Effects of Perioperative Immunonutrition on Cell-mediated Immunity, T helper type 1 (Th1)/Th2 Differentiation, and Th17 Response after Pancreaticoduodenectomy

Objective
This study was completed to investigate whether perioperative immunonutrition can influence cell-mediated immunity, T helper cell differentiation and response, and can reduce the rate of infectious complications after pancreaticoduodenectomy (PD).

Methods
This was a prospective randomized clinical trial where 30 consecutive patients that met inclusion criteria were enrolled in one of the following three groups:

A. Perioperative group received ORAL IMPACT® containing supplementary arginine, omega-3 fatty acids and nucleotides for 5 days before surgery and at least 7 days of enteral infusion via jejunostomy after surgery.
B. Postoperative group received the same immunonutrition for at least 7 days after surgery.
C. A second postoperative group received total parenteral nutrition (TPN) for at least 7 days after surgery.

Enteral feeding began 12-18 hours after PD at a 10 mL/hour rate and was progressed daily by an 20 mL/hour until 25 kcal/kg/day was reached. The three regimens were approximately isocaloric before and after surgery. PD included the Whipple procedure and a pylorus-preserving PD.

Results
As per intention to treat analyses:

- **Cell-mediated immunity.** On POD 7, concanavalin A (Con A) or phytohemagglutinin (PHA)-stimulated lymphocyte proliferation was significantly higher in group A than other groups (p<0.05). On POD 14, natural killer (NK) cell activity was higher in group A than others (p<0.05).
- **Th1/Th2 differentiation.** On POD 3, mRNA expression levels of T-bet (transcription factor for Th1) and the ratio of T-bet/GATA-3 (transcription factor for Th2) were significantly higher for group A vs other groups (p<0.05). A hallmark cytokine for Th1 cells, IFN-γ, helps to activate microbicidal activity, and was also found to be significantly higher in group A vs. others (p<0.01).
- **Th17 response.** On PODs 0, 1 and 3, mRNA expression of RORyt (transcription factor for Th17), and on PODs 3 and 7, mRNA expression of IL-17F were significantly higher in group A vs other groups (p<0.05). Plasma IL-6 levels peaked on POD 0 for all groups, and on PODs 1 and 2, IL-6 was significantly lower for group A than group C (p<0.05).
- **Infectious complications.** Defined as intra-abdominal abscess, bacteremia, cholangitis, colitis, pneumonia, superficial or deep wound infections and UTI, the rate of infectious complications in group A was significantly lower (10%) than in groups B (60%) or C (60%) (p<0.05). The duration of SIRS was significantly lower in group A (2.4 days) than in group C (3.6 days; p<0.05).
- **Compliance.** Group A drank more than 90% of the 1000 kcal ordered preoperatively. Overall, the full nutritional goal was reached in 80% of patients.

Conclusion
Investigators suggest that the reduction in infectious complications may be due to the reduction in stress induced immunosuppression, correction of impaired Th1/Th2 balance and stimulation of Th17 response when perioperative immunonutrition is used with patients undergoing PD.

Summary prepared by Nestlé Healthcare Nutrition. To view the study abstract, please use the following link:  http://www.ncbi.nlm.nih.gov/pubmed/20227099

*IMPACT ADVANCED RECOVERY® Drink is the oral form of IMPACT® formula offered in the United States. IMPACT ADVANCED RECOVERY® is a trademark of Société des Produits Nestlé S.A., Vevey, Switzerland.

May 2013