P-Value <0.05) which is considered statistically significant.
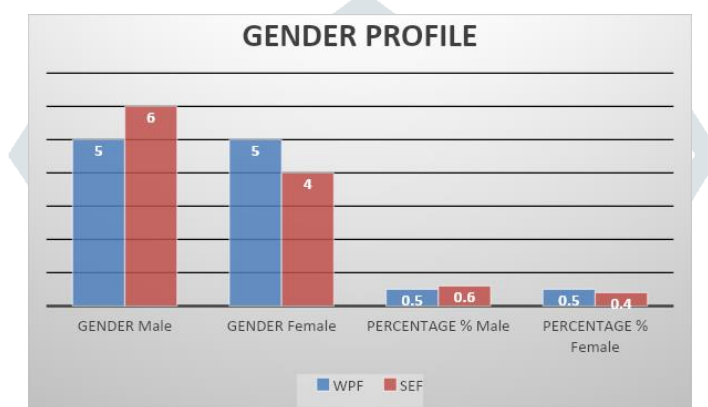
II. RESULTS AND DISCUSSION

GENDER CLASSIFICATION:

The total number of patients assessed were 20.A mix of male and females were present in both WPF and SEF groups.

Table(1) gives the break up of both the groups.

TABLE (1)

GENDER PROFILE

| GENDER	WPF		SEF	
	NUMBER(n= 10)	PERCENTAGE(%)	NUMBER(n= 10)	PERCENTAGE(%)
Male	5	50%	6	60%
Female	5	50%	4	40%

- The patients assessed had equal no of males and females(50%) in the WPF group &
- The majority of the patients assessed were males(60%) in the SEF group

BMI PROFILE:

The patients were assessed as per BMI and classified according to their nutritional status in both WPF and SEF groups. The details are shown in the table.

TABLE (2)

BMI RANGES	WPF GROUP		SEF GROUP	
	NUMBER	PERCENTAGE (%)	NUMBER	PERCENTAGE (%)
UNDER WEIGHT(<18.5)	0	0	0	0
NORMAL (18.5 - 24.9)	5	50	8	80
OBESE GRADE - 1(25 - 29.9)	3	30	2	20
OBESE GRADE - 2(30 - 39.9)	2	20	0	0
OBESE GRADE - 3(> 40)	0	0	0	0
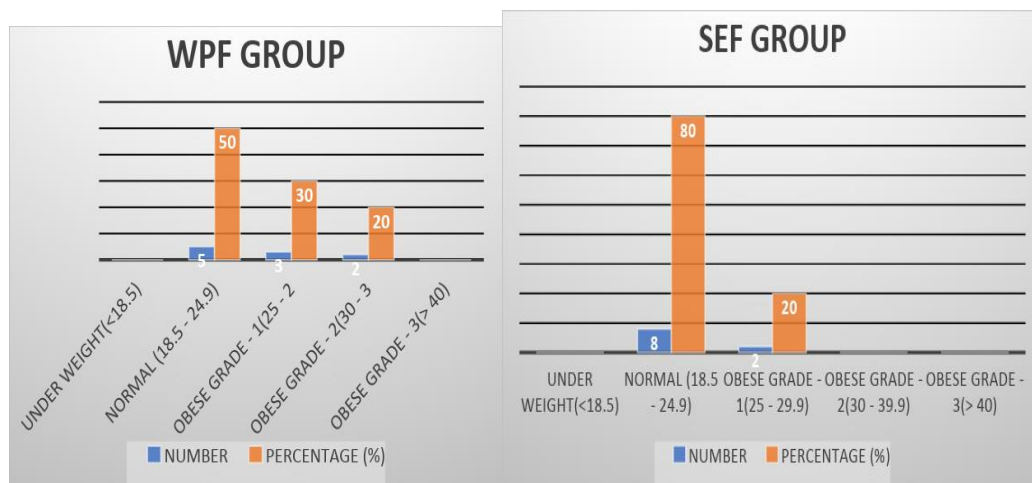
- Half of the patients assessed in the WPF group were normal and the other half were of obese grade – 1 and grade – 2 category.

Most of the patients assessed in the SEF group were normal

BIOCHEMICAL VALUES:

The biochemical data of the patients in both WPF and SEF groups were evaluated and interpreted. The details are shown in the tables.

TABLE (3)   **BIOCHEMICAL ANALYSIS**

NUMBER OF PATIENTS	ALBUMIN(Normal range 3.5 – 5g/dL)	
(n=10)	SPF	WPF
1	2	2.18
2	2.8	2.23
3	1.5	2.00
4	2.00	2.35
5	3.2	2.5
6	2.9	2
7	3.2	3.2
8	1.8	3.5
9	2.8	2.7
10	2.6	3.45

ALBUMIN (Normal range 3.5 - 5g/dL)
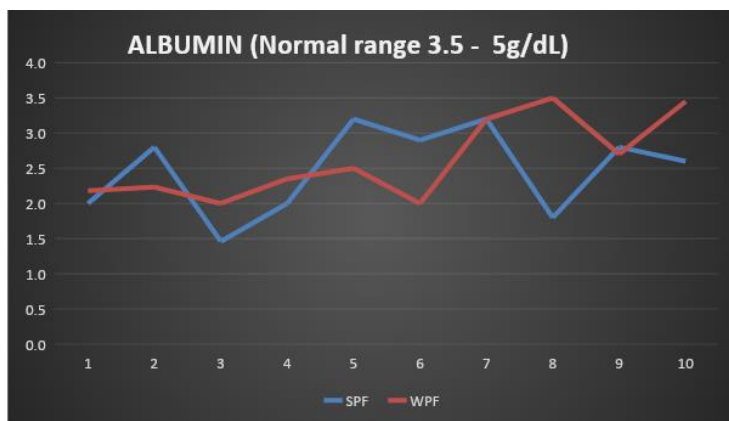
TABLE (4)

NUMBER OF PATIENTS	PRE ALBUMIN(Normal range 18-35.7mg/dL)	
(n=10)	WPF	SEF
1	12	9
2	14	19
3	17	6
4	30	19
5	16	17
6	8	22
7	11	14
8	12	17
9	14	22
10	12	18

PRE ALBUMIN (Normal range 18-35.7mg/dL)
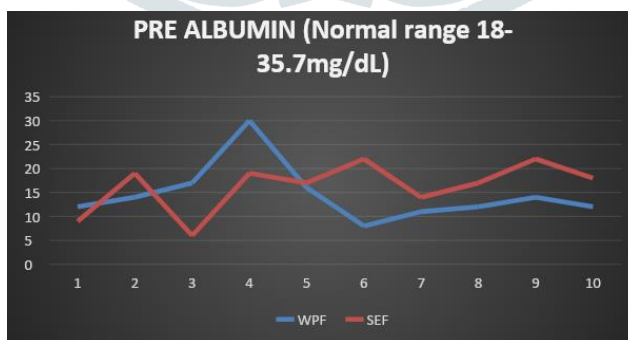
- In the above figure, pre albumin levels were better in SPF group than WPF whereas ,albumin levels were good in WPF group when compare to SPF group.

- In a study it was reported increase in serum pre albumin and albumin in both groups but levels reached statistical significance in the 100% WHP diet group only, indicating improved nutrient assimilation in the semi-elemental group.(24)

SOFA SCORE:

SOFA scores of both WPF and SEF groups is shown in Table (14)

TABLE (14)

NUMBER OF PATIENTS	SOFA SCORE (0-24)	
(n=10)	WPF	SEF
1	6	9
2	16	16
3	3	3
4	13	9
5	7	1
6	16	4
7	6	1
8	9	4
9	8	4
10	13	3

- Patients included in the WPF group have HIGH SOFA scores when compared to SEF group indicating high risk of mortality.
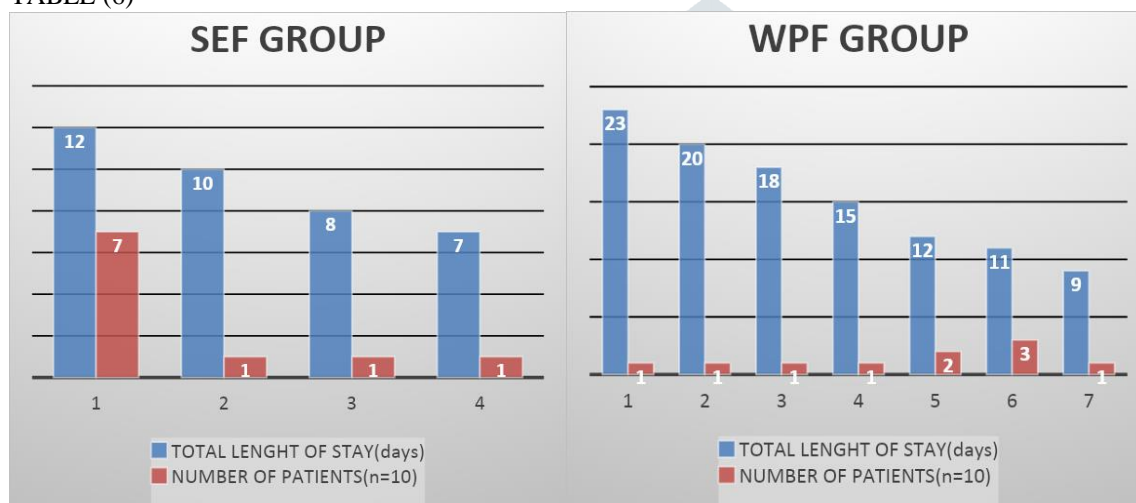
TOTAL LENGTH OF STAY CLASSIFICATION:

The total length of stay in the hospital of the patients in both WPF and SEF groups is shown in Table (5) and (6)

SEF GROUP	
TOTAL LENGTH OF STAY(days)	NUMBER OF PATIENTS(n=10)
12	7
10	1
8	1
7	1

TABLE (5)

WPF GROUP	
TOTAL LENGTH OF STAY(days)	NUMBER OF PATIENTS(n=10)
23	1
20	1
18	1
15	1
12	2
11	3
9	1

TABLE (6)

- Total length of stay was more in patients belonging WPF group when compared to SEF group
- Oral nutritional standard supplement may be associated with reduced LOS, hospitalization cost, and readmission risk in hospitalized Medicare patients(24)

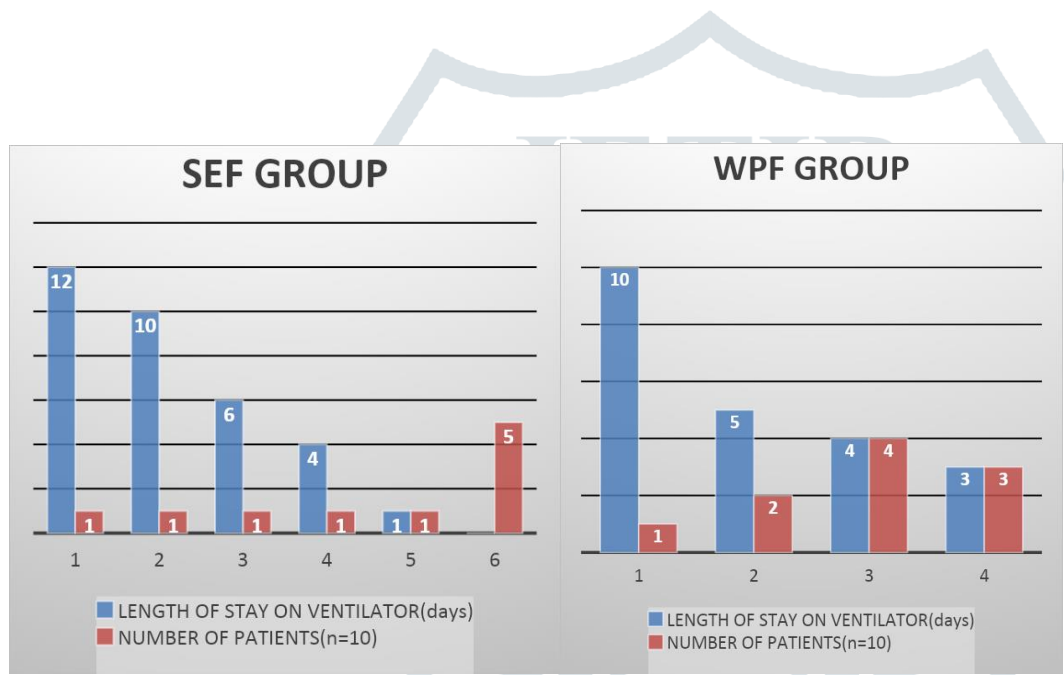**LENGTH OF STAY ON VENTILATOR CLASSIFICATION:**

The length of stay on ventilator of the patients in both WPF and SEF groups is shown in Table (7) and (8)

WPF GROUP	
LOS ON VENTILATOR(days)	NUMBER OF PATIENTS(n=10)
10	1
5	2
4	4
3	3

TABLE (7)

SEF GROUP	
LENGTH OF STAY ON VENTILATOR(days)	NUMBER OF PATIENTS(n=10)
12	1
10	1
6	1
4	1
1	1
0	5

TABLE (8)

- **Length of stay on ventilator was more in patients belonging WPF group when compared to SEF group**

In a study conducted that critically ill patients should be fed intermittently with a whey-based formula which contains omega-3 fatty acids. is likely to limit muscle atrophy and promote metabolic stability (23)
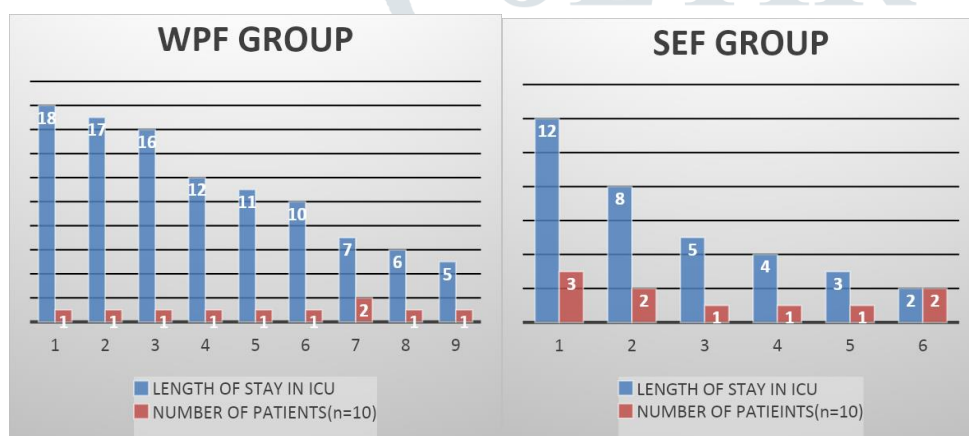
LENGTH OF STAY IN ICU CLASSIFICATION:

The length of stay in ICU of the patients in both WPF and SEF groups is shown in Table (8) and (9)

SEF GROUP	
LENGTH OF STAY IN ICU	NUMBER OF PATIEINTS(n=10)
12	3
8	2
5	1
4	1
3	1
2	2

TABLE (8)

WPF GROUP	
LENGTH OF STAY IN ICU	NUMBER OF PATIENTS(n=10)
18	1
17	1
16	1
12	1
11	1
10	1
7	2
6	1
5	1

TABLE (9)

- The above data shows the Length of stay in ICU was more in patients belonging WPF group when compared to SEF group
- In the study ,it was observed that the use of semi-elemental formula instead of standard EN can result in cost savings through the reduction in length of ICU stay if >7% of GI intolerance cases are avoided.(20)

A pilot study suggests that feeding a peptide-based formula to ICU patients may be associated with a statistically significant reduction in the number of days, during which adverse events occurred as compared to a standard formula.(17)

GI SYMPTOMS:

The GI symptoms towards tolerance in both WPF and SEF groups is shown in Table (10)

(TABLE 10)

	OBSERVATION	
GROUP	NO DIARRHEA	NO CONSTIPATION
SEF	80%	100%
WPF	100%	100%
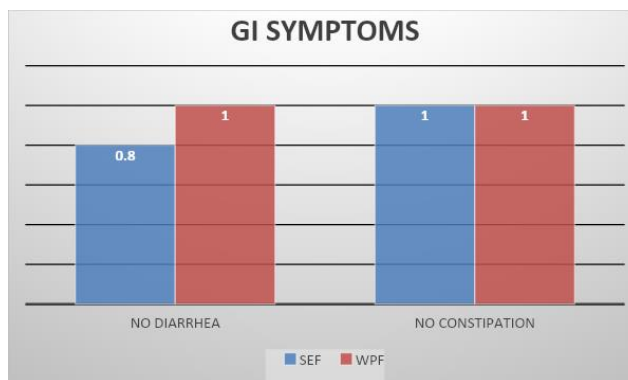
- Patients of both the groups showed no symptoms of constipation
- 20% of the patients belonging SEF group showed diarrhea
- Patients belonging WPF group showed no symptoms of diarrhea

- The European Society for Parenteral and Enteral Nutrition guidelines also note that the clinical trial evidence for the impact of semi-elemental EN versus standard EN in ICU patients is contradictory with two trials showing a reduction in diarrhoea, one showing an increase in diarrhoea (16)
- it was concluded that peptide enteral formula was well tolerated in patients with severe hypoalbuminemia when compared to a standard isotonic enteral formula.(21)

TOLERANCE :

Tolerance towards feed in both WPF and SEF groups is shown in Table (11)

(TABLE 11)

GROUP	OBSERVATION	
	TOLERANCE	NO ASPIRATION
SEF	100%	100%
WPF	100%	100%

- Patients of both the groups showed good tolerance towards the feed given.

- A study reported that a 100% whey semi elemental formula would lead to fewer cases of GI intolerance than a standard formula because the enzymatically hydrolyzed whey protein helps facilitate gastric emptying and reduces the risk for reflux and aspiration(26)
- It was concluded that by taking Oral nutritional supplements with peptides and n-3 fatty acids, for a 3 month period were well tolerated and resulted in body weight gain (20)
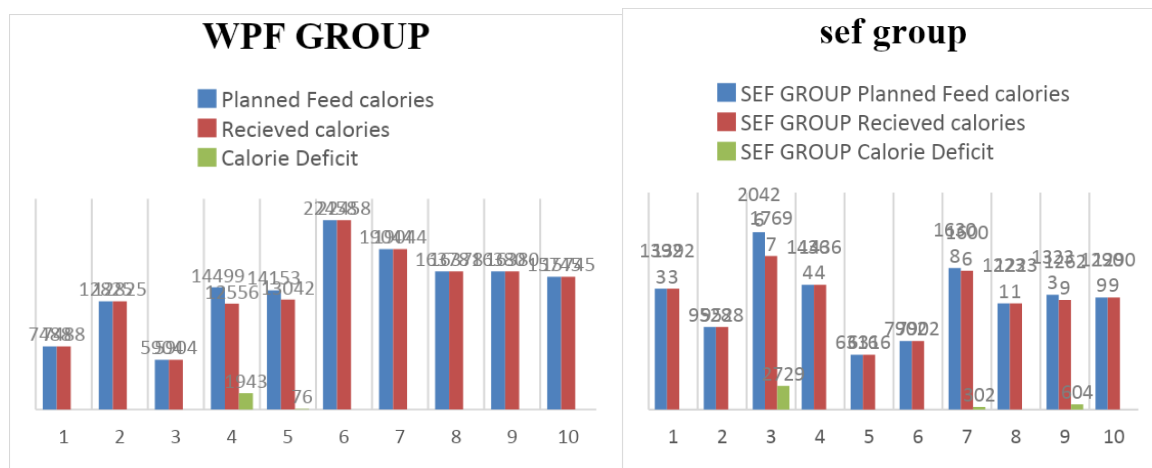
FEED INTAKE DETAILS:

Calorie intake details in both WPF and SEF groups is shown in Table (12)

NO OF PATIENTS(n=10)	WPF GROUP		
	Planned Feed calories	Received calories	Calorie Deficit
1	7488	7488	0
2	12825	12825	0
3	5904	5904	0
4	14499	12556	1943
5	14153	13042	76
6	22458	22458	0
7	19044	19044	0
8	16378	16378	0
9	16380	16380	0
10	15745	15745	0

TABLE (12)

NO OF PATIENTS(n=10)	SEF GROUP		
	Planned Feed calories	Received calories	Calorie Deficit
1	13923	13923	0
2	9528	9528	0
3	20426	17697	2729
4	14364	14364	0
5	6316	6316	0
6	7902	7902	0
7	16308	16006	302
8	12231	12231	0
9	13233	12629	604
10	12909	12909	0

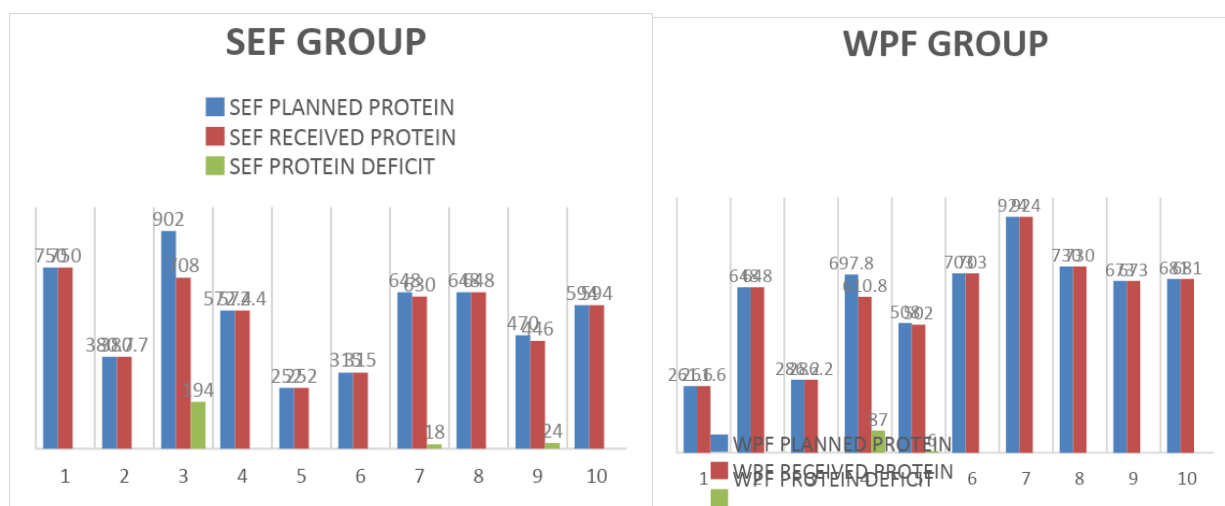- Calorie deficit was observed in both WPF and SEF groups due to feed disturbances like tracheostomy, ECG,X-RAY tests.

FEED INTAKE DETAILS:

Protein intake details in both WPF and SEF groups is shown in Table (13)

TABLE(13)

NO OF PATIENTS(n=10)	WPF GROUP		
	PLANNED PROTEIN	RECEIVED PROTEIN	PROTEIN DEFICIT
1	261.6	261.6	0
2	648	648	0
3	286.2	286.2	0
4	697.8	610.8	87
5	508	502	6
6	703	703	0
7	924	924	0
8	730	730	0
9	673	673	0
10	681	681	0
	SEF GROUP		
NO OF PATIENTS(n=10)	PLANNED PROTEIN	RECEIVED PROTEIN	PROTEIN DEFICIT
1	750	750	0
2	380.7	380.7	0
3	902	708	194
4	572.4	572.4	0
5	252	252	0
6	315	315	0
7	648	630	18
8	648	648	0
9	470	446	24

10	594	594	0

- Protein deficit was observed in both WPF and SEF groups due to feed disturbances like tracheostomy, ECF, X-RAY tests.

III. ACKNOWLEDGMENT

This aknowlegdment is not only formality but also it is a way by which we are getting an opportunity to show our deep sense of gratitude and obligation to all the people who have provided us ,with inspiration, guidance and help during the preparation of the project successfully.

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This acknowledgement will be incomplete if we fail to express our deep sense of gratitude and indebtedness to our group members and friends, for their patience and support without which this would not have been successfully completed.

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