## ORIGINAL ARTICLES

# NUTRITIONAL FOLLOW-UP OF CRITICALLY ILL INFANTS RECEIVING SHORT TERM PARENTERAL NUTRITION

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SUMMARY: Few studies have tried to characterize the efficacy of parenteral support of critically ill infants during short period of intensive care.

We studied seventeen infants during five days of total parenteral hyperalimentation. Subsequently, according to the clinical conditions, the patients received nutritional support by parenteral, enteral route or both up to the 10th day. Evaluations were performed on the 1st, 5th, and 10th days. These included: clinical data (food intake and anthropometric measurements), haematological data (lymphocyte count), biochemical tests (albumin, transferrin, fibronectin, prealbumin, retinol-binding protein) and hormone assays (cortisol, insulin, glucagon).

Anthropometric measurements revealed no significant difference between the first and second evaluations. Serum albumin and transferrin did not change significantly, but mean values of fibronectin (8.9 to 16 mg/dL), prealbumin (7.7 to 18 mg/dL), and retinol-binding protein (2.4 to 3.7 mg/dL) increased significantly ($p < 0.05$) from the 1st to the 10th day. The hormonal study showed no difference for insulin, glucagon, and cortisol when the three evaluations were compared. The mean value of the glucose/insulin ratio was of 25.7 in the 1st day and 15.5 in the 5th day, revealing a transitory supression of this hormone. Cortisol showed values above normal in the beginning of the study.

We conclude that the anthropometric parameters were not useful due to the short time of the study; serum proteins, fibronectin, prealbumin, and retinol-binding protein were very sensitive indicators of nutritional status, and an elevated glucose/insulin ratio, associated with a slight tendency for increased cortisol levels suggest hypercatabolic state. The critically ill patient can benefit from an early metabolic support.

DESCRIPTORS: **Hyperglycemia. Nutritional status. Nutritional profile.**

Cuthbertson in 1932 was the first to describe the metabolic events occurring in response to trauma, consisting of wasting of body nitrogen (N)[1,2]. Only after many years was the metabolic response better understood. Trauma and sepsis cause a hypermetabolic state, resulting in an increasingly negative N balance. This negative N balance is generally proportional to the intensity of the injury. There is hyperglycemia and resistance to insulin[3,4,5]. Cortisol, catecholamines, and glucagon are invariably high. The basic substrate to cope with the increased nutritional needs comes from Acetyl coenzyme A (acetyl-CoA) in the Krebs cycle. Acetyl-CoA is produced by carbohydrates, fats, and amino acids. Alanine and glutamate are the principal sources of amino acids for gluconeogenesis. Exogenous amino acid administration can minimize the large amount of catabolism that occurs after trauma, increasing N retention[6–10]. The early diagnosis of acute protein deficiency is important for prescribing adequate metabolic support[11–13].

Nutritional status can be assessed by clinical and laboratory procedures. Feeding evaluation and anthropometric measurements are fundamental to the diagnosis. Laboratory tests are indicated according to the clinical situation of the patient; serum proteins (transferrin, retinol binding protein, prealbumin, and fibronectin), serum amino acids, and number of lymphocytes have special importance[14–19].

We present data concerning the nutritional profile of severely ill infants while receiving early nutritional support. Our objective was to identify

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those serum proteins that can be considered as good markers of body protein depletion. We also present data concerning the hormonal profile during recovery from the hypermetabolic phase.

## PATIENTS AND METHOD

Seventeen infants (11 males and 6 females) aged between 2 and 6 months, with a median age of 3 months 20 days, were studied during recovery from acute respiratory distress caused by bronchopneumonia. They were admitted to the Intensive Care Unit of Instituto da Criança, Hospital das Clínicas, São Paulo University Medical School, between October of 1992 and October of 1993.

All patients were evaluated at admission, but the data were incomplete for three patients who died after a few days.

The severity of the patient's condition was assessed by the PRISM Score (Pediatric Risk of Mortality)[20].

After initial stabilization, clinical and laboratory evaluation were performed, and total parenteral hyperalimentation was prescribed within one week.

The nutritional evaluation comprised a complete 24-hour feeding inquiry questionairre (anamneses, neonatal data, recent diet) and physical examination with anthropometric measures (body weight, height, mid-arm circumference, and some skin folds). Z scores were calculated for body weight/age, height/age, and weight/height.

The laboratory workup included prealbumin, transferrin, retinol-binding protein, and fibronectin, which were analyzed by radial immunodiffusion.

The following hormones were measured by radioimmunoassay: glucagon, insulin, and cortisol[21].

The evaluations above described were repeated in the 5$^{th}$ and 10$^{th}$ day after initial stabilization and initiation of nutritional support. Parenteral hyperalimentation consisted of 100 ml/100 kcal/kg day of a 10% dextrose solution containing 2 g/kg/day amino acids and 2 to 3 g/kg of fat emulsion. The ratio of N/calories varied between 1/150 and 1/200. Trace elements, minerals, and vitamins were administered in basal amounts daily to critically ill patients.

The data were tabulated and analyzed (mean $\pm$ SD). Means were compared using the Student's *t* paired test. The non-parametric tests of Friedman and Wilcoxon were calculated, using the 5% significance level.

## RESULTS

The mean of the PRISM score was less than 10 (8.4 $\pm$ 7.1) at the beginning of the study and did not change signifcantly by the second evaluation (4.5 $\pm$ 3.8).

Table 1 shows the z score for weight for age, height for age, and weight for height at admission, as well as for the subsequent evaluations. The majority of the patients were nutritionally normal or slightly malnourished. The intake of food was adapted for the

**Table 1** - Mean "Z"scores at admission, 5$^{th}$ and 10$^{th}$ day (N = 14).

| Parameters | Admission | 5$^{th}$day | 10$^{th}$day |
|---|---|---|---|
| Weight/Age | -0.94±0.89 | -1.00±0.98 | -0.92±0.97 |
| Height/Age | -1.02±0.79 | -1.02±0.79 | -1.02±0.79 |
| Weight/Height | -0.14±0.60 | -0.23±0.79 | -0.12±0.80 |

Weight = Kilogram
Height = centimeter

**Table 2** - Mean serum Retinol-Binding-Protein, Fibronectin, Prealbumin, Albumin at admission, 5$^{th}$day and 10$^{th}$day.

| Serum Proteins | Admission | 5$^{th}$day | 10$^{th}$day |
|---|---|---|---|
| RBP (3-6 mg/dL) | 2.40±1.79 | 3.45±2.32 | 3.75±1.31* |
| Fibronectin (25-40 mg/dL) | 8.9±6.62 | 11.6±6.58 | 16.0±5.57* |
| Prealbumin (20-50 mg/dL) | 7.7±5.59 | 18.0±17.7 | 20.7±11.9* |
| Albumin (g/dL) | 3.2±0.46 | 3.34±0.53 | 3.30±0.50 |

*p< 0.05

**Table 3 -** Mean serum glucose, insulin, glucagon, cortisol, and glucose/insulin ratio at admission, 5$^{th}$day, and 10$^{th}$ day.

| Parameters | Admission | 5$^{th}$day | 10$^{th}$day |
|---|---|---|---|
| Glucose (70-110mg/dL)* | 135±43 | 118±30 | |
| Insulin (3-305pcg/mL) | 6.5±5.1 | 11.3±10.4 | 16.0±22.7 |
| Glucagon (4-130pcg/mL) | 27.3±17.7 | 93.8±141 | 66.2±75 |
| Cortisol (5-20mcg/mL) | 22±12.6 | 18.4±14 | 18.6±14.1 |
| Glucose/Insulin Ratio (4) | 25.7±18.3 | 15.5±8.4 | |

* Normal range

age of patients. Energy intake calculated was estimated until a deficit of 10% of the recommended intake.

Table 2 shows the values for serum proteins at admission and at the 10$^{th}$ day of follow-up. Prealbumin, retinol-binding protein, and fibronectin were significantly higher at the end of the study ($p< 0.05$) compared with first day.

Table 3 shows the values for glucagon, cortisol, and insulin at the beginning and end of the study. Mean insulin and glucagon were maintained in the normal range in all periods. But the ratio of serum glucose/insulin was elevated, with a mean of 25.7 at admission and 15.5 on the 5$^{th}$ day ($p< 0.06$). Serum cortisol levels were slightly increased on the first day and were normal on the 5$^{th}$ and 10$^{th}$ day of the study.

There was positive linear correlation between retinol-binding protein and insulin, prealbumin and cortisol, and retinol-binding protein and prealbumin.

The lymphocyte count was less than 1800/cm$^3$ in two patients in the first day and in three patients at the 5$^{th}$ day with no statistical difference found using the Student's *t* paired test.

## DISCUSSION

Few studies have emphasized the efficacy of parenteral nutritional support of critically ill infants after the admission to the ICU[13,22]. In this study we evaluated the role of early metabolic support in stressed infants. In the last decade several investigators have tried to establish a correlation between clinical and laboratory parameters and the prognosis of critically ill patients[9,13,23]. The ideal parameter should have sensitivity, specificity, and predictive value capable of identifying groups with a difference in the rate of morbidity-mortality.

In this study, nutritional status was evaluated and associated with a specific and standardized metabolic support. As was expected by the short term of the study, there was no important body gain weight. In spite of the severity of the infection in these patients, they maintained body weight. However, factors such as edema and vascular permeability disturbances could influence the sequential analysis of the anthropometric parameters. Other anthopometric indexes as triceps and biceps skin thickness, as well as arm muscle circumference and arm muscle area were similar at admission and at the end of the study.

The muscle evaluation is more significant when one considers the important muscle atrophy described in the severely infected infant[8,24].

Serum albumin and lymphocyte count are not good nutritional indicators when the nutritional depletion is assessed for a short period of time. The correlation between serum albumin and body protein mass is more accurate in large numbers of people, with a low individual sensitivity and specifity[3,17]. Thus, the greater half-life of albumin (15 to 20 days) is not correlated with acute nutritional alterations. A lymphocyte count less than 1500 to 1800/cm$^3$ seems to be related to a high mortality rate. Relating these findings to nutritional status is of doubtful value, since the method has low sensitivity and specificity. Sequential counts are more reliable for detection of slight nutritional alterations[25,26] .

Retinol-binding protein, fibronectin, and prealbumin have a shorter half-life[17,27]. Our data suggest that these serum proteins were significantly higher at the 10th day, compared with admission. Yoder et al. and Bondestam et al. have described the reliability of these proteins in the nutritional evaluation of children with chronic infection of the respiratory airways or during recovery from protein-energy malnutrition[27,28]. Yoder et al. called attention to the better specificity of changes in prealbumin and fibronectin occurring with malnutrition or nutritional recovery, independent of the presence of inflammatory response. The positive linear correlation in our study supports this idea. Schlichtig and Ayres pointed out the better sensitivity of fibronectin in acute nutritional disturbances in critically ill adults[3]. There have been only few studies in pediatrics in which

retinol-binding protein has been evaluated. But, the superior value of retinol-binding protein over albumin or tranferrin during nutritional recovery has been emphasized[18,27].

Several hormones function as mediators of intermediary metabolic alterations in patients with severe infections. The hyperglycemic hormones, which are related to the protein catabolism, show systematically elevated serum concentrations, although the factors responsible for these actions remain to be clarified. Insulin, the principal anabolic hormone, has extremely variable concentrations in different phases of acute disease. The more constant finding for this hormone is a blunted response, secondary to diminished pancreatic perfusion and counteraction by catecholamines[2,3,24,29]. We observed a tendency for our patients to be hyperglycemic. After observing the behavior of the insulin concentrations during the follow-up, we note the possibility that the decreased insulin values at the end of the study (elevated glucose concentration/insulin concentration) might be a factor in the hyperglycemia in view of the normal glucagon and cortisol concentrations. Cortisol decreased during the study, but the values were not statistically different. The clinical stability of the patients at the beginning could explain the hormonal findings. Recently, a study has shown that the serum concentrations of thyroid hormones and cortisol are sensitive indices in critically ill patients.[30] Accordingly, the positive linear correlation ($p<0.05$) in our study between retinol-binding protein and insulin, which was similar to prealbumin and cortisol, indicates a high specificity of these indices.

Metabolic support administered until the 10$^{th}$ day was sufficient to prevent deterioration of the nutritional status of these patients. The early administration of the nutritional support is important for prevention of acute protein-energy depletion in hospitalized infants treated in intensive care units.

## CONCLUSION

Serum proteins (fibronectin, prealbumin and retinol-binding protein) and an increased glucose/insulin ratio were useful in evaluating nutritional recovery in infants with respiratory distress during intensive care. Early metabolic support results in clinical benefit in those conditions.

## RESUMO

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DELGADO AF e col. - Avaliação nutricional seqüencial de lactentes gravemente doentes recebendo terapia nutricional parenteral por curto período. **Rev. Hosp. Clín. Fac. Med. S. Paulo 55** (1):3-8, 2000.

A avaliação nutricional seqüencial é muito importante para a adequação e monitoramento da terapia nutricional. Raros estudos caracterizaram a eficácia da terapia nutricional parenteral em lactentes gravemente doentes.

Foram estudados 17 lactentes submetidos à terapia nutricional parenteral total por cinco dias. Posteriormente, de acordo com as condições clínicas, os pacientes recebiam terapia nutricional parenteral, enteral ou mista até o décimo dia de internação. As avaliações nutricionais eram realizadas no primeiro, quinto e décimo dias e constavam de: dados clínicos ( história alimentar e medidas antropométricas), dado hematológico (contagem de linfócitos), testes bioquímicos (albumina, transferrina, fibronectina, pré-albumina e proteína ligada ao retinol) e dosagens hormonais (cortisol, relação glicemia/insulina, glucagon).

As medidas antropométricas não revelaram diferença significante entre a primeira e seguunda avaliações. Os níveis de albumina e transferrina não se modificaram significativamente, mas os valores médios de fibronectina (8.9 a 16mg/dL), pré-albumina (7.7 a 18mg/dL) e proteína ligada ao retinol (2.4 a 3.7mg/dL) aumentaram significativamente ($p < 0.05$) do primeiro ao décimo dia. O estudo hormonal não revelou diferenças para insulina, glucagon e cortisol nas três

comparações. O valor médio da relação glicemia/insulina foi de 25.7 no primeiro dia e 15.5 no quinto dia, revelando supressão transitória deste hormônio. O cortisol mostrou valores acima do normal no início do estudo.

Neste estudo concluiu-se que os parâmetros antropométricos não foram úteis no curto período de avaliação. As proteínas viscerais foram de boa sensibilidade e a relação glicemia/ insulina aumentada, associada com uma tendência de elevação do cortisol, sugerem estado hipercatabólico. Os lactentes gravemente doentes podem se beneficiar de uma terapia nutricional precoce.

DESCRITORES: **Glicemia. Terapia nutricional parenteral. Lactente gravemente doente. Avaliação nutricional.**

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