8. Metabolic/Nutrition – Free Papers

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EFFECT OF EARLY ENTERAL NUTRITION ON INCIDENCE OF SEPSIS, SEPTIC SHOCK AND ORGAN FAILURE IN CRITICALLY ILL PATIENTS

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OBJECTIVES: Early enteral nutrition (EN) has been advocated as a means of possible improving survival rate in critically ill patients. The aim of the study was to evaluate the effect of EN on incidence of sepsis, septic shock and organ failure in critically ill patients requiring ventilatory support.

METHODS: An observational study was carried out in 35 critically ill patients admitted to the ICU. The study was conducted in two groups: Group A (n=17) received enteral nutrition (EN) and Group B (n=18) received parenteral nutrition (PN) as a control. The following parameters were evaluated: sepsis incidence, septic shock, organ failure, length of ventilatory support and clinical outcome.

RESULTS: EN was associated with a lower incidence of sepsis (29% vs 55% in PN, p=0.02), septic shock (18% vs 44% in PN, p=0.01) and organ failure (29% vs 50% in PN, p=0.05) when compared to PN. The length of ventilatory support was also shorter in the EN group (7 vs 10 days, p=0.03). Clinical outcome was better in the EN group with a higher survival rate (76% vs 50% in PN, p=0.05).

CONCLUSIONS: Early EN appears to be beneficial in critically ill patients requiring ventilatory support, with a reduction in sepsis, septic shock and organ failure, and a shorter length of ventilatory support.

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A RANDOMIZED CONTROLLED TRIAL OF THE ENTRAL IMMUNONUTRITION ‘IMPACT’ IN THE CRITICALLY ILL

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OBJECTIVE: To assess the effects of enteral immunonutrition on hospital mortality and length of stay in a heterogeneous group of critically ill patients.

Design: Prospective randomized double-blind controlled clinical trial comparing ‘IMPACT’ (Sandoz Nutrition Ltd, Berne, Switzerland), an enteral feed supplemented with arginine, nucleotides and omega-3 fatty acids and with an iso-osmotic, iso-nitrogenous control enteral feed. A prior sub-group analysis was according to the volume and rate of feed delivered and the presence of admission on the systemic inflammatory response syndrome.

Patients: 396 patients were enrolled and data from 390 (193 fed with ‘IMPACT’; 197 fed with the control feed) were analysed on an intention to treat basis. 390 patients actually received some enteral nutrition (184 - ‘IMPACT’, 186 - control) of whom 101 patients (50 ‘IMPACT’, 51 -control) received more than 2.5L within 72 hours of ICU admission.

Results: Overall hospital mortality was 48.2% reflecting severity of illness on ICU admission (mean APACHE II score 18.4 ± 7.1; APACHE risk of death 31 ± 22%). Whilst there was no significant difference in hospital mortality between the two groups on an 'intention to treat' analysis (‘IMPACT’ group 48%, control group 44%) nor in any other predefined subgroup analysis, patients randomised to receive a 'heavier' tended to have higher APACHE II scores (20.1 ± 7.1 versus 18.7 ± 7.1 [p = 0.07] for the 'intention to treat' cohort; 20.1 ± 7.2 versus 18.5 ± 7.1 [p = 0.035] for the 'received feed' cohort). In the 101 patients achieving successful early enteral nutrition (2500 ml within 72 hours of ICU admission), there was a significant reduction in the requirement for mechanical ventilation (days of ventilation 9 ± 8.5 versus 13.5 ± 12.4, p = 0.03) with an associated reduction in the length of hospital stay (‘IMPACT’ group 21.0 ± 20.5 days, control 26.4 ± 46.0 days, p = 0.03).

Conclusions: Whilst the administration of enteral immunonutrition (‘IMPACT’) to a general, critically ill population of patients did not affect overall mortality, those patients in whom it was possible to achieve early enteral nutrition had a statistically significant reduction in the duration of mechanical ventilation and length of hospital stay.

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OUTCOME AND COST OF INTENSIVE CARE PATIENTS GIVEN GLUTAMINE-SUPPLEMENTED NUTRITION.

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OBJECTIVES: To study whether giving glutamine containing feeds to the critically ill improves recovery, reduces late mortality and hospital costs.

DESIGN: A prospective block-randomised, double-blind treatment study comparing L-Glutamine (Gln) supplemented (Oxford Nutrition, UK) enteral (EN) or parenteral nutrition (PN) with isonitrogenous, isosinergentic control (CNTL) feeds.

SUBJECTS: In critically ill patients admitted to ICU, to ensure consistency of management policies, 156 critically-ill adult patients, with APACHE II score > 10, required nutrition support were studied.

METHODS: Standard clinical decision making with enteral nutrition being preferred unless contraindicated or unsuccessful and nutrition support continued to a general, critically ill population of patients did not affect overall mortality, those patients in whom it was possible to achieve early enteral nutrition had a statistically significant reduction in the duration of mechanical ventilation and length of hospital stay.

RESULTS: Selected clinical results are presented in the table.

Incidence of Group EN Group TN P value
Sepsis 11 (73%) 10 (100%) NS
Septic shock 2 (13%) 6 (60%) <0.05
Lung failure 7 (46%) 7 (70%) NS
Hepatic failure 1 (6%) 0 (0%) NS
Renal failure 1 (6%) 6 (50%) <0.05
Gut failure 0 (0%) 0 (0%) NS
Coagulation failure 2 (13%) 0 (0%) NS
Mortality 2 (13%) 6 (60%) <0.05

DISCUSSION: EN seems to be safe and efficative method in improving clinical outcome and should be employed whenever is possible as a standard part of any nutritional protocol in critically ill patients.

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GLUTAMINE Dipeptide (L-Alanyl-L-Glutamine) Supplemented Total Parenteral Nutrition (TPN) Improves N-Balance and Shortens Hospitalization in Surgical Patients

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Objectives: To assess the efficacy of a glutamine (Gln) dipeptide-supplemented total parenteral nutrition on selected metabolic and clinical variables in surgical patients.

Design: A randomized, double-blind, controlled study in a university hospital.

Subjects and methods: Eighty-eight patients (age range 42-88 years, mean 68 years) undergoing elective resections of colon or rectum were allocated, after randomization, into two groups to receive isonitrogenous (0.24 g N kg⁻¹ day⁻¹) and isosinergetic (2500 kcal/1200 kcal kg⁻¹ day⁻¹) TPN over days. Controls received 1.5 g amino acids (AA) kg⁻¹ day⁻¹ (Amnustell®/KET10%) and the testgroup 1.5 g AA including 0.3 g L-Alanyl-L-Glutamine (Ala-Gln) kg⁻¹ day⁻¹ (mixture of Amnustell®/KET10% and Dippeptiven®/Fresenius AG). Venous heparinized blood samples were obtained preoperatively and on postoperative days 1 and 3 and postoperatively for routine clinical chemistry and for measurement of plasma free amino acids (automated on-line HPLC system). N-balances were calculated on days 1, 2 and 5 postoperatively.

Results: Controls n=13□ -4,0 t 3,0□ 15,5 ± 0,7□ 30 t 6□ 37 t 3 Controls n=13□ 526 ± 48□ 427□± 28□ 30 ± 6□ 37 ± 3 Controls n=13□ -18,9 t 21□ 5□ 43 t 9□ 21,7 t 2,8□

Mean±SD, SEM; Gln and glutamate (Glu) in nmol/ml plasma *p<0.01 and †p<0.05 controls vs Ala-Gln; p<0.05 day 6 vs day 1

Conclusion: No side effects or complaints were noted. There is no indication for Gln dipeptide are less catabolic, revealing improved N-balances. Postoperative hospital stay (days) was significantly shorter in the dipeptide supplemented group, supporting patient care and indicating economic implications.

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DIFFERENTIAL CLEARANCE OF INTRAVENOUSLY INFUSED EMULSIONS IN THE RAT. EFFECT OF HEPARIN.

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Introduction: Two lipases, lipoprotein lipase (LPL) and hepatic lipase (HL) are thought to act in concert in the hydrolysis of Triglyceride-rich particles. Intravenous injection of heparin increased both plasma LPL and HL activities. In various clinical situations, heparin (which is widely used as an anticoagulant) and lipid emulsion (which is widely used as an integral component of parenteral nutrition) are employed simultaneously (i.e. hemodialyzed patients). The aim of this present work was to compare the effect of heparin on the elimination kinetics of a MCT/LCT and a LCT emulsion.

Methods and materials: Under light ether anesthesia, male Wistar rats of 200-250 g were injected with an unique dose of heparin (20 UI/100 g). After 90 sec, rats were injected with 20 mg of TG of MCT/LCT (MEDALIPIDE® 20 %, B. BRAUN MEDICAL SA) or LCT emulsion (INTRALIPIDE® 20 %, PHARMACIA®) (n=5). Blood aliquots (200 μl) were drawn from the jugular vein at 0, 2, 4, 6 and 8 min after heparin. Plasma were separated by centrifugation for determination of TG and non esterified fatty acids (NEFA). Statistical significances were calculated using the ANOVA-test (mean ± S.D).

Results: Half lives (T1/2) of lipid emulsions were determined from the slope of disappearance: TG and NEFA after 2 min. T1/2 of TG (40±2 vs. 83±7 min) and of NEFA (T1/2, 67 vs. 10,19 min) were cleared more rapidly from circulation in the MCT/LCT group. TG were significantly lower at 4, 6 and 8 min after heparin in MCT/LCT treated rats than in the LCT one (p<0.05). NEFA were significantly higher only 2 min after heparin in MCT/LCT group (p<0.001) but not later.

Conclusion: MCT/LCT was eliminated from plasma at a higher rate (16,81 vs. 23,85 min) than LCT alone. The presented results clearly show that: 1) Heparin may strongly promote hydrolysis of MCT/LCT, 2) Tissue uptake of NEFA is not a limiting step in the use of MCT/LCT.

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PERIOPERATIVE ADMINISTRATION OF AN ENRICHED ENTERAL FORMULA: EFFECT ON INFLAMMATORY, IMMUNE AND GUT FUNCTIONS.

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OBJECTIVE: To evaluate if the perioperative administration of an enriched enteral formula might modulate the inflammatory and immune responses and the gut function in critically ill patients.

DESIGN: Prospective, randomized, double-blind trial.

SUBJECTS: Patients undergoing major surgery for cancer of the stomach or colon-rectum.

METHODS: Seven days before surgery the patients drunk 1 litre/day of an enteral formula improved intestinal perfusion and oxygenation and modulated the gut function. The formula improved intestinal perfusion and oxygenation and modulated the gut function. The formula was administered for 72 hours after surgery. Patients were randomized to receive an enteral formula enriched with arginine, RNA and n-3 fatty acids (n=20). Blood aliquots (200 μl) were drawn from the jugular vein at 0, 2, 4, 6 and 8 min after heparin. Plasma were separated by centrifugation for determination of TG and non esterified fatty acids (NEFA). Statistical significances were calculated using the ANOVA-test (mean ± S.D).

RESULTS: Compared to PN15, PN75 stimulated more CO2 production (by 30±4% vs. 6,02±0,14% after 2 min. T1/2 of TG (40±2 vs. 83±7 min) and of NEFA (T1/2, 67 vs. 10,19 min) were cleared more rapidly from circulation in the MCT/LCT group. TG were significantly lower at 4, 6 and 8 min after heparin in MCT/LCT treated rats than in the LCT one (p<0.05). NEFA were significantly higher only 2 min after heparin in MCT/LCT group (p<0.001) but not later.

Conclusion: MCT/LCT was eliminated from plasma at a higher rate (16,81 vs. 23,85 min) than LCT alone. The presented results clearly show that: 1) Heparin may strongly promote hydrolysis of MCT/LCT, 2) Tissue uptake of NEFA is not a limiting step in the use of MCT/LCT.

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Gastric acidity and duodeno-gastric reflux during jejunal tube feeding in mechanically ventilated patients.

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OBJECTIVES: In order to prevent gastric microbial overgrowth which may compromise nasogastric feeding, administration of nutrients more distally into the gut has been advocated in ITU patients, as it offers the advantage of maintaining the stomach acid and empty. In this study, we assessed the incidence of duodenogastric reflux ( bile and nutrients) as well as variations of gastric pH during jejunal tube feeding in ITU patients.

DESIGN: Each patient admitted in our ITU during a 5 months period and requiring ventilatory assistance was considered for inclusion, provided that enteral feeding was not contraindicated. Were excluded postoperative patients and patients with history of digestive disease. The day before study, a double lumen naso-gastro-junal tube (Floracath®) was positioned in the jejunum. H2 antagonists were stopped 12 hours before study in order to maintain the stomach acid before investigation.

Gastric pH was recorded over a 4 hours period of fasting followed by a 4 hours period of naso-jejunal feeding, by means of a glass electrode (Engedi®) connected to a laboratory pHmeter (Elsolab®). Data from the pHmeter were stored in a personal computer (1 measurement per minute) for later analysis. During the feeding period, a polymeric diet (Nutrition standard®) traced with DTPA Indium 111 was infused at a rate of 100 mL/hr. Gastric contents were aspirated every 30 minutes, and samples were analysed for determination of radioactive and bile acids concentration.

RESULTS: Gastric pH was monitored in 21 pts (M/F=11/10, Age: 55 ± 15 years) and duodeno-gastric reflux was analysed in 15. Mean pH increased from 2.06 ± 1.7 during fasting to 2.90 ± 1.81 during feeding (p=0.031, Wilcoxon signed-rank test). The duration of pH >4 increased during feeding (median: 9 min (feeding) vs 1 min (fasting); p=0.026), as well as the bile acids in the stomach (448±1 305μmol/L (feeding) vs 578±819 μmol/L (fasting); p=0.01). Duodeno-gastric reflux, as defined by detection of the presence of radioactive material in the stomach during feeding, was observed in 14 patients on 15.

CONCLUSION: A slight but significant increase in gastric pH occurs during jejunal tube feeding in ITU patients. This gastric alkalisation is related, at least partly, to reflux of bile and nutrients from the duodenum. Whether such alkalisation may favor gastric microbial overgrowth is unknown and deserves further investigations.

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Effects of the carbohydrate content of isocaloric parenteral nutrition on CO2 production and energy expenditure in critically ill patients.

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OBJECTIVES: Administration of carbohydrate (CHO) in hypercaloric amount enhances respiratory work by increasing CO2 production, whereas it is commonly admitted that CO2 excretion is not dependent on glucose load in isocaloric conditions. However, recent observations suggest that de novo lipogenesis from CHO is increased in critically ill patients. Such a process is expected to stimulate both CO2 production and energy expenditure due to its high energy requirement. It is also expected that 13C-labeled exogenous CHO converted into fat will not be recovered as expired 13CO2. This study was performed to assess the relationship between CHO administration, non oxidative exogenous CHO disposal (NOxCHO) and the thermic effect (TE) of parenteral nutrition (PN).

DESIGN AND SUBJECTS: Observational study in 11 critically ill patients.

METHODS: During continuous isonitrogenous-isotonic PN, containing 75% CHO (PN75: n=6) or 15% CHO (PN15: n=5), indirect calorimetry was performed before (t1) and after 72 hrs (t2). At t2, 13C6 glucose (1.5 mg/kg/min) was also infused to label exogenous CHO and 13CO2 production was measured.

RESULTS: Compared to PN15, PN75 stimulated more CO2 production (by 165±4% vs. 452±% (p<0.05). NOxCHO was 42% and 36% of infused CHO in PN75 and PN15 respectively (ns). TE was positively correlated with NOxCHO (R2=0.40, p<0.05). The slope of the regression line indicated that TE amounted to 22% of the energy content of non oxidized CHO, suggesting that de novo lipogenesis from CHO is increased in critically ill patients. Surgical intensive care unit, and Institute of Physiology, CH-1011 Lausanne University Hospital, Switzerland.
OBJECTIVES: Cardiopulmonary effects of fat emulsion containing long chain triglycerides (LCT) and medium chain triglycerides (MCT) on cardiopulmonary system in septic patients with respiratory failure were evaluated in our critical Care Unit.

METHODS: A Swan-Ganz catheter was placed in all patients to monitor their hemodynamic status by calculating a variety of measurements. The measurements were made every four hours. Every patient was subjected to three measurements daily during glucose infusion+LCT or glucose plus fat infusion (MCT+LCT) correspondingly. The group A (10 patients), received their non protein caloric load as glucose+fat (LCT) and the group B (11 patients) as glucose+mixture fat emulsion (MCT+LCT). Data were measured before, during and after the infusion and when serum lipemia cleared.

RESULTS: The PAP increased from 267.4±4.5 mmHg to 337.5±5.8 mmHg in group A (p<0.05) during the infusion but in group B from 262.6 to 271.6 no statistical significance. The venous index (Qva/Qc %) from 23.2±4.5 to 38±8.5 (p<0.05) in group A and from 23.7±4.5 to 28.5±5.5 in group B (p=not significant). The PaO2/FiO2 precipitated a significant reduction in group A from 240±40 to 180±59 (p<0.05) but in group B the reduction was smaller from 251±48 to 241±42 (no significant difference).

CONCLUSION: We conclude that fat emulsion containing medium chain triglycerides (MCT) induce less alterations in pulmonary hemodynamics and gas exchange in compare to fat emulsions with long chain triglycerides (LCT). This result is probably due to reduced prostandin formation because fat emulsion containing MCT provide less prostanoids precursors than pure LCT emulsions.

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PREOPERATIVE IMMUNONUTRITION IMPROVES THE POSTOPERATIVE IMMUNE RESPONSE

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OBJECTIVES: Postoperative enteral feeding with an omega-3 fatty acid, arginine and RNA enriched formula (IMPACT®, Sandoz Nutrition, Switzerland) may improve the depressed postsurgical immune response. The aim of this study was to evaluate the immune response in 40 patients who were to undergo upper gastrointestinal surgery receiving preoperatively either the supplemented diet (n=20) or a placebo diet (n=20).

METHODS: Following randomization patients did consume 1000 ml per day of freshly prepared enteral diet for 5 days preoperatively. After surgery patients were fed via a needle catheter jejunostomy starting on the first POP day with 20 ml/h and increasing the volume up to 80 ml/h on POP day 5. IgM, B-lymphocytes and activated T-lymphocytes were determined 5 days preoperatively, on the day of operation and on POP-day 1, 5 and 10. B- and T-lymphocytes were determined by FAC-Scan and the IgM by laser nephelometry.

RESULTS: IgM levels were similar in both diet groups preoperatively and on the day operation as well as on POP day 1. However, on POP day 5 and 10 IgM levels were 177 mg/ml and 245 mg/ml in the supplemented diet group versus 128 and 185 mg/ml in the control group (p<0.05). B-lymphocytes were suggestively higher in the immunonutrition diet on the first and fifth POP day as compared to the placebo diet. The activated T-lymphocytes were significantly higher in the supplemented diet group on the first POP day (167 cells/ml versus 88 cells/ml, p<0.05). On POP day 5 the amount of activated T-lymphocytes was suggestively higher in the immunonutrition group.

CONCLUSION: Our data show a significant modulation of immune parameters by preoperative application of immunonutritional enteral diet. Preoperative feeding with an immunonutritional diet may shift the positive cellular and humoral immune response to the early postoperative period. This may help reducing the infectious complications within the early postoperative period.

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MODULATION OF LEUKOTRIENE SYNTHYSIS AND EPA-LEVELS IN SERUM AFTER APPLICATION OF OMEGA-3 FATTY ACIDS ENRICHED FAT EMULSION IN SURGICAL PATIENTS

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OBJECTIVES: Application of omega-3 fatty acids (ω-3 FA) in the postoperative (POP) period is known to influence the postoperative immune response. The aim of this study was to investigate the alteration of the lipid mediators leukotriene B4 and B5 and to determine the EPA serum levels in surgical patients.

METHODS: In a prospective, randomized and double-blind clinical trial we investigated the effect of parenteral application of ω-3 FA on the immune response of 40 patients (n=40) who underwent surgery for colorectal cancer. Patients were randomized to receive either the ω-3 fatty acids supplemented 20% MCT/LCT fat emulsion (Lipofundin® B Braun Melsungen AG, Germany) or a 20% MCT/LCT standard fat emulsion (MCT/LCT:1:1) as control substance within 24 h after surgery. TPN with a total of 50 g fat on the first 2 POP-days and 100 g on the third day has been applied via a central venous catheter. Both diets were tolerated well. Serum lipids were assayed for phospholipid fatty acids composition by gas chromatography. Additionally, the leukotrienes B5 (LTB5) and B4 (LTB4) release by Ca2+-ionophore stimulated leukocyte cultures was determined preoperatively and on the POP days 1, 5, 10 and on the day 15. The ratio of LTA4 and arachidonic acid (AA) as well as the ratios of LTB5 and LTB4 have been determined.

RESULTS: In the ω-3 FA supplemented diet group a dose-dependent increase of the EPA / AA ratio in serum and in erythrocyte membrane has been found. The increase of the EPA / AA ratio correlated well with increased infusion of ω-3 FA (Correlation coefficient r = 0.660). Furthermore, we have found a dose-dependent increase of the ratio of the leukotrienes LTB5 / LTB4 (Correlation coefficient r = 0.660).

CONCLUSION: Our data show a significant modulation of serum lipid composition and eicosanoid release after postoperative parenteral nutrition with a ω-3 FA containing fat emulsion. There is an increase of the amount of the inflammatory less active LTB5 and an increase of the EPA serum levels in surgical patients as compared to controls. This may help reducing the infectious complications within the early postoperative period.