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Role of Glutamine Supplementation in Management of Burn Patients

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Abstract: *Glutamine is the most abundant free amino acid in the body[1]. In the presence of critical illness and catabolic stress, the body's glutamine consumption exceeds the normal supply and the gut mucosal cells, deprived of glutamine, cease to perform their barrier function and allow entry of luminal toxins and bacteria directly into the portal bloodstream.[2] Supplementation with glutamine or glutamine-containing dipeptides improves nitrogen balance and maintains the intracellular glutamine pool[3]. Our aim is to study the role of glutamine supplementation in burn patients. This prospective observational study was conducted among burn patients who were admitted in the burn ward from August 2017 to March 2018. A total of 60 patients were included in the study. Patients receiving glutamine supplementation had overall better survival and showed significantly (<0.05) less morbidity and mortality.*
Hence the above study showed that Glutamine being a semi-essential amino acid improves outcome in burn patients and therefore, should be supplemented for better prognosis.

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I. Introduction

Nutrition therapy is a cornerstone of burn care from the early resuscitation phase until the end of rehabilitation[4]. While several aspects of nutrition therapy are similar in major burns and other critical care conditions, the pathophysiology of burn injury with its major endocrine, inflammatory, metabolic and immune alterations requires some specific nutritional interventions[4]. Glutamine being a semi-essential amino acid in the body fulfils many roles including facilitating nitrogen metabolism, fueling the cells that line the intestine, supporting protein synthesis, and serving as a critical substrate for the cellular immune response[5]. In the presence of critical illness and catabolic stress, the body's glutamine consumption exceeds the normal supply and the gut mucosal cells, deprived of glutamine, cease to perform their barrier function and allow entry of luminal toxins and bacteria directly into the portal bloodstream[2]. Supplementation with glutamine or glutamine-containing dipeptides improves nitrogen balance and maintains the intracellular glutamine pool[3]. The current study aims to study the overall effect of glutamine supplementation among patients of burn.

II. Material And Methods

This prospective comparative study was carried out among patients of Burn admitted in the burn ward, Department of Surgery at Rajendra Institute of medical sciences (RIMS), Ranchi, from August 2017 to March 2018. A total of 60 burn patients were included in this study.
Study Design: Prospective open label observational study.
Study Location: This was a tertiary care teaching hospital based study done in the Burn ward, Department of General Surgery, at Rajendra Institute of Medical Sciences (RIMS), Ranchi, Jharkhand.
Study Duration: August 2017 to March 2018.
Sample size: 60 patients.

Inclusion criteria:
1. Burn patients having 30-40 % of burn injuries.
2. Female sex
3. Aged ≥ 18 years,

Exclusion criteria:
1. Patients with burn injuries more than 40% and less than 30%.
2. Patients having deep facial burns.
3. Patients with seizure disorders.
4. Patients with injuries from high voltage electrical shock

5. Patients who are moribund
6. Patients having age less than 18 years.
7. Received glutamine supplement for > 24 hrs prior to randomization
8. Known allergy to maltodextrin, corn starch, corn, or corn products
9. Pregnant patients.
10. Liver cirrhosis - Child's class C liver disease
11. Absolute contra-indication for enteral nutrition; intestinal occlusion or perforation, abdominal injury
12. Patients admitted more than 48hrs after burn

Procedure methodology

After written informed consent was obtained, a well-designed questionnaire was used to collect the data of the recruited patients retrospectively. The questionnaire included socio-demographic characteristics such as age, gender, height, weight, mode of burn injury acquired and biochemistry laboratory investigations such as haemoglobin levels, total and differential leukocyte count, ESR and serum albumin levels. All biochemical assays was carried out using the same method, throughout the study period. Wound culture was repeated weekly.

Route of Glutamine administration

Where there is a choice, enteral feeding is preferable to parenteral[6]. The gastrointestinal tract is particularly at risk during the early burn resuscitation phase due to the major stress resulting from burn injuries and from the treatment required to maintain life. As a result of the early massive capillary leak causing a hypovolumic shock, large amounts of crystalloids are required during the first 24-48 hrs to maintain blood pressure. The fluid resuscitation causes generalized edema, including in the gut, contributing to the development of a paralytic ileus in case the gastrointestinal tract is not used early on. Intestinal permeability is also significantly increased shortly after injury compared to other ICU conditions[7]. Very early enteral feeding, i.e. initiated within the first 6-12 hrs after injury by the gastric route is associated with numerous clinical and biological advantages, such as attenuation of the stress hormone levels, of the hypermetabolic response[4,8], results in increased immunoglobulin production[9], reduction of stress ulcers, while reducing the risk of malnutrition and of energy deficit[10,11]. Studies have shown that either enteral or parenteral provision of glutamine dipeptides can maintain the intracellular or extracellular glutamine pool[12]. Hence, we preferred enteral route of glutamine supplementation in patients. Glutamine or a placebo was given every 6 hours at 0.5 gm/kg/day as boluses, until complete healing. Resuscitation, nutritional support, pain management, infection control and surgical care was done according to standardized procedures.

Statistical analysis

Data was analyzed using SPSS version 20. Student's *t*-test was used to ascertain the significance of differences between mean values of two continuous variables. Chi-square and Fisher exact tests were performed to test for differences in proportions of categorical variables between two or more groups. The level $P < 0.05$ was considered significant.

III. Result

Table no 1 : Showing the differences between groups with and without glutamine supplementation.

	Cases taking glutamine supplementation(n=30)	Cases having placebo(n=30)	'P' value
Age (in years)	31+/- 2.1	30+/- 1.94	0.0603
BSA of burn (in %)	32.3+/-12.35	37.52+/-15.88	0.16
Positive wound cultures (no. of times)	4+/-2.2	6.52+/-4.42	0.007
Length of Hospital Stay (in days)	23.8+/-5.0	34.4+/-7.8	0.0001
Mortality	3(10%)	12(40%)	0.0153

The mean age among two groups i.e.- Burn patients having glutamine supplementation and the other group not having it, was 31+/- 2.1 years and 30+/-1.94 years respectively, P value being 0.0603, hence not

significant. So, we compared the effect of glutamine among two groups having almost similar age group as we excluded extremes of ages in the study and included burn patients having age more than 18 and less than 60 years.

Burn Surface area of the two groups, i.e, the one receiving glutamine supplementation and the other not receiving it was 32.3+/-12.35 and 37.52+/-15.88 % respectively (P -0.16), hence the percentage of burn among the two groups were comparable.

The mean number of positive wound cultures was 4+/-2.2 and 6.52+/-4.42 among groups receiving glutamine supplementation and not receiving it respectively which is a significant value. (*P* value 0.007)

The mean length of stay in hospital was 23.8+/-5.0 and 34.4+/-7.8 days in groups having glutamine supplementation and not having it respectively which shows again a significant difference (*P*-0.0001).

Mortality was also significantly low in the group receiving glutamine supplementation [3(10%) compared to 12(40%)] having P value 0.0153.

Thus from the above table we can clearly say that glutamine supplementation improves outcome among burn patients and improves both morbidity and mortality significantly.

IV. Discussion

Glutamine use is supported by clinical nutrition guidelines worldwide[13,14,15,16,17]. Enteral formulations with glutamine appeared to benefit patients with burns or trauma [17]. Benefits were dose-dependent, with >0.3 g/kg/day required for benefit; 0.5 g/kg/day (in divided portions) was more effective[17]. A meta-analysis of all glutamine randomized controlled trials (both enteral and parenteral) showed a statistically significant reduction in mortality in ICU patients of all types (21 studies, more than 1,500 patients) [17]. In a 2003 study, mortality was significantly lower in the glutamine group than in the control group. By intention-to-treat analysis, there were two deaths vs. 12 deaths ($P < .05$), and by protocol analysis, there were no deaths vs. eight deaths ($P < .01$), respectively[19,23]**.**Decreased mortality was also found in another study with enteral glutamine administration[23] similar to the result as in this study, though few studies showed no significant reduction in mortality[18].

Earlier studies showed a significant reduction in hospital stay (WMD 4.73 days, 95 % CI −8.53 to −0.90; p =0.02)[14]. Garrel et al reported that glutamine supplementation reduced hospital stay significantly and wound healing was faster[19]**.**Glutamine supplementation was associated with a significant reduction in hospital length of stay(WMD −4.73, 95 % CI −8.56 to −0.90; p =0.02; heterogeneity $I^2 = 52$ %) in another study also,[18] however few studies showed no benefit[24]. Our study also showed significant reduction in length of hospital stay as earlier studies.

Earlier studies have shown that glutamine supplementation reduces the rate of infection, inflammation, length of hospital stay, and mortality, and improves gut barrier function and immune function, especially cell-mediated immunity in critically ill patients[25]. Length of care in the survivors was not different between groups (0.9 vs. 1.0 days/percent total body surface area for glutamine vs. control, respectively)and positive blood culture was three times more frequent in control than in glutamine treatment (4.3 vs. 1.2 days/patient, p <.05)[19] Another study showed that enteral glutamine supplementation using a commercially available dipeptide supported plasma glutamine levels, improved gut permeability, and initially decreased plasma endotoxin levels in severely thermally injured patients. These alterations were associated with a reduction in the length of hospitalization and lower costs[26]. Our study also showed results similar to above studies.

V. Conclusion

Enteral Glutamine supplementation in adult burn patients significantly reduces length of hospital stay, improves overall clinical outcome and reduces mortality, hence should be given to all burn patients.

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