

TITLE: EFFECTS OF GROWTH HORMONE (GH) AND TOTAL PARENTERAL NUTRITION (TPN) IN PATIENTS WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE (COPD) AND MALNUTRITION

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**Introduction.** COPD is often associated with malnutrition which is manifested by diminished nitrogen retention (NR) and reduced lean body mass (LBM). We have studied the effects of refeeding in patients with COPD and ventilator dependence and have demonstrated a positive response with aggressive nutritional therapy.<sup>1</sup> However, aggressive refeeding of these patients may result in increased production of CO<sub>2</sub> related to the metabolism of carbohydrates which can lead to respiratory failure and complicate ventilator management in susceptible individuals.<sup>2</sup> GH is a potent anabolic hormone expected to enhance protein synthesis, NR and fatty acid utilization. This study was designed to determine whether the combination of GH and TPN could be safely administered to COPD patients with malnutrition to accelerate recovery of nutritional and respiratory status.

**Methods.** Six COPD patients (FEV<sub>1</sub> .32 - 1.88 L) with malnutrition (weight loss > 10% ideal body weight) were entered for study after signing informed consent. The patients received two days of D5W (340 kcal) followed by 4 days of TPN (1680 kcal, 85 gm protein), 4 days of TPN + GH 30 ug/kg/d sc, and 4 days of TPN + GH 60ug/kg/d sc. The TPN regimen was designed to approximate an energy intake of 1.3 X REE with a low calorie to nitrogen ratio (99:1). NR was calculated daily (N intake - N output) using measurements obtained on an Antek analyzer. Resting Energy (REE), VO<sub>2</sub>, VCO<sub>2</sub> and RQ were measured daily using indirect calorimetry (Datex Cart, Sensormedics Corp). LBM was measured daily using a bioelectrical impedance unit (BIA 101, RJL, Inc.). Whole blood and serum were collected on days 1, 3, 7, 11 and 15 for CBC, chemistry profile, lipid profile (cholesterol, triglycerides, HDL, LDL, FFA, glycerol) and hormone response (GH, IGF I, cortisol, epinephrine, norepinephrine, insulin, glucagon). Handgrip dynamometry and ventilatory muscle strength were tested on days 2, 6, 10, and 14.

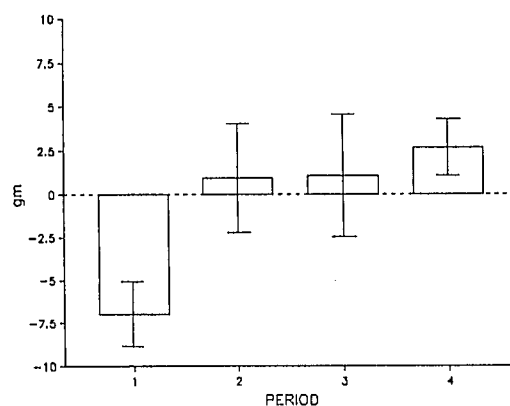
**Results.** GH administration had a profound effect on NR, increasing it more than twofold (0.9 ± 3.1 vs. 2.7 ± 1.6 gm/day, p=.046) over TPN alone. An increase in REE of about 15% was observed during GH corresponding to an increase of VO<sub>2</sub> (3.8 ± 0.26 vs. 4.4 ± 0.4 ml/min/kg) with an moderate increase of VCO<sub>2</sub> (3.2 ± 0.13 vs. 3.5 ± 0.28 ml/min/kg). The increase in REE resulted in negative energy balance in the final study period (198 ± 117 vs. -42 ± 77 kcal). RQ decreased during GH (.854 ± .066 vs. .825 ± .076). D5W and TPN without GH resulted in weight loss (128 ± 17 vs. 124 ± 18 lbs), reduction in LBM, and reduced muscle strength (20.7 ± 7.74 vs. 18.3 ± 6.4 kg/cm<sup>2</sup>). Low dose GH prevented further weight and LBM loss and the higher dose produced weight gain (127 ± 19 lbs), increased LBM, and increased

muscle strength (20.7 ± 7.74 kg/cm<sup>2</sup>). GH administration resulted in increased levels of IGF I (1.04 ± 0.6 vs. 2.71 ± 1.4 U/ml) and insulin (16.3 ± 2.2 vs. 28.1 ± 2.8 uU/ml) with a mild elevation of glucose (108 ± 21.5 vs. 114 ± 14.3 mg/dl).

**Discussion.** Malnourished COPD patients respond to GH during parenteral hypocaloric feeding with an increase in NR, LBM and VO<sub>2</sub> without significantly increasing VCO<sub>2</sub> or RQ. The GH effect on NR is sufficiently potent to overcome negative energy balance. However, no improvement was seen in muscle function suggesting the importance of energy balance in addition to NR. GH administration produces elevations in IGF I and insulin but only mild increases of glucose, glucagon and cortisol. Minimal effects were observed on the CBC and serum chemistry profiles. The combination of GH and TPN may permit a reduction of calorie intake and reduce complications associated with refeeding patients with COPD or ventilator dependence.

#### References.

1. Goldstein SA, Thomashow B, Askanazi J: Functional changes during nutritional repletion in patients with lung disease. Clin Chest Med 7:141-151, 1986
2. Askanazi J, Nordenstrom J, Rosenbaum SH, et al: Nutrition for the patient with respiratory failure: glucose vs. fat. Anesthesiology 54:373-377, 1981



Mean nitrogen balance of 6 COPD patients during study. Period 1 = D5W, period 2 = TPN alone, period 3 = TPN + GH 30 ug/kg/d sc, period 4 = TPN + GH 60 ug/kg/d sc (period 4). TPN + GH resulted in 289% increase in NR over TPN alone (p=.046).