Early immuno-enhancing enteral feeding in a cohort study of critically ill patients with severe traumatic brain injury

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INTRODUCTION: Effective and sensible clinical nutrition practice is of paramount importance in critically ill patients and may influence outcome. The role of early enteral immuno-nutrition in critically ill patients is highly disputed and in the sub-group of severe traumatic brain injury (TBI) is poorly investigated. Optimal nutrients constitution, dose scheme, starting point and duration still remain subjects of debate. Recent data from microdialysis studies in patients with TBI argue for a role of NO metabolism (closely related to arginine's). Increased plasma cytokine levels (IL-6, IL-8), have been associated with poor outcome in patients with TBI[1] and biphasic elevation of IL6 with late MODS in patients with trauma[2]. The goal of this study was to compare the effects of early administration of arginine supplemented immuno-enhancing enteral feeding VS standard isocaloric feeding in TBI patients in terms of clinical indices / outcome as well as parameters of nutrition and inflammation.
[1]Venetsanou K et al, Eur Cytokine Netw 2007; 18(4):206-9, [2]Maier B et al, Shock 2007; 28(6):668-674

METHODS: Prospective, randomized, controlled trial, recruiting consecutive patients. The study was approved by the Cyprus Bioethics Committee and the Hospital authorities. Two groups: A = isocaloric, standard enteral feeding 1kcal/ml (Nutrison STD) and B = isocaloric, immuno-enhancing feeding, 13 g/L Arginine (Impact, Novartis, oral/enteral) – (protein 22% of total energy, carbohydrates 53%, fat 25%, ω3/ω6 FFA, RNA, vitamins, minerals, trace elements). Patients with GCS< 5 were excluded. Follow up was up to 30 days. Clinical assessment (gender, age, type of trauma/neurotrauma, clinical history, GCS, intubation circumstances, neurosurgical complications, type of surgery, ICP, ABGs, daily follow up for fever-infection, cardiac and respiratory function, enteral feeding and side effects, outcome variables) / nutritional assessment (anthropometry, nutritional assessment scoring, energy/protein/fluid requirements, laboratory assessment) up to 30 days, inflammatory mediators profile – cytokines (IL-6, IL-8, IL-10, TNF-α, measured with ELISA standardised on 50 healthy individuals), pre-albumin, CRP, Cortisol, PCT, NO derivatives (admission, 1st, 4th, 7th day of feeding), std labs (every day), cortisol (admission, 1st, 4th, 7th day) severity scores (Apache-II, GCS, GOS) and mortality to 30 days. Enteral feeding practice followed standard protocol, its implementation audited before starting the PRCT (Poster 1018, ESICM 2007). Primary end points were (a) Percentage of infectious complications and time-frame of fever and inflammation (days free of fever), length of mechanical ventilation and inflammatory status at a cellular level. Secondary end-point was 30 days mortality. Results were analyzed with SPSS (descriptive statistics, means, ANOVA, t-tests, Pearson correlation coefficients).

RESULTS: From Sep.2007 to Jul.2008, 48 patients enrolled (A=25, B=23, M/F = 38/10, Age 34.2 ± 15, GCS 9.6 ± 3.9, Apache II score 17.6 ± 6.5), enrollment paused due to positive results. We had 6 deaths by the 30th day. 52% of patients started enteral feeding before the 2nd day and 83% by the 3rd day post-admission, 75% met their theoretical nutritional needs (Harris Benedict, 5.7 +/- 2.2 VS 6.2 +/- 1.8, total 5.9 +/- 2). The two groups were comparable regarding demographics and severity of disease / TBI (Apache: 17.4 +/- 7.6 VS 18 +/- 5, total 17.6 +/- 6.5 and GCS: 9.6 +/- 4 VS 9.6 +/- 3.9, total 9.6 +/- 3.9). Prevalence of Sepsis (SIRS with T>38.2 plus documented / suspected infection) during the first 10 days after injury was significantly lower in the immunonutrition group compared to Std nutrition.
Length of mechanical ventilation did not show similar differences (9±8 VS 9±6 days, NS). Mortality (1/19=5.3% VS 5/22=22.7%) was significantly less in Immunonutrition group (x^2=20.512, d.f.=1, p<.0001). Pre-albumin levels at the 7th day were higher in the immunonutrition group (13.8±2 VS 17.8±9.2, p<0.05), see *figure 3*. Cytokine plasma levels profile has also clear differences between the 2 groups, with immunonutrition group having lower values of IL6, IL8 and IL10 as early as within 24 hrs from the injury.

CONCLUSION: It seems that enteral immunonutrition (based mainly on high Arginine content) in a small cohort of critically ill ventilated patients with severe TBI, is most probably beneficial compared to standard nutrition even if both regimens are administered early and effectively. The benefit refers to decreased sepsis rate retained up to 10 days post admission as well as decreased mortality, though the small number of patients does not permit definite conclusions. Pro-inflammatory Cytokines profile is different showing an attenuation of the trauma-related inflammatory process in TBI patients fed with immuno-enhancing diet, a fact that probably contributes to the observed results. Larger, multi-center PRCTs are urgently needed.

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