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A COMPARISON OF GLUTAMINE AND PROBIOTICS AS A NUTRIENT IN SEPTIC PATIENT.

Clinical Research

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ABSTRACT

The aim of the present study is comparison of glutamine and probiotics as a nutrition supplement in patients with sepsis in terms of Length of hospital stay, Mechanical Ventilaton free days, Mortality rate, Frequency of infectious complications. The final sample comprises of 120 patients- 60 patients in each group on the basis of quota system i.e patients receiving glutamine and probiotics as standard diet. One sample of 10 ml blood sent for culture/sensitivity as to clinically diagnose septicemia, and second sample of 10 ml blood for culture/sensitivity after two weeks of enteral feed. They are evaluated by history, clinical examination and relevant investigations. Group 1 will receive glutamine 30gm/ day and Group 2 will receive probiotics 10 billion CFU/day. This prospective, clinical study was designed to detect differences in clinical outcomes between two enteral formulas after admission to an ICU. There was marked reduction in length of hospital stay with patients receiving enteral glutamine in comparison to probiotics. There was no significant difference in mechanical ventilator free days & frequency of infectious complications in between patients receiving enteral glutamine and probiotics. There was significant difference in mortality between two groups i.e mortality rate decreases more in patients receiving enteral glutamine supplementation than probiotics. Our study therefore concludes exogenous enteral glutamine supplementation in sepsis patients have shown benefits related to anti-inflammatory roles, immune modulation, preservation of tissue function and antioxidant capacity.

KEYWORDS

Sepsis, Glutamine, Probiotics, Enteral Nutrition

INTRODUCTION

Sepsis with associated multisystem organ dysfunction is a leading cause of death in patients hospitalized in intensive care units (ICU). During critical illness, alterations in gut microflora are due to several factors that include changes in circulating stress hormones, gut ischemia, immunosuppression, the use of antibiotics and other drugs, possible bacterial translocation and the lack of nutrients. Providing adequate nutritional support through enteral and parenteral routes may improve clinical outcomes such as wound healing, infection rates, and hospital length of stay, mechanical ventilation free days, mortality rate, frequency of infectious complications. Four SIRS criteria were defined namely tachycardia (heart rate >90 beats/min), tachypnea (respiratory rate >20 breaths/min), fever or hypothermia (temperature >38 or <36 °C), and leukocytosis, leukopenia or bandemia (white blood cells >1,200/mm3, <4,000/mm3 or bandemia ≥10%). Patients who met two or more of these criteria fulfilled the definition of SIRS. Sepsis-1 was defined as infection or suspected infection leading to the onset of SIRS. Sepsis complicated by organ dysfunction was termed severe sepsis, which could progress to septic shock, defined as "sepsis-induced hypotension persisting despite adequate fluid resuscitation." [1,2]. Under the Sepsis-2 definition, as with Sepsis-1, an individual must have atleast 2 SIRS criteria and a confirmed or suspected infection [3]. The authors recommended use of SOFA scoring to assess the severity of organ dysfunction in a potentially septic patient.

Glutamine (C5H10N2O3) is a conditionally essential amino acid, produced in large quantities by skeletal muscles, brain and lungs. In human blood, glutamine is the most abundant free amino acid [4]. Studies of exogenous glutamine supplementation in critically ill patients have shown benefits related to anti-inflammatory roles, immune modulation, preservation of tissue function, and antioxidant capacity. Under normal conditions, glutamine is a nonessential amino acid. However in catabolic patients, glutamine has been postulated to be a conditionally essential nutrient. Glutamine plays a central role in nitrogen transport, intestinal mucosal integrity, nucleotide and arginine synthesis & renal angiogenesis [4].

Probiotics are live microorganisms that when administered in adequate amounts, confer a health benefit on the host. The most common probiotics are the bacteria lactobacilli and bifidobacteria and the yeast Saccharomyces .boulardii. The health benefits of specific strains involve effects on infections, immune function, inflammation and gastrointestinal transit, which result from microbial competition, bacteriocin production & specific & nonspecific immune stimulation [5,6].

MATERIAL & METHODS

The present study was approved by the Committee of Ethics in Research of the S.N Medical College & Hospital Agra. Sample size selected on the basis of quota system. 120 consecutive patients admitted to our 12-bedded ICU who fulfil our inclusion and exclusion criteria during the study period of 1 year were selected as sample of the study. The final sample comprises of 120 patients- 60 patients in each group ie patients receiving gutamine and probiotics as a standard diet (each group, n=60). The main end points in the study are-

(1) The length of hospital stay (L.O.H.S) in the ICU
(2) The Mechanical Ventilation Free Days (M.V.F.D)
(3) Mortality rate
(4) Frequency of infectious complications (F.I.C)

Eligibility for the study included : Patients admitted in ICU with sepsis, Patients on ventilatory support, Patients in which enteral feed is allowed, Patients age 15-60 years admitted in ICU with sepsis, An individual must have atleast 2 SIRS criteria, 7 or more sequential organ failure assessment score (SOFA score), therapeutic intervention scoring system (TISS) score >20.

The exclusion criteria were:- Attendant/Patient not giving consent, Patient not tolerating enteral feed, Immuno-suppressive conditions (AIDS, chronic corticosteroid use and immuno-suppressive drugs), Severe brain injury (Glassgowscale score <5), Chemotherapy or radiotherapy in the last 6 months, cancer, pregnancy, indication of TPN (Total Parenteral Nutrition), Patients were excluded if the diet was interrupted for 2 or more consecutive days or for more than 5 days during the period of study. Duration of enteral feed (glutamine or probiotics) is upto two weeks in our study.

Systemic inflammatory response syndrome	
Finding	**Value**
Temperature	<36 °C (96.8 °F) or >38 °C (100.4 °F)
Heart rate	>90/min
Respiratory rate	>20/min or PaCO2<32 mmHg (4.3 kPa)
WBC	<4x10^9/L (<4000/mm^3), >12x10^9/L (>12,000/mm^3), or 10% bands

SOFA score	0	1	2	3	4
Respirationa PaO_2/FIO_2 (mm Hg) SaO_2/FIO_2	>400	<400 221–301	<300 142–220	<200 67–141	<100 <67
Coagulation Platelets $10^3/mm^3$	>150	<150	<100	<50	<20
Liver Bilirubin (mg/dL)	<1.2	1.2–1.9	2.0–5.9	6.0–11.9	>12.0
Cardiovascular[b] Hypotension	No hypotension	MAP <70	Dopamine </=5 or dobutamine (any)	Dopamine >5 or norepinephrine </=0.1	Dopamine >15 or norepinephrine >0.1
CNS Glasgow Coma Score	15	13–14	10–12	6–9	<6
Renal Creatinine (mg/dL) or urine output (mL/d)	<1.2	1.2–1.9	2.0–3.4	3.5–4.9 or <500	>5.0 or <200

One sample of 10ml blood sent for culture/sensitivity as to clinically diagnose septicemia, and second sample of 10 ml blood for culture/sensitivity after two weeks of enteral feed. They are evaluated by history, clinical examination and relevant investigations.

Group 1 will receive glutamine 30gm/ day and Group 2 will receive probiotics 10 billion CFU/day. This prospective, clinical study was designed to detect differences in clinical outcomes between two enteral formulas after admission to an ICU ward.

Formulas were administered by nasoenteric, nasogastric, gastrostomy or jejunostomy tube at the discretion of the physician-investigator. Enteral nutrition is started within 36 hrs of the diagnosis of sepsis and the total intake of caloric needs is scheduled to be reached by day 4 after entry to the study . Both formulas were similar in form (powder).

The calculation for caloric needs is based on the Harris-Benedict formula.

After admission of patient and before starting the enteral glutamine/probiotics, routine investigations (CBC, B.Urea, S.Creatinine, S.electrolyte, SGOT, SGPT, S.billirubin, Urine routine & microscopy, ABG) were sent, then test feed was given to the patient. If test feed was accepted, enteral feed was started. Enteral nutrition allowed with addition of glutamine/probiotics powder mix in 100-200 ml water. 30gm glutamine & 10 billion CFU probiotics given in two divided doses per day. Glutamine/Probiotics given upto 14 days, then observe the patients clinically, with lab investigations & examination . The frequency of acquired infections after study inclusion was recorded for each patient according to criteria of the Centers for Disease Control including type of infection, organism, localization, and required treatment. Length of stay in the ICU was also recorded, although the patient was not followed up through hospital stay, nor were data available before entry to the study. Digestive complications caused by enteral nutrition, such as nausea, vomiting, abdominal distention, and diarrhea, were also recorded for each patient for each day.

Significance testing for the univariate, between group differences was performed by using when appropriate, analysis of variance, Student's t-test. P value less than 0.05 considered significant.

RESULTS & DISCUSSION

Both the groups of patients receiving glutamine and probiotics are demographically comparable with maximum patients in the age group of 21-30 yrs in both the groups.

Sex wise distribution is- M:F=1:1.4 for glutamine M:F=1:1.5 for probiotic group.

Table 1: SOFA Score

Sofa Score	Glutamine(N=60)	Probiotic(N=60)
<12	51(85.00)	51(85.00)
13-18	9(15.00)	9(15.00)
19-24	0	0
Mean	9.70	9.97
SD	2.40	2.25
t-value	-0.6357	
p-value	0.5262	

The mean (±SD) sofa score was 9.70 ±2.40 and 9.97±2.25 in group received enteral glutamine and probiotics respectively with P-value 0.5262 . The groups were statistically insignificant, majority of patients (85%) have <12 sofa score in our study who received glutamine and probiotics.

Table 2: L.O.H.S (DAYS)

L.O.H.S(days)	Glutamine(N=60)	Probiotic(N=60)
≤5 days	16(26.67)	13 (21.67)
6to 10	32 (53.33)	21 (35.00)
11 to 15	7 (11.67)	17 (28.33)
16 to 20	3 (5.00)	1 (1.67)
21 to 25	2 (3.33)	3 (5.00)
26 to 30	0 0.00	5 (8.33)
>30 days	0 0.00	0 0.00
Mean	8.45	10.95
SD	4.47	6.97
t-value	-2.3387	
p-value	0.0213	

L.O.H.S for glutamine was 8.45+-4.47 days while for probiotics L.O.H.S was 10.95+- 6.97.

P value was 0.0213 that was significant value (<0.05).

Table 3: M.V.F.D

M.V.F.D(days)	Glutamine(N=37)	Probiotic(N=24)
1 to 3 days	32	17
4 to 6	5	6
10 days	0	1
Mean	2.73	3.00
SD	0.90	1.98
t-value	-0.6273	
p-value	0.5353	

The mean (±SD) M.V.F.D was 2.73 ±0.90 days and 3.00±1.98 days in group received enteral glutamine and probiotics respectively with P-value 0.5353 , the groups were statistically insignificant.

Table 4: MORTALITY

	No.	%
Glutamine(N=60)	21	35.00
Probiotc(N=60)	30	50.00
Over all (N=120)	51	42.50

Mortality rate 35% and 50% in group received enteral glutamine and probiotics respectively which was statistically significant. Glutamine shows decrease in mortality rate more than probiotics.

Table 5: F. I .C (frequency of infectious complications)

F. I .C	Glutamine(N=60)		Probiotc(N=60)	
	No.	%	No.	%
BSI	5	8.33	9	15.00
FUNGAL	4	6.67	6	10.00
UTI	7	11.67	7	11.67
VAP	6	10.00	10	16.67

The blood stream infection(BSI) 8.33% and 15% in groups received enteral glutamine and probiotics respectively, fungal infection 6.67% and 10.0%, urinary tract infection(UTI) 11.67% and 11.67% Ventilator associated pneumonia (VAP) 10.0% and 16.67% in group received enteral glutamine and probiotics respectively. with P-value 0.867. The difference was statistically insignificant.

DISCUSSION

Glutamine helps to maintain gastrointestinal structure, reduces intestinal permeability, and decreases the risk of bacterial translocation and development of infection. Supplementation has also been shown to attenuate cytokine release, preserve tissue function after sepsis, and attenuate insulin resistance. Under normal conditions, glutamine is a nonessential amino acid. However, in catabolic patients, glutamine has been postulated to be a conditionally essential nutrient

The two groups were comparable in following profile which include Age, sex , SIRS Criteria (temp, Heart rate, Resp rate, WBC count), SOFA Score (P:F ratio, platelets count, bilirubin, vassopresor, GCS, S.Creatinine).

There was a significant difference between glutamine and probiotics in relation to L.O.H.S, both causes decrease in the length of hospital stay but there were lesser no. of days of hospital stay with glutamine in relation to probiotics. In our study L.O.H.S for glutamine was 8.45+-4.47 days while for probiotics L.O.H.S was 10.95+- 6.97, P value was 0.0213 that was significant value (<0.05)

Enteral GLN supplementation does not confer significant clinical benefit in critically ill patients, with the exception of reduced hospital stay. There may be a significant benefit in patients with burns[7].

In our study there was no significant difference found in glutamine and probiotics in relation to mechanical ventiatory free days.

echanical ventilator free days for glutamine was 2.73+-0.90 and for probiotics was 3.0+-1.98, P value was 0.5353 which was not significant (significant P<0.05), glutamine and probiotics both are reducing ventilator days i.e. increasing mechanical ventiatory free day till the patient is in ICU. However some other studies shows glutamine delivered via the parenteral route has been associated with decreased length of mechanical ventilation, decreased risk of pneumonia, and decreased bacteremia and fungemia incidence [8].

Same result of reduction in mechanical free days in patients taking probiotics were also found in other studies [9].

In our study there was 42.50% total mortality, 35% mortality in those patients (n=60) who taken glutamine, and 50% of total mortality in those patient (n=60) who taken probiotics as nutrition. This means there was significant difference in mortality in those taken glutamine or probiotics. The percentage of mortality in glutamine low in comparison to probiotics.

Other studies also suggested the reduction in mortality with the use of glutamine and probiotics [10].

While a few studies suggested that early provision of high-dose glutamine administered separately from artificial nutrition was not beneficial and may be associated with increased mortality in critically ill patients with multiorgan failure [11]

In our study out of 120 patients 45.0% patients suffered from infectious complication .

36.67% infectious complications occur in those patients, who had taken glutamine (n=60). 53.33% infectious complications occur in those patients, who had taken probiotics (n=60). There was no significant difference found between glutamine and probiotics in relation to frequency of infectious complication, while both glutamine and probiotics reduced frequency of infectious complications individually.

In previous studies Glutamine supplementation conferred no overall mortality and length of hospital stay benefit in critically ill patients. However, this therapy reduced nosocomial infections among critically ill patients, which differed according to patient populations, modes of nutrition and glutamine dosages [12].

Some previous studies shows the administration of probiotics did not result in any improvement in the incidence of clinically suspected VAP, antimicrobial consumption, duration of mechanical ventilation, mortality and length of hospital stay [13,14].

CONCLUSION

Our study therefore concludes exogenous enteral glutamine supplementation in sepsis patients have shown benefits related to anti-inflammatory roles, immune modulation, preservation of tissue function, and antioxidant capacity. Glutamine helps to maintain gastrointestinal structure, reduces intestinal permeability, and decreases the risk of bacterial translocation and development of infection.

Glutamine and probiotics both reduce length of hospital stay but more with glutamine.

Both glutamine and probiotics increase mechanical ventilation free days but no significant difference between these groups.

Glutamine and probiotics both decrease mortality rate but glutamine decrease more than probiotics.

Both glutamine and probiotics resist infectious complications but no significant difference between them

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