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Effect of Nutritional Support Containing Arginine, Glutamine and β-hydroxy-β-methylbutyrate on the Protein Balance in Patients with Major Burns

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Abstract

Objective: To evaluate the effect of a supplementary nutritional product containing arginine, glutamine and β-hydroxy-β-methylbutyrate (HMB) on the nutritional parameters of patients with major burns.

Methods: In a total of 40 patients with major burns treated in the Burns Unit, standard nutritional support was administered to 20 patients, and the study product was added to the standard nutritional support of the remaining 20 patients. The biochemical laboratory test results and burn severity were recorded on the first day of treatment and on Days 14 and 28. The 40 patients were divided as the study and the control group, and their results were compared.

Results: An increase in the albumin, prealbumin and total protein values in the group administered with the study product was found to be statistically significant compared to the control group ($p=0.021$, $p=0.02$, $p<0.001$, respectively). The decreases in haemoglobin and C-reactive protein (CRP) were at the levels expected in burn trauma.

Conclusion: The results obtained in this study demonstrated that the addition of arginine, glutamine and HMB to the nutrition of patients with burns had a positive effect on the protein balance.

Keywords: Arginine, β-hydroxy-β-methylbutyrate, burn, glutamine, nutrition, prealbumin

Introduction

Despite the efforts to reduce the incidence with preventative measures, major burns continue to be a healthcare problem worldwide. In the early stage, the extent of the burn injury constitutes a high risk of death followed by an acute burn shock. The depth of the injury determines the outcome with respect to the development of long-term temporary or permanent sequelae. Changes in the metabolism that start in the period of acute shock can continue for a long time after the burn.

It is well known that the metabolism is increased in patients with burns. The calorie requirements change with increasing metabolism. Therefore, most of the recommendations to meet the requirements of the metabolism are directed towards preventing the patient from a prolonged catabolic process and negative effects of malnutrition on the immune system (1). Before widespread acceptance and application of an early excision, recent improvements regarding the better understanding of the burn hypermetabolism, and better critical patient care, the energy expenditure of patients with burns was accepted as 1.5 to 2.5 times higher than the one calculated for the nonburn controls. Today, energy requirements that are 1.3 to 1.5 times greater have been reported in the recent studies.

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The guidelines recommend providing 50% to 60% of calories from carbohydrates and approximately 15% from fat (2).

In the catabolic process, one of the first deposits to be consumed is the skeletal muscle. Loss of the muscle protein causes a reduction in the lean body mass and the development of several secondary complications (3, 4). The recommended amount of proteins is 1.5 to 2 g kg^{-1} per day for adults with burns, and protein levels that are greater than the recommended cause the urea load and azotaemia, with a limited additional impact on the skeletal muscle loss (2).

Albumin, which is particularly focussed on as a colloid during shock resuscitation, maintains a role as a long-term nutritional follow-up parameter in the subsequent period. Albumin and prealbumin are good indicators of the patient nutritional status in the acute and chronic periods. Following burn injuries, while albumin levels are a better indicator of morbidity and mortality than other biochemical parameters and anthropometric measurements, prealbumin is accepted as a good nutritional parameter (5).

A general approach in the formulas of the recommended guidelines for fluid resuscitation of patients with major burns is directed towards the administration of colloids as a necessity. Albumin is the colloid recommended in the guidelines for use following the first 24 hours of major burn resuscitation. However, there is no consensus on what dosage should be used or on the duration of albumin application. Some authors have recommended the administration of fresh frozen plasma rather than albumin (6).

An increased metabolism and the catabolic process are well known in patients with burns. Several studies have been conducted related to a good management of this process, and there are also many studies including patients with burns which have evaluated formulas containing amino acids. The formula used in the current study contained arginine, glutamine and β-hydroxy-β-methylbutyrate (HMB). Arginine is a precursor of nitric oxide in the body, and it plays a role in trauma, wound healing and immune modulation. Glutamine is a regulator of muscle proteolysis. HMB takes on the function of reducing the muscle destruction to a minimum, stimulating the protein synthesis and preventing proteolysis (3, 7, 8).

Prealbumin is a protein with a half-life of 2 days and is a better nutritional marker than albumin. Following major burns, its decrease in the blood is often seen in the first week. A decrease in prealbumin is observed in cases of an infection, a prolonged hospital stay and delayed wound healing. As the inflammatory status effects (alter) the C-reactive protein (CRP) plasma level, it must be measured together with prealbumin. An increase in the acute phase proteins such as CRP is seen together with low prealbumin levels. When CRP remains stable, and there is a decrease in prealbumin plasma concentrations, this is related to a nutritional disorder (5, 9).

Although several studies have examined the subject of nutrition in burn cases, no consensus has yet been reached on a nutritional regime. Furthermore, although glutamine, arginine and formulas containing some other products have been individually evaluated, to the best of our knowledge, there have been no previous studies which have included HMB. Therefore, in this present study, we aimed to investigate the effect of nutritional support containing arginine, glutamine and HMB on the nutritional status of patients with major burn.

Methods

This study examined patients with major burns admitted to the Burn Treatment Centre of our hospital. The number of patients planned to be included in the study was reached between September 2011 and September 2015. The study included adult inpatients with burns covering more than 30% of the body surface, no concomitant injury, those who were conscious, not morbidly obese, and who had a sufficient oral nutritional intake or were fed by a nasoenteric tube. Patients were excluded if they were younger than 18 years, unconscious, had a body mass index (BMI) >35, and could not use the enteral route and were applied parenteral nutrition. A total of 20 patients received standard nutritional support, and a total of 20 patients received the study product in addition to the standard nutritional support.

Approval for the study was granted by the Ankara Numune Training and research Hospital local Ethics Committee (336-2014), and informed consent was obtained from all the patients. All the tests applied were those routinely used in the monitoring of patients, and no additional financial cost was incurred for either the institution or the patient. All the tests were performed in the laboratory of our hospital.

As the clinical approach, all patients were closely monitored, and the Parkland formula was used for calculating the initial amount of fluid. Resuscitation was maintained by titrating the amount of fluid administered according to the urine output of the patient, the central venous pressure and the vital signs. After the first 24 hours, colloid resuscitation with fresh frozen plasma was started in all patients and was continued in the period after resuscitation for as many days as seen to be clinically appropriate for the patient. No patient in either the study or the control group received albumin during the treatment period.

The nutritional support of the patients was started immediately after bringing the burn shock resuscitation under con-

trol. First, oral nutrition was given to all patients, and in those who could not tolerate oral intake, nasoenteral feeding was applied. No patient received parenteral nutrition support, and no nutrition was administered in a manner more invasive than the nasogastric feeding. After calculating the patient's daily calorie requirement with the Harris-Benedict formula multiplied with 1.5 as the burn coefficient**,** a standard nutritional product was used in addition to the hospital food (Ensure, Original Abbott Nutrition). All patients received 1.5 g kg^{-1} proteins per day.

The control group received this standard product, and the study group was given an additional mixture of arginine, glutamine and HMB in the formula of 3 gr HMB, 14 gr arginine and 14 gr glutamine (Abound, Original Abbott Nutrition). This supplement was administered in the morning and in the evening in two equal doses, and all the patients in the study group were fed in this manner for 28 days.

The age, body surface area burn percentage, Baux index, height, weight, BMI, comorbidities and length of hospital stay were recorded for each patient. On the first day of treatment and on Days 14 and 28, blood samples were taken from the patients for the assessment of routine biochemical parameters to determine the nutritional status. The biochemical parameters examined were albumin, prealbumin, total protein, alanine-transaminase, aspartate-transaminase, gamma glutamyl-transferase, alkaline phosphatase, lactic dehydrogenase (LDH), C-reactive protein, creatine kinase, total cholesterol, low-density lipid, ferritin, blood urine nitrogen, haemoglobin

Table 1. Comparison of the demographic and clinical data of the groups

	Standard nutrition + abound (Study group)	Standard nutrition only (Control group)	p
Age	35.85±1.52	32.75±10.96	NS
Burn percentage	52.15±16.32	46.50±14.00	NS
Baux index	84.80±16.96	82.35±39.38	NS
Height	171.85±6.86	173.15±6.08	NS
Weight	77.45±11.94	73.10±13.8	NS
Body mass index	25.11±3.26	24.58±3.51	NS
Hospital stay	56.30±22.70	49.15±17.96	NS

NS: not significant

Table 2. Evaluation of the test results of the group administered with the HMB formula (Abound)

Parameter (min-max)	1st sampling	2nd sampling	3rd sampling	p
Albumin (35-52 g L^{-1})	25.83±3.98	30.98±894	34.25±11.81	0.003
Prealbumin (20-40 mg dL^{-1})	10.83±1.75	11.49±4.30	12.40±5.26	0.329
Total Protein (66-87 g L^{-1})	42.90±7.66	56.72±10.85	57.71±9.45	0.001
ALT (3-50 U L^{-1})	26.50 (6-214)	51.70±50.00	42.57±26.52	0.455
AST (4-50 U L^{-1})	33.50 (7-971)	36.00 (9-345)	34.31±18.44	0.135
GGT (6-55 U L^{-1})	40.25±45.74	57.85±45.06	51.10±45.01	0.182
ALP (52-171 IU L^{-1})	83.65±53.26	108.85±93.55	99.47±94.60	0.282
LDH (25-248 U L^{-1})	374 (187-2098)	419.85±245.31	279.63±158.97	0.053
CRP (<5 mg L^{-1})	131±65.67	111.90±94.69	69.00±61.80	0.007
Creatine kinase (10-171 U L^{-1})	745.00±860	60.50 (19-1453)	56 (4-1150)	<0.001
Total cholesterol (20-200 mg dL^{-1})	115.15±28.59	112.45±29.19	112.79±26.16	0.711
LDL (<100 mg dL^{-1})	65.65±28.10	65.35±22.70	64.57±18.60	0.911
Ferritin (23.9-336.2 ng mL^{-1})	291.04±105.14	283.02±120.17	271.66±107.87	0.621
BUN (17-43 mg dL^{-1})	28.45±17.64	34.21±11.91	35.82±12.27	0.311
Haemoglobin (12.6-17 g dL^{-1})	10.20±2.73	9.55±1.71	9.02±1.83	0.034
Haematocrit (38%-49%)	30.81±7.41	29.08±4.71	27.52±5.31	0.036
Eosinophil percentage (0.9%-4%)	0.95 (0.20-10.70)	2.27±2.31	1.47±0.92	0.326
Neutrophil (45.5-73.1%)	69.17±10.73	72.09±8.71	74.42±4.05	0.161
GFR (>60)	60 (41-60)	60.00 (40-60)	60 (41-60)	0.984

ALT: alanine transaminase; AST: aspartate transaminase; GGT: γ-glutamyl transferase; ALP: alchalen phosphatase; LDH: lactate dehydrogenase; CRP: C-reactive protein; BUN: blood urea nitrogen

(Hb), haematocrit (Htc), eosinophil percentage, neutrophil and glomerular filtration rate.

For randomisation, the order of patient admittance was taken as the basis, and alternate patients were allocated to the study group. Without exception, the patients were consecutively monitored, and no patient was excluded from the study after starting the nutritional supplement.

Statistical analysis

Whether there was a difference between the groups with respect to the burn severity and demographic parameters was evaluated with Student's t-test. Then the differences between the first, second and third samplings of the biochemical parameters in each group and the differences between the groups at these sampling times were evaluated with the analysis of variance and Student's t-test, respectively.

Table 3. Comparison of the parameters showing a significant difference over time in the group administered with the HMB formula (Abound)

Measurement Comparison	1st versus 2nd	2nd versus 3rd	1st versus 3rd
Albumin	0.09	0.217	0.007
Total Protein	0.006	0.561	<0.001
CRP	0.440	0.011	0.002
Creatine kinase	0.004	0.053	0.003
Haemoglobin	0.138	0.194	0.028
HCT	0.194	0.206	0.036

CRP: C-reactive protein; HCT: hemotocrit

Results

A total of 40 patients were included in the study: 20 patients in the study group and 20 in the control group. In all patients, the target caloric intake (1.5 times of calories calculated by the Harris-Benedict equation and 1.5 gr kg^{-1} protein per day) was ensured via oral intake, but the naso-enteric tube feeding was applied for a short time in 3 patients from the study group and 4 patients from the control group. The mean age of the patient group was 34.3±13.2 years (median, 31.5 years), the percentage of the mean body surface area affected by the burn was 49.32%±15.28% (range, 20%-95%) and the mean length of hospital stay was 52.73±20.52 days. No difference was found between the groups with respect to age, the burn percentage, Baux index, height, weight, BMI, comorbidities and the length of hospital stay (Table 1).

The results of the blood tests showing a statistical difference and those which were useful in the sense of evaluation of the nutritional support are presented in Tables.

Following the blood sample analysis of the study group, it was observed that there was a significant improvement in the parameters of albumin, total protein, CRP and creatine kinase and a decrease in Hb and Htc (Table 2). The comparison of the first, second and third measurements of the parameters with significant changes and the times of the significant changes are shown in Table 3.

Table 4. Evaluation of the test results of the control group

Parameter (min-max)	1st sampling	2nd sampling	3rd sampling	p
Albumin (35-52 g L^{-1})	27.48±5.98	26.09±4.45	27.42±4.54	0.503
Prealbumin (20-40 mg dL^{-1})	8.72±1.16	8.68±0.64	8.47±0.59	0.207
Total protein (66-87 g L^{-1})	71.2±93.95	55.06±5.34	61.10±9.60	0.637
ALT (3-50 U L^{-1})	32.0 (14-168)	31.5 (18-125)	38 (12-1560)	0.413
AST (4-50 U L^{-1})	41.0 (23-646)	36.5 (15-127)	35.0 (13-823)	0.195
GGT (6-55 U L^{-1})	31.95±26.09	62.75±49.26	60.40±58.85	0.069
ALP (52-171 IU L^{-1})	63.8±39.84	96.95±40.09	102.80±68.61	0.034
LDH (25-248 U L^{-1})	418.0 (177-1580)	387.50±143.82	337.0±132.28	0.012
CRP (<5 mg L^{-1})	63.25±42.43	47.0±24.34	28.80±16.78	<0.001
Creatine kinase (10-171 U L^{-1})	1057.0 (39-7620)	307.0 (51-4545)	207.0 (12-1154)	0.048
BUN (17-43 mg dL^{-1})	32.0±15.06	32.25±18.40	28.70±18.31	0.859
Haemoglobin (12.6-17 g dL^{-1})	13.82±3.40	9.1±1.28	9.57±1.87	<0.001
Haematocrit (38%-49%)	40.88±9.80	27.04±4.29	29.48±5.89	0.301
Eosinophil percentage (0.9%-4%)	0.15 (0.00-3.80)	0.65 (0.0-4.6)	1.10 (0.0-8.40)	0.147
Neutrophil (45.5%-73.1%)	72.00±16.26	75.84±8.37	72.14±10.61	0.498
GFR (>60)	60	60.00 (42.7-60)	60.0 (46.21-60)	0.277

ALT: alanine transaminase; AST: aspartate transaminase; GGT: γ-glutamyl transferase; ALP: alchalen phosphatase; LDH: lactate dehydrogenase; CRP: C-reactive protein; BUN: blood urea nitrogen

When the evaluation was made within the control group, it was determined that LDH, CRP, creatine kinase and Hb decreased, while alkaline phosphatase increased. No significant change was observed in albumin or prealbumin levels in the control group (Table 4). The comparison of the first, second and third measurements of the parameters with significant changes and the times of the significant changes is presented in Table 5.

Parameters showing a difference according to the measurement times in the study and control groups are presented in Table 6.

Table 5. Comparison of the parameters showing a significant difference over time in the group administered with standard nutrition only (Ensure)

Measurement Comparison	1st versus 2nd	2nd versus 3rd	1st versus 3rd
ALP	0.033	0.016	0.760
LDH	0.028	0.005	0.106
CRP	<0.001	<0.001	0.031
Creatine kinase	0.072	0.107	0.023
HG	<0.001	0.165	<0.001

ALP: alchalen phosphatase; LDH: lactate dehydrogenase; CRP: C-reactive protein; HG: haemoglobine

Discussion

A better understanding of burn pathophysiology by sharing the experience in the literature and modern developments in medical equipment has reduced the mortality rates in recent years. There are also ongoing studies aiming to correct the clinical course of cases with major burns, which still have severe morbidity and sequelae. Some of these are oriented towards improving the nutritional status of patients and meeting the increased metabolic requirements. The gastrointestinal system is important in the early resuscitation of patients with burns. Following shock resuscitation, the administration of enteral support products is recommended. Products that contain fibre and are high in protein and nitrogen are recommended (1). In our study, after achieving patient stabilisation with resuscitation, enteral nutrition was started in the early stage. That no patient experienced complications related to enteral nutrition supports the view that enteral nutrition is appropriate in the early stage.

In addition to indicating chronic nutrition disorders, albumin may also be an indicator in the acute phase. To increase the blood oncotic pressure, albumin is among the colloids used in the resuscitation of burn patients (6). Due to the risk of the development of pulmonary side-effects and compartment syn-

Table 6. Parameters showing a difference according to the test times in the study and control groups

	Sampling time	Study group	Control group	p
Albumin (35-52 g L^{-1})	1st sampling	25.83±3.9	27.48±5.9	0.310
	2nd sampling	30.98±8.9	26.90±4.4	0.035
	3rd sampling	34.25±11.8	27.42±4.5	0.021
Prealbumin (20-40 mg dL^{-1})	1st sampling	10.83±1.7	8.72±1.1	0.000
	2nd sampling	11.49±4.3	8.68±0.6	0.006
	3rd sampling	12.4±5.2	8.47±0.5	0.002
Total Protein (66-87 g L^{-1})	1st sampling	42.90±7.6	71.20±9.3	0.319
	2nd sampling	56.72±10.8	55.06±5.3	0.5
	3rd sampling	57.71±9.4	61.10±9.6	0.439
LDH (25-248 U L^{-1})	1st sampling	374.95±461.75	418.35±229.20	0.78
	2nd sampling	419.85±245.3	387.5±143.8	0.614
	3rd sampling	279.63±36.4	337.0±132.28	0.227
CRP (<5 mg L^{-1})	1st sampling	131.84±65.6	63.25±42.40	0.000
	2nd sampling	111.89±94.6	47.0±24.3	0.05
	3rd sampling	69.0±61.8	28.8±16.7	0.08
Haemoglobin (12.6-17 g dL^{-1})	1st sampling	10.20±2.7	13.8±3.4	0.001
	2nd sampling	9.5±1.7	9.1±1.2	0.361
	3rd sampling	9.02±1.8	9.5±1.8	0.365
Haematocrit (38%-49%)	1st sampling	30.81±7.4	40.88±9.8	0.001
	2nd sampling	29.08±4.7	27.07±3.6	0.208
	3rd sampling	27.52±5.3	29.48±5.8	0.291

CRP: C-reactive protein; LDH: lactate dehydrogenase

drome, albumin has been given to virtually no patients in our clinic for the past 10 years. As albumin was not given to any patient in the study or control groups, the change in albumin levels can be obviously associated with the nutrition and the metabolic process of the patient. An increase in the albumin levels in the study group was seen in all three evaluations. In addition, the increase was determined to be significant in comparison with the control group. By the fourth week, the albumin levels were observed to have returned to normal in those who received HMB. In the control group, however, this increase was not observed. A decrease in albumin was expected in the control group as this is a known status after burns shock. The predicted albumin decrease was not observed in the control group, and this is considered to be a consequence of the administration of the supplementary formula in that group. It is likely that a better control of nutrition and the careful control of the increased metabolism created the opportunity for albumin to be synthesised in the control group. When comparing the two groups, although there was no difference at the beginning of the treatment, a significant difference in favour of the study group was observed in the evaluations on Day 14 and Day 28. This demonstrates that the nutritional support given together with the formula used in the study made a positive contribution to raising the albumin level.

Prealbumin is a good indicator of acute nutritional status (3, 5). Its short half-life allows the acute status to be well reflected. In the study group, statistical significance was not obtained within the group; however, a continuous increase was observed throughout the treatment period. In the control group, however, a continuous decrease in the prealbumin level was observed. When comparing the two groups, a significant increase was observed in every measurement period. Although the initial difference between the two groups could account for the following difference, this is not true as the group receiving the formula supplement showed a continuous gradual increase in the prealbumin level. Further studies conducted on larger groups and with a longer follow-up period are necessary to determine the continuation of the increase and the significance of the difference.

When total protein levels were examined with respect to reflecting the general protein status, a gradual increase was observed in all three measurements in the study group, and this was statistically significant. In the control group, although there was a decrease, it was not statistically significant. When both groups were compared, the difference was significant, and an improvement was observed in the study group. This result is in compliance with other studies which have been conducted using this formula (4, 10).

Lactic dehydrogenase is a parameter which shows the muscle damage. In the examination of the LDH levels of the groups, an increase in the blood and a later decrease is expected as a response to burn shock. In the study group, LDH was seen to increase with the burn trauma in the early stage and decrease on the 28th day. There was no statistical significance between the two groups with respect to the decrease in LDH levels. However, in a review by Wilson et al. (10), it was reported that HMB caused significant decreases in LDH levels.

High levels of CRP were determined at the beginning of study in both groups, secondary to systemic inflammation of the burn. During the follow-up period, a significant reduction in these levels was observed in both groups. Although there was no difference between the groups with respect to the percentage of the total body surface area covered by the burn and the Baux index, the burn percentage and Baux index values were higher in the study group, which may have been due to the CRP values in this group being two times higher than those of the control group at the beginning of the study. From the second measurement onwards, a rapid decrease was observed in the CRP levels of the study group. Previous studies have reported that HMB lowers infection, modulates immune functions, and contributes to a positive nitrogen balance, and these could explain the decrement of the infection indicator of CRP levels (11). As a result, if a reduction in the CRP level is achieved, it can be considered that the difference is preserved because of the ongoing healing period. With a longer follow-up, a more accurate interpretation could be made.

A decrease in the Hb levels in the control group was more significant than in the study group. In both groups, a decrease in Hb values observed in the second week was evaluated as the decrease expected in the chronic period as a response to burn trauma. Although patients underwent various surgical procedures in this period, there was no requirement for blood transfusion. The significant difference between the two groups at the start of treatment, which was thought to be due to more severe burns in the study group, was closed by the study group in the follow-up period. The product used in the study is known to increase the number of red blood cells, eosinophils and lymphocytes and Hb and Htc levels (12).

Prealbumin is an appropriate acute-stage nutritional monitoring parameter. In the treatment of patients with burns, transferrin and ferritin blood levels are not routinely examined. They were not examined in this study, and this could be considered a study limitation.

Conclusion

The nutrition of patients with burns is one of the major components determining treatment outcomes. There is as yet no consensus on the nutritional regime that should be applied to patients with major burns. Studies examining various nutrients are still ongoing. The results of our study, that relatively

better values of albumin and prealbumin levels were obtained in patients who were administered arginine, glutamine and HMB compared to those who were not, demonstrate that these can be used as an appropriate nutritional support in patients with major burns.

Ethics Committee Approval: Ethics committee approval was received for this study from the ethics committee of Ankara Numune Training and Research Hospital (336-2014).

Informed Consent: Written informed consent was obtained from patients who participated in this study.

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References

1. Rousseau AF, Losser MR, Ichai C, Berger MM. ESPEN endorsed recommendations: nutritional therapy in major burns. Clin Nutr 2013; 32: 497-502. **[CrossRef]**
2. Carson JS, Khosrozadeh H, Norbury WB, Herndon DN. Nutritional Needs and Support for the burned patient. Total Burn Care, Elsevier, 5th Ed., Editor Herndon DN. pp. 287-300.
3. Clark RH, Feleke G, Din M, Yasmin T, Shingh G, Khan FA, et al. Nutritional treatment for acquired immunodeficiency virus-associated wasting using beta-hydroxy beta-methylbutyrate, glutamine, and arginin: a randomized, double-blind, placebo-controlled study. JPEN J Parenter Enteral Nutr 2010; 24: 133-9. **[CrossRef]**
4. Erdem D, Akan B, Albayrak MD, Aksoy E, Unal S, Ornek D, et al. The use of nutritional supplement containing arginine, glutamine and beta-hydroxy-beta-methylbutyrate in the treatment of pressure ulcers in an ıcu patient. Analg Resusc: Curr Res 2015; 4: 1.
5. Rodriguez NA, Jeschke MG, Williams FN, Kamolz LP, Herndon DN. Nutrition in Burns: Galveston Contributions. JPEN J Parenter Enteral Nutr 2011; 35: 704-14. **[CrossRef]**
6. Warden GD. Fluid resuscutation and early management. In: Total Burn Care 3rd edition, Ed. Herndon DN, Saunders Elsevier, 2007: 107-18.
7. JJ Lin, XJ Chung, CY Yang, HL Lau A. Meta-analysis of trials using the intention to treat principle for glutamine supplementation in critically ill patients with burn. Burns 2013; 39: 565-70. **[CrossRef]**
8. Yan H, Peng X, Huang Y, Zhao M, Li F, Wang P. Effects of early enteral arginine supplementation on resuscitation of severe burn patients. Burns. 2007; 33: 179-84. **[CrossRef]**
9. Prelack K, Washek M, Sheridan RL. Pre-albumin and C-reactive protein are predictive of nutritional adequacy in burned children. JBCR 2002; 23: S126.
10. Wilson GJ, Wilson JM, Manninen AH. Effects of beta-hydroxy-beta-methylbutyrate (HMB) on exercise performance and body composition across varying levels of age, sex, and training experience: A review. Nutr Metab 2008; 5: 1. **[CrossRef]**
11. Prelack K, Dylewski M, Sheridan RL. Practical guidelines for nutritional management of burn injury and recovery. Burns. 2007; 33: 14-24. **[CrossRef]**
12. Rathmacher JA, Nissen S, Panton L, Clark RH, Eubanks May P, Barber AE, et al. Suplemention with a combination of beta-hydroxy-beta-methylbutyrate (HMB), arginin, and glutamine is safe and could improve hematological parameters. JPEN J Parenter Enteral Nutr 2004; 28: 65-75. **[CrossRef]**