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# EFFECT OF GLUTAMINE-ENRICHED TOTAL PARENTERAL NUTRITION ON INFLAMMATORY BOWEL DISEASE

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The aim of this study was to asses the effect of glutamine-supplemented total parenteral feeding on clinical and nutritional states in severe inflammatory bowel diseases (IBD).

Twenty seven patients with severe IBD were qualified to total parenteral feeding with or without glutamine. The clinical, metabolic and nutritional improvements have been analyzed after 14-day treatment.

Though, we were able to notice some improvements in hemoglobin and transferrin concentrations as well as nitrogen balance, it still cannot be strongly concluded that these effects were due to glutamine supplementation. There were any beneficial effects of glutamine on immunological, biochemical nor anthropometric parameters of nutritional status.

## INTRODUCTION

In the late 1960's, the introduction of total parenteral nutrition (TPN) provided a life saving solution to children with short bowel syndrome and other diseases that precluded natural feeding by mouth or by enteral nutrition. Intravenous administration of nutrients in some cases became the only possible way to avoid progressive malnutrition leading to death [Dudrick *et al.,* 1968; Elia *et al.,* 1989].

Inflammatory Bowel Diseases (IBD) refers to two chronic diseases that cause inflammation of the intestines: ulcerative colitis and Leśniowski-Crohn's disease, often associated with nutritional disturbances, such as protein-calorie malnutrition, vitamins and trace elements deficiencies. Although same important improvement has recently been made in the management of IBD, the major controversial issues in the field of nutritional support remain open [Alan *et al.,* 2001; Geerling *et al.,* 1999; Han *et al.,* 1999]. Prevalence of malnutrition in IBD ranges from 23% in outpatients to 85% in hospitalized patients. In IBD some nutrients can help to maintain intestinal structure and function. In IBD tissue damage can be determined by some nutritional factors, *e.g.:* (1) diminished availability of all nutrients; (2) lower availability of antioxidant nutrients (glutathione, zinc, selenium, vitamins A, C and E); (3) insufficient supply of enterotrophic nutrients (glutamine, short-chain fatty acids);, and (4) diminished cellular capacity of using trophic nutrients (growth hormone resistance).

Glutamine, the most abundant nonessential amino acid in mammals is released in large quantities from skeletal muscle and serves as an important donor of nitrogen playing a pivotal role in nitrogen balance and acid base homeostasis [Elia *et al.,* 1989]. This amino acid is a main energy fuel for rapidly dividing cells such as lymphocytes and enterocytes [Calder *et al.,* 1994]. The metabolic response to chronic inflammation and sever malnutrition is characterized by the breakdown of skeletal muscle protein. During muscle protein degradation intracellular level of glutamine falls and its production and turnover increase leading to decreased plasma level. These findings have led to the hypothesis that protein catabolism can be corrected by providing exogenous glutamine.

Studies have shown that the glutamine-enriched parenteral nutrition in patients after elective abdominal surgery results in reduction of hospital stay (by 4 days on average) [Morlion *et al.,* 1998] and costs [Mertes *et al.,* 2000]. Patients also had a better nitrogen balance, higher intracellular concentrations of glutamine in the skeletal muscle,a higher muscle protein synthesis rate and an improved lymphocyte count [Morlion *et al.,* 1998]. In postoperative patients glutamine supplementation has also helped to maintain intestinal permeability [Jiang *et al.,* 1999; Wilmore *et al.,* 1998, 2001]. Up to now, available data showed that glutamine should be considered as an essential part of parental nutrition in various pathological states [Seo *et al.,* 1999].

In IBD, the TPN's aims are perioperative nutrition, fulfilling postoperative nutritional requirements and correcting malnutrition. It is also used as primary therapy for IBD when there are contraindications for feeding *via* the gastrointestinal tract [Geerling *et al.,* 1999; van der Hulst *et al.,* 1993].

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The aim of the study was to asses the effect of glutamine-supplemented total parenteral feeding on clinical and nutritional states in severe, active IBD.

## MATERIAL AND METHODS

**Patients.** Twenty seven patients with active IBD scheduled for total parenteral nutrition were studied (active Leśniowski-Crohn's disease, n=18, ulcerative colitis n=9). The indications for TPN were severe malnutrition, severe diarrhea and contraindications for enteral nutrition. Patients were qualified to total parenteral feeding without (n=15) or with (n=12) glutamine at a dosage of 20 g (Dipeptiven, Abbott). The clinical (CDAI > 350, Truelove-Witts score – severe), metabolic and nutritional (anthropometry, bodystat, laboratory data) parameters did not different significantly among the studied groups.

**Blood and urine analyses.** The blood count, total lymphocyte count, hemoglobin, albumin, trensferrin concentrations, have been analyzed in 0, 7 and 14 day of treatment. Daily nitrogen balance was calculated using urine creatinine, urea and ureic acid 24-h excretion method.

**Anthropometry and body composition.** Body mass index (BMI) was calculated from height and weight. Anthropometric parameters, triceps skin-fold thickness (TSF) measured with a Harpenden Compass, and mid-arm circumference (MAC) measured half-way between the olecranon and the acromion with a tape measure, were recorded on the nondominant side three times by the same investigator and the results were averaged. Body composition measurement was performed using a Bosystat®1500 medical analyzer.

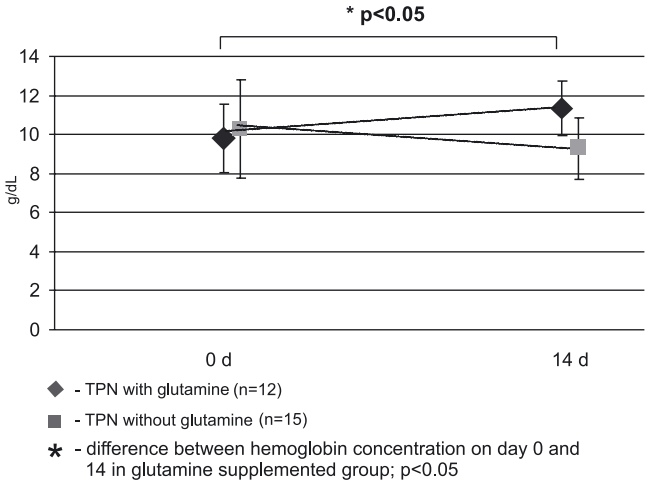


FIGURE 1. Hemoglobin concentration in patients with and without glutamine-enriched TPN.

## RESULTS

We observed a high, but not statistically significant, increase in albumin concentration in the group supplemented with glutamine as compared to the non-glutamine group after 2 weeks (2.5±0.6 *vs*. 2.8±0.35 g/dL). After that period of treatment, hemoglobin concentration raised significantly higher in the glutamine-enriched TPN group (10.26±2.51 *vs*. 9.29±1.56 g/dL, p<0.05) as compared to the group without glutamine (Figure 1). In the group without glutamine

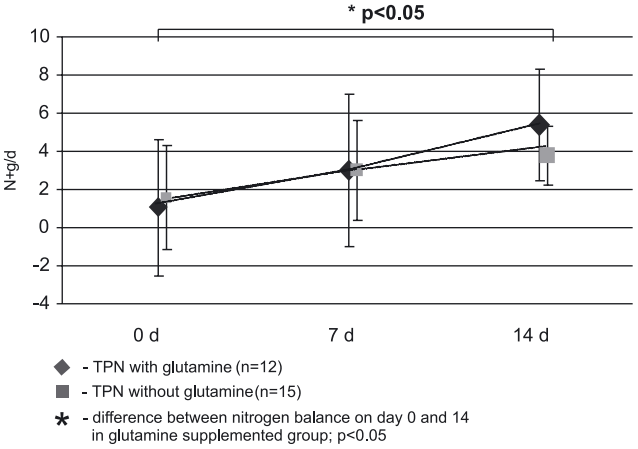


FIGURE 2. Nitrogen balance in patients with and without glutamine-enriched TPN.

supplementation, the concentration of hemoglobin was observed to even slightly decrease during the treatment. Transferrin concentration in the glutamine group was higher after 2 weeks of the treatment (148.06±26.96 *vs*. 145.17±33.40 µg/dL, p<0.05). Transferrin concentration in patients not receiving supplementation remained unchanged. There was a small beneficial effect on the nitrogen balance in the group with glutamine-enriched TPN, but it could be noticed until 2 weeks of the treatment (5.38±2.92 *vs*. 3.79±1.55 g N/day, p<0.05) (Figure 2). In both groups, a similar increase in total lymphocyte count and a decrease in platelets count have been noticed. We were not able to detect any statistically significant, beneficial effect of glutamine on anthropometric measurements, body composition and BIA as compared to the group without glutamine supplementation. The observed changes in disease activity, length of TPN and hospital stay, were independent of glutamine supplementation.

## DISCUSSION

Increasing research on the mechanisms by which nutritional management improves the clinical well being of patients has led to novel formula design. Hypothesized mechanisms have postulated the idea of "bowel rest", reduced antigenic impact, and improved nutritional status [Ruemmele *et al.,* 2000]. The immunonutrition term has been used to describe molecular compounds that, while being nutrients, such as omeg-3 polyunsaturated fatty acids, glutamine, arginine, ribonucleic acid, also influence immunological mechanisms when added to standard TPN solutions or enteral nutrition. It has been suggested that parenteral or enteral glutamine supplements could attenuate the GALT function and inhibit the mucosal hypoplasia associated with prolonged TPN. Studies carried out on a rat-IBD model suggest that supplementation of total parenteral nutrition with glutamine reduces intestinal inflammation, improves nitrogen

balance and may alter the activity of the disease. However, human data supporting these benefits are missing.

Though we were able to notice some improvements in hemoglobin and transferrin concentration as well as nitrogen balance, it still cannot be strongly concluded that these effects were due to glutamine supplementation. Although limited by the sample size and heterogeneity of the patients studied, these results do not support the hypothesis that glutamine-enriched TPN has an obvious biochemical or clinical benefit on patients with active IBD. However, we are aware of the fact that 2 weeks is too short period of treatment to reach any changes in antrophometric measurements.

In patients receiving home parenteral nutrition and in those with liver-function abnormalities some side effects of glutamine have been described. On the basis of currently available clinical data, it seems to be inappropriate to recommend glutamine for therapeutic use in any condition [Akobeng *et al.,* 2000; Fujita *et al.,* 1995]. Moreover, the limited data concerning the supplementation of glutamine suggest that there is no strict evidence of its therapeutic role in IBD [Powell-Tuck *et al.,* 1999; Shinozaki *et al.,* 1997; Wischmeyers *et al.,* 1993; Zachos *et al.,* 2001].

## CONCLUSIONS

Though glutamine parenteral supplementation seems to be beneficial in same critically ill patients, further studies are required in patients suffering from IBD, to evaluate the effect of disease duration and location.

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# WPŁYW SUPLEMENTACJI GLUTAMINY W ŻYWIENIU POZAJELITOWYM NA PRZEBIEG NIESWOISTYCH CHORÓB ZAPALNYCH JELIT

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Celem pracy była ocena wpływu suplementacji glutaminy w trakcie pozajelitowej terapii żywieniowej chorych z ciężkim rzutem nieswoistych chorób zapalnych jelit (IBD). Oceniano parametry kliniczne, metaboliczne i stanu odżywienia u 27 pacjentów zakwalifikowanych do TPN z dodatkiem lub bez dodatku glutaminy po 14-tu dniach leczenia. Chociaż autorzy odnotowali lepszą poprawę stężenia hemoglobiny, transferryny oraz bilansu azotowego w grupie chorych, którzy otrzymywali glutaminę, to nie można było na podstawie analizy danych określić ścisłej zależności korzyści od prowadzonej suplementacji. Nie stwierdzono, aby chorzy odnieśli korzyści w postaci poprawy parametrów immunologicznych czy parametrów oceniających stan odżywienia.