EFFECT OF EARLY NUTRITIONAL SUPPORT ON CLINICAL COURSE AND SEPTIC COMPLICATIONS IN PATIENTS WITH SEVERE BURNS

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SUMMARY. Retrospective and prospective analyses of methods for nutritional support were carried out to assess their efficiency in covering the calculated caloric and protein needs of patients with severe burns. The energy and protein needs of the patients in Group 1 (study group) with nutritional support started 24 h after the thermal trauma were determined by the Toronto formula or by means of indirect calorimetry. Nutritional support of patients in Group 2 (control group) were initiated on day 4 post-trauma. The patients in the two groups were similar in respect to age, gender, body surface area burned, and injury severity score. We found statistically significant differences in the metabolic response of both groups as measured by nitrogen balance, serum proteins, and absolute lymphocyte count. Significant differences were also registered in body weight loss, number of positive haemocultures, and the complications rate.

Introduction

The causes of the development of post-traumatic hypermetabolism following severe burns are multifactorial, and still incompletely elucidated. Nevertheless, contemporary knowledge provides the possibility to determine with precision the basic principles for the treatment of patients with major burns, including control of the primary injury site, recovery of oxygen transport, management of septic complications, and adequate nutritional support (NS).

The purpose of this study is to assess the effect of the early initiation of NS, with high caloric and nitrogen intake, on the development and severity of hypercatabolic changes and septic complications in patients with severe burns.

Material

This study included 20 consecutive adult patients with major burns (Group 1) treated in the ICU of the Centre for Burns and Plastic Surgery, Pirogov Emergency Medicine Hospital, Sofia, over a 3-yr period (1 Jan. 2000 - 31 Dec. 2002) and a control group of 25 patients (Group 2) treated in the same unit in the period 1 Jan. 1996 - 31 Dec. 1999. All the patients were admitted to the Centre not later than 48 h after their injury. Surgical procedures were initiated within 48 h after the accident, and were performed later at various time intervals. To exclude the mortality factor, all the patients studied concluded their treatment with clinical healing. The study was carried out during the first 30 days post-injury; NS (parenteral and enteral) was started in Group 1 after the first 24 h, and in Group 2 72 h post-injury. *Table I* presents the demographic analysis of the patients in both groups. Group 1 includes patients with an age range of 21-76 yr and body surface area burned (BSAB) of 36-80%, while Group 2 includes patients with an age range of 18-69 yr and BSAB of 36-60%. The number of Group 1 patients with burns exceeding 50% BSAB was 7 (35%), while there were 11 such patients in Group 2 (44%), with no statistical difference.

Table I - Demographic analysis

	Group 1			Group 2			*p*
	No.	Mean	SD	No.	Mean	SD	
Age (yr)	20	40.85	± 16.21	25	42.40	± 8.97	n.s.
Sex (m/f)		18/2			18/7		n.s.
BSAB (%)		47.35	± 11.49		47.20	± 8.13	n.s.
ABSI*		8.85	± 1.23		884	± 1.21	n.s.

*ABSI - abbreviated burn severity index[14]

Methods

Daily caloric requirements were estimated using the Toronto formula[1] recommended for patients with major burns and chosen by our team because of its advantages and reliability, provided by the inclusion of multiple adequate parameters and the possibility for dynamic changes in the course of treatment (*Table II*).

Resting energy expenditures (REE) were measured using indirect calorimetry (IC) twice weekly with patients in Group 1 in the course of the 30 days after trauma.

Nitrogen balance (NB), calculated according to the formu-

Table II - Formulas used for estimation of daily energy requirements and nitrogen balance

Toronto formula
MEE = -4343 + (10.5 BSAB) + (0.23 CI) + (0.84 HBEE) + (114 T)-(4.5 DPB)
MEE = metabolic energy expenditure
BSAB = body surface area burn
CI = caloric intake
HBEE = Harris-Benedict energy expenditure
T = mean daily temperature °C
DPB = day post burn
Nitrogen balance
Nitrogen balance (g/24h) = Nin - [UUN + 4 + (BUNe -BUNs/100 x BW x F)]
Nin = nitrogen intake (g/24h)
UUN = urinary urea nitrogen (g/24h)
BUN = blood urea nitrogen (mg/dl) (s = at start, e = at end of 24 h)
BW = body weight (kg)
F = body water factor (male: F = 0.60, female: F = 0.55)

la presented in *Table II*, was measured every day for 30 days.

The following parameters were used for the monitoring of the patients' nutritional status and the complications that set in during the 30-day period after the injury:

- body weight
- serum albumin
- absolute lymphocyte count (ALC)
- number of positive haemocultures
- complications: sepsis, multiple organ failure (MOF), acute respiratory failure (ARF)

All statistical analyses were performed by computer, using the statistic software package SPSS-11.01 for Windows.

Results and discussion

Daily energy intake

Prolonged starving and insufficient caloric delivery have a negative effect on the course of a severe trauma. That is why our efforts were directed to maximum shortening of the period without nutritional support. Within 48 h of trauma all patients in Group 1 were brought to a state of stabilized haemodynamic parameters, with tissue perfusion and adequate diuresis, which allowed the initiation of parenteral nutrition with carbohydrate and amino acid solutions and an additional extension with lipidic emulsions over the next day. Enteral nutrition was initiated within 24-48 h post-trauma, depending on the recovery of gastrointestinal passage, and was postponed in cases with stomach excretions > 500 ml/3 h, persistent interstitial oedema, and serum albumin levels < 30 g/l. The oxygen consumption measured using IC over the first and second day post-trauma was very high: 234 ml/min/m^2-423 ml/min/m^2. These data confirm once again that adequate infusion therapy during the first hours post-injury can significantly shorten the so-called shock phase. Hypermetabolic processes occur very quickly and NS must be initiated as early as possible. REE values measured using IC exceeded those of basic metabolic expenditures by 120-130%, the highest values being registered during the second and third weeks. *Fig. 1* shows the mean daily caloric intake over the 30-day period in both groups. Patients in Group 1 had a high caloric intake - 30 kcal/kg/24 h on the third day of admission, which was maintained over the second and third weeks, while patients in the control group reached this level on day 9 post-trauma. A statistically significant difference was observed during the first 6 days (p = 0.001).

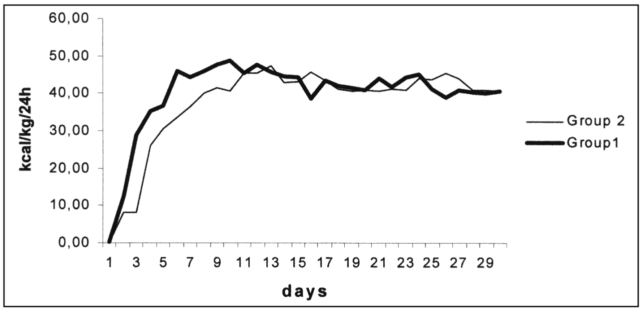

Fig. 1 - Mean daily caloric intake (kcal/kg/24 h).

Daily nitrogen intake

The exact assessment of protein needs in patients with major burns is a difficult task and one that is still insufficiently defined. This is due to the difficulties related to the exact measurement of nitrogen loss with urine excretion, on the one hand, and the determination of nitrogen losses through the wound surface, which are significant over the first two weeks post-trauma, on the other. Nevertheless, there is a consensus about the quality of proteins in the form of amino acid solutions that must be received by severely burned patients. Although the recommended amino acid intake in middle-aged patients with a moderately severe burn is 2.0-2.5 g/kg/24 h, some researchers have recently successfully administered a higher protein intake - over 3 g/kg/24 h in patients with burns > 45% BSAB.[2] The ratio between caloric and nitrogen intake has also significantly changed. Some studies present encouraging results using a kcal:N/g/ratio of 100:1 and even 85:1,[3] which differs significantly from the generally accepted level of kcal:N/g of 150:1. *Fig. 2* shows the daily nitrogen intake g/kg/24 h over the 30-day period. As early as day 3, patients in Group 1 received a nitrogen intake of 0.20 g/kg/24 h, which was increased over the following days to reach 0.35-0.40 g/kg/24 h during the second and third weeks, when the catabolic processes were more expressed because, on the one hand, of the infectious complications that occurred and, on the other, of the increased number of operations over the period. The initiation of nitrogen intake was delayed in patients in control Group 2 and was comparatively lower over the whole period. A statistically significant difference was found between the two groups during the first three weeks of the period (p = 0.001). It is nowadays generally accepted that a nitrogen intake of 0.25

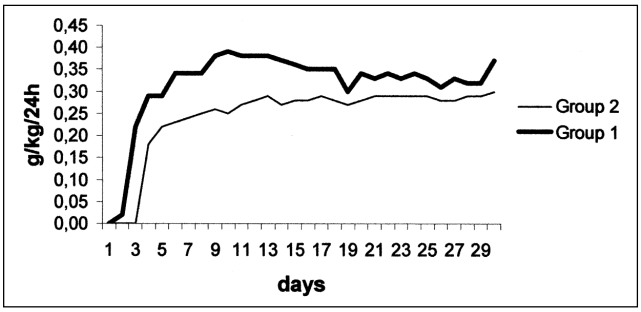

Fig. 2 - Mean daily nitrogen intake (g/kg/24 h).

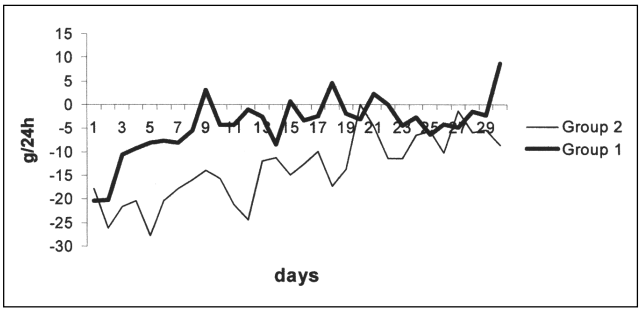

Fig. 3 - Nitrogen balance (g/24 h).

g/kg/24 h can reduce nitrogen losses by 60% when energy intake is adequate.[4] That is why the early inclusion of amino acid solutions in parenteral nutrition is of significant importance for the improvement of the nitrogen balance.

When assessing the daily caloric and nitrogen intake we paid special attention to the following important aspects:

– the inclusion as early as possible of energy and protein resources in the nutritional regimen of patients with major burns
– the adjustment of caloric and nitrogen intake according to the severity of the burn
– the reaching of the optimal dosage and its maintenance over the successive four weeks in patients with burns over in 35% BSAB

Nitrogen balance (NB)

The severity of the trauma and the complications that occur influence the NB. The level of urea nitrogen in urine is one of the basic parameters for assessing the extent of catabolic processes and protein needs. The enhanced catabolism of tissue proteins causes a significant increase of the nitrogen losses through urine excretion.[5] In clinical practice it is sufficiently reliable to measure urea nitrogen because it is about 80% of total urine nitrogen. Nitrogen loss during the first days after thermal trauma is very large and leads to a significant negative NB, which can be compensated only with difficulty.[4] The extent of proteinolysis increase is closely related to the severity of the injury, and the highest nitrogen losses, often exceeding 30 g/24 h, are observed in patients with major burns. These are caused by the increased protein catabolism, occurring mainly in the skeletal muscles, connective tissues, and non-stimulated bowels.[6] On the other hand, intensive NS leads to a significant acceleration of anabolic processes, but can influence the intensity of catabolism only to a limited extent.[2] When a constant daily nitrogen intake is maintained, NB can become positive only when the import of non-protein caloric sources covers the daily energy needs.[7] If this import is not sufficient, some of the proteins delivered by the diet are used as an energy source, and this leads to a negative NB. The aim of NS is to maintain a positive NB of 4-6 g/24 h, which requires an adequate import of non-protein energy sources and proteins as well. An NB between -2 and 2 g/24 h indicates the achievement of an adequate balance; when the values are under -2 g/24 h, more proteins and more calories are needed.[8] *Fig. 3* shows the NB of patients in both groups measured daily over the 30-day period post-trauma. In Group 1 patients, the NB turned positive at the end of the first week and remained unchanged until the end of the study period. In Group 2 patients, the NB was negative during the first three weeks, with very low values (-15 to -24 g/24 h. A statistically significant difference was observed ($p < 0.001$). The rapid achievement of a positive NB can be explained by the early initiation of a high nitrogen and caloric import. *Table III* shows the day when the NB became positive, and the number of days it remained positive. The statistical analysis demonstrated a significant difference when both parameters were considered.

Table III - The first day NB became positive, the number of days it remained positive, body weight loss (BWL), and the number of positive haemocultures

	Group 1		Group 2		*p*
	Mean	SD	Mean	SD	
First day with positive NB	5.10	± 2.40	10.96 ±	5.89	< 0.001
Number of days with positive	10.30	± 4.29	6.40	± 5.25	< 0.01
BWL (kg)	6.82	± 4.29	12.19	± 4.13	<0.001
Number of positive haemocultures	1.70	± 1.49	2.84	± 1.65	< 0.021

Serum albumin (SA)

Although the plasma proteins albumin and transferrin have a long half-life and do not correspond exactly to the changes in the nutritional regimen, they are widely accepted as a basic criterion for assessing nutritional status and as an exact prognostic sign for the course and outcome of a disease.[9] An SA concentration under 35 g/l indicates failure by the patient's organism to successfully combat the effects of a severe trauma and its related complications.[7] However, a body weight loss of more than 10% can have a different effect on the clinical course of the thermal trauma, depending on the SA level.[10] A combination of a low level of SA with a significant body weight loss is an alarming sign.[11] When an analysis is made of

SA levels, the type of trauma, time of examination, and the juxtaposition on other parameters for the assessment of nutritional status should be taken into consideration. Hypoalbuminaemia after resuscitation, in cases of a severe trauma, is usually caused to a large extent by an increase of extracellular fluids, while in patients with major burns hypoalbuminaemia is the result of many factors. During resuscitation a dramatic increase of extracellular fluids occurs because of the significant impairment of vascular permeability and the high volume of infused solutions, on the one hand, and the enormous loss of proteins from the wound surfaces and the interstitial matrix, on the other. That is why the assessment of existing hypoalbuminaemia is complex, as it is mainly influenced in the first post-trauma days by the injury itself. If hypoalbuminaemia persists for more than 7-8 days post-injury, it should be accepted that it is caused by malnutrition or else arises from septic complications. A body weight loss of more than 10% post-trauma has no definite prognostic significance if it is not related to hypoalbuminaemia (< 32 g/l), disorders of consciousness, or organ dysfunction. If these signs are present, the possibility for the appearance of septic complications is very high.[9] *Fig. 4* shows the mean values of SA. In Group 2 patients the SA level was < 35 g/l over the whole period of observation, while in Group 1 patients it increased to over 35 g/l after day 2 post-trauma and remained at that level until termination of the observation. During the second and third weeks, a statistically significant difference was registered (< 0.001). These data confirm once again the importance of SA for the assessment of nutritional status.

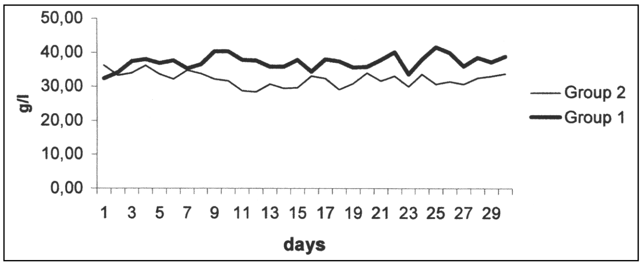

Fig. 4 - Serum albumin (g/l).

Absolute lymphocyte count (ALC)

Depending on the severity of tissue damage, a significant post-trauma depression of lymphocyte activity is observed, which to a greater extent affects cell-mediated immunity.[12] For this reason, early-initiated NS can positively influence the immune response and the course and success of trauma treatment in patients with major burns. *Fig. 5* presents the mean values measured of ALC in both groups. A statistically significant difference was found during the second half of the observed period. In control Group 2, ALC was 1000 mm^3 on average during the first and second weeks, which is a sign of malnutrition, and remained < 1500/mm^3 over the third and fourth weeks. In Group 1 ALC was 1406 ± 520.09/mm^3 during the first week, and increased over the next weeks to more than 1500/mm^3. A statistically significant difference was recorded during the second and third weeks (p = 0.019).

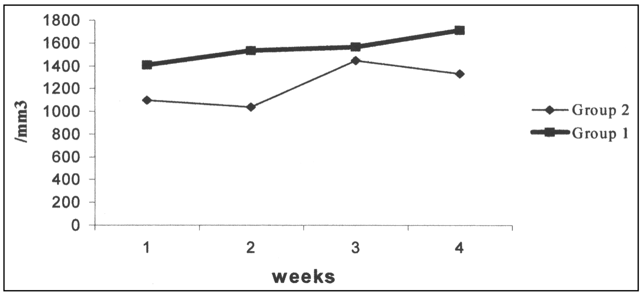

Fig. 5 - Absolute lymphocyte count/mm^3.

Body weight loss

Significant body weight loss increases the possibility of the development of septic complications and causes delays in wound healing. Especially in patients with an insufficient protein import, the reduction of body weight is connected with muscle weakness, which leads to disturbed mobilization, a delay in weaning from mechanical ventilation, an ineffective cough, and the development of respiratory infections. It has been reported that until wound surfaces are covered, no rise in body weight can be expected.[13] *Table III* presents the mean body weight reduction over the 30-day post-trauma period, i.e. 12.19 ± 4.13 kg (more than 10%) in Group 2 patients and 6.82 ± 4.29 kg (less than 10%) in Group 1 patients. The difference is statistically significant. Reduction of body weight is a relatively late criterion for the assessment of nutritional status in burn patients. During the first days after a major burn there is a rapid increase in body weight, and a real reduction in body weight may be objectively registered later. That is why this criterion has a predominantly confirmative character, especially after the first week post-trauma. Body weight loss after a major burn is significant, resulting in muscle mass reduction, loosening of joint ligaments, and complete exhaustion of fat deposits. The maintenance of body weight up to 90% or more of the ideal body weight is a sign of adequate NS.

Number of positive haemocultures during the observed period

Table III shows the incidence of positive haemocultures in both groups: the mean number of positive haemocultures was 1.70 ± 1.49 in Group 1 and 2.84 ± 1.65 in Group 2, which is a statistically significant difference (p < 0.021).

Complications

The analysis of the complications observed is of great

Table IV - Complications

	Group 1		Group 2	
	No.	Percentage	Number	Percentage
Sepsis	12	60	19	76
MOF	3	15	6	24
ARF	7	35	7	26
ARF/MV (n of days)	7.28	SD ± 5.08	16	SD ± 8.75

importance for the assessment of the course and outcome of burn injuries, and it is thought that the adequacy of NS plays a significant role in reducing the complications rate. *Table IV* demonstrates the data related to the characteristics and incidence of complications observed: sepsis, MOF, and ARF/days of mechanical ventilation. The incidence of septic complications and MOF in Group 1 patients was significantly lower than in Group 2 patients. The number of cases with ARF was the same in both groups. However, the duration of mechanical ventilation in cases with ARF in Group 1 was significantly shorter (7.28 ± 5.08 days) than in similar patients in Group 2 (16.00 ± 8.75 days). A 50% shortening of this period was observed, which could also to some extent be attributed to the adequate NS applied.

Conclusion

The findings of this study provide encouraging evidence that adequately planned complex treatment, including early nutritional support, can lead to a significant reduction of all the detrimental aspects of the specific processes that affect the organism after a severe thermal trauma. Early initiation of adequate nutrition would appear to support the positive effects of the organic response to the metabolic stress in cases of major burns.

RÉSUMÉ. Les Auteurs ont effectué des analyses rétrospectives et prospectives des méthodes de support nutritionnel pour évaluer leur capacité de couvrir les exigences calculées caloriques et protéiques des grands brûlés. Les besoins énergétiques et protéiques des patients du premier groupe 1 (groupe d'étude), qui recevaient un support nutritionnel initié 24 h après la brûlure, ont été déterminés avec la formule de Toronto ou avec la calorimétrie indirecte. Le support nutritionnel des patients du deuxième groupe (groupe témoin) a commencé quatre jour après la brûlure. Les patients des deux groupes étaient comparables pour ce qui concerne l'âge, le sexe, la surface corporelle brûlée et le score de la sévérité de la lésion. Les Auteurs ont trouvé des différences statistiquement significatives dans la réponse métabolique des deux groupes mesurée moyennant le bilan d'azote, les protéines sériques et le compte absolu des lymphocytes. Ils ont noté en outre des différences significatives dans les pertes de poids corporel, le numéro des hémocultures positives et le taux des complications.

BIBLIOGRAPHY

1. Allard J.P., Pichard C. et al.: Validation of a new formula for calculating the energy requirements of burn patients. JPEN, 14: 115, 1990.
2. Gore D.C, Chinkes D.L., Hart D.W. et al.: Hyperglycaemia exacerbates muscle protein catabolism in burn-injured patients. Crit. Care Med., 30: 2438-42, 2002.
3. Cunningham J.J., Prelack K., Sheridan R., Remennyder J.P.: Nutrition support during the acute care of moderately or severely burned patients. In: "Artificial Nutrition Support in Clinical Practice", 2nd edition, pp. 575-89, Payne-James J., Grimble G., Silk D. (eds), London, San Francisco, 2000.
4. Pitkänen O., Takala J., Pöyhönen M., Kari A.: Nitrogen and energy balance in septic and injured intensive care patients: Response to parenteral nutrition. Clin. Nutr., 10: 258-65, 1991.
5. Takala J., Suojaranta-Ylinen R., Pitkänen O.: Nutrition support in trauma and sepsis. In: "Artificial Nutrition Support in Clinical Practice", 2nd edition, pp. 575-89, Payne-James J., Grimble G., Silk D. (eds), London, San Francisco, 2000.
6. Dahn M.S., Wilson R.F., Lange M.P. et al.: Hepatic parenchymal oxygen tension following injury and sepsis. Arch. Surg., 125: 441, 1990.
7. Christou N.V., Tellado-Rodriguez J. et al.: Estimating mortality risk in pre-operative patients using immunologic, nutritional, and acute phase response variables. Ann. Surg., 210: 69-77, 1989.
8. Schneeweiss B., Graninger P., Ferenci P. et al.: Short-term energy balance in patients with infections: Carbohydrate-based versus fat-based diets. Metabolism, 41: 125-30, 1992.
9. Serra A.S., Franch-Arcas G.: Nutrition assessment. In: "Artificial Nutrition Support in Clinical Practice", 2nd edition, pp. 165-76, Payne-James J., Grimble G., Silk D. (eds), London, San Francisco, 2000.
10. Windsor J.A., Hill L.: Weight loss with physiologic impairment: A basic indicator of surgical risk. Ann. Surg., 20: 290-6, 1988.
11. Blackburn G.L., Bistrian B.R., Maini B.S. et al.: Nutritional assessment of the hospitalized patient. JPEN, 1: 11-22, 1977.
12. Ninnemann J.L., Stein M.D., Condie J.T.: Lymphocyte response following thermal injury: The effect of circulating immunosuppressive substances. J. Burn Care Rehabil., 2: 196, 1981.
13. Newsome T.W., Mason A.D., Pruitt B.A., jr: Weight loss following thermal injury. Ann. Surg., 178: 215-7, 1973.
14. Tobiasen J., Hiebert J.M., Edlich R.F.: A practical burn severity index. J. Burn Care Rehabil., 3: 229-32, 1982.

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