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Short Bowel Syndrome, Gut Failure and Nutrition

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Definition of Short Bowel Syndrome

The normal small intestine length is 300 to 800 cm, dependent on the mode of measurement, either radiological, surgical or necropsy [1-3]. Short bowel syndrome is generally considered to occur when there is less than 200cm remaining. Short bowel may be consequent to congenital abnormalities, necrotizing enterocolitis, extensive agangliosis, and volvulus in children, and following surgery for ischemia, Crohn's disease, tumors and trauma in adults. A "functional short bowel" may result from refractory celiac sprue, chronic intestinal pseudo-obstruction, and radiation enteritis. Short bowel syndrome may be defined as "reduction of functioning gut mass below the minimum amount necessary for adequate water and electrolyte absorption and adequate digestion and absorption of nutrients" [4,5].

Absorption in the small bowel

Most digestion and absorption in the small bowel occurs in the first 150 cm. Vitamin B12 and bile salts are absorbed in the distal ileum. The distal ileum provides a brake, through the effects of peptide YY, GLP-I, neurotensin and the ileocecal valve [6-8]. PYY and GLP-1 are produced by the neuroendocrine (L) cells of the ileum and colon, as well as in nerves of the enteric nervous system and stimulated by incompletely digested fats. PYY and GLP-1 inhibits vagally stimulated gastric acid secretion, and gastric and intestinal motility [7-10]. The ileocecal valve also prevents contamination of the small bowel with colonic bacteria [11]. Removal of the ileocecal valve therefore increases the risk of bacterial overgrowth in the small bowel.

Following small bowel resection, possibly as a consequence of increased gastrin levels, and decreased PYY and GLP-1 in patients without a colon, gastric hypersecretion occurs in the first 6 months [12,13]. This may result in inactivation of pancreatic secretion, and irritation of the ileum resulting in more diarrheas. Proton pump inhibitor therapy is therefore required in the early management of short bowel patients.

The ileum, in particular, has the capability of adapting over a period of 1 to 2 years, with increase in height and diameter of the villi leading to a greater absorptive area. Glucagon-like peptide 2 (GLP-2), is secreted by endocrine cells in the ileum and colon, and stimulates hyperplasia, and increases the absorptive capacity of the residual small bowel [14,15]. Intestinal adaption is also thought to be enhanced by enteroglucagon, growth hormone, epidermal growth factor, cholecystokinin, gastrin, insulin, neurotensine as well as the amino acid glutamine [16,17].

Because of reduced surface area for absorption, as well as reduced bile salts, patients with short gut syndrome will have significant fat malabsorption. Hydroxylation of the fats by colic bacteria, if the colon is intact, will result in the production of hydoxy-fatty acids, which have cathartic activities, and may aggravate the diarrhea [18-20]. Fats also compete with oxalate for absorption to calcium. Increased fats will therefore increase the availability of oxalate for absorption in the colon, and increases the risk of oxalate renal stones. A low fat, high calcium diet may therefore be indicated in patients with short gut with intact colons.

Non-absorbed carbohydrates (monosaccharides and oligosaccharides) may be fermented by lactobacilli, and other bacteria in the colon to produce D-lactate [21,22]. D-lactate cannot be metabolized by L-lactate dehydrogenase, possibly resulting in a severe metabolic acidosis and encephalopathy.

Importance of the colon

The presence of the colon is important in short bowel syndrome. The presence of the colon is associated with increased PYY levels, providing a "colonic brake" [8,23,24]. With increased delivery on non-absorbed carbohydrates, particularly fiber, colonic bacteria produce short chain fatty acids which are absorbed, together with water and electrolytes and contribute significantly to nutrient and fluid balances. The presence of at least 50% of the colon is equivalent to an additional 50cm of small bowel [25]. Up to 1000kcal/day may be salvaged by the colon [26].

Problems of fluid and electrolyte balance generally occur when there is less than 120cm small bowel remaining. Less than 60cm of small bowel (with an intact colon), and less than 100 cm without a colon invariably necessitates long-term parenteral nutrition [27].

Therapeutic interventions

A variety of therapeutic interventions have been tried in patients with short bowel syndrome to reduce the dependence on TPN.

Szkudlarek et al. [28] randomized 8 patients with short bowel syndrome, who had been dependent on parenteral nutrition for an average of 7 years, to a double blind crossover study of placebo and growth hormone (mean 0.12 mg/kg/day) with oral glutamine (mean 28 g/day) and parenteral glutamine (mean 5.2 g/day) for 28 days. Results showed that growth hormone with glutamine did not improve intestinal absorption of energy, (baseline, placebo, treatment, mean 46%, 48%. 46% of oral intake, respectively), carbohydrate (71%, 70%, 71%), fat (20%, 15%, 18%), nitrogen (27%, 18%, 19%) compared to placebo or baseline [28]. The authors concluded that high dose growth hormone and glutamine with a normal diet administered for 4 weeks did not improve intestinal absorption.

Seguy et al. [29] investigated the role of low dose growth hormone in patients with short bowel syndrome who were parenteral nutrition dependent [29]. Twelve adult patients with short bowel syndrome who had received home parenteral nutrition for a mean of 7 ± 1 years

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were randomized in a double-blind, placebo-controlled, crossover study to receive growth hormone 0.05mk/kg/day and placebo for two 3-week periods separated by a 1-week washout period. Patients were all on an unrestricted hyperphagic diet providing 2.1 ± 0.2 times the basal metabolic rate (53±6 kcal/kg/day) with 0.34±0.05 g nitrogen/kg/day. Results revealed that treatment with growth hormone increased intestinal absorption of energy (15%± 5%, P < 0.002), nitrogen (14%6%, P<0.04), and carbohydrates (10%±4%, P<0.04). The effects on fat absorption were not significantly different (12%±8%, NS). This represented 37%±16% of total parenteral energy delivery. D-xylose absorption also increased with growth hormone treatment (1.2±0.2 vs 0.8±0.2 mmol/l). Body mass increased significantly (57.2±2.4 kg vs. 55.2±2.2 kg, P< 0.003), as did lean body mass (46.9±2.7 kg vs 45.2±2.5 kg, P<0.002). Citrulline levels were not significantly different (20 μmol/l vs. 17±2 μmol/l)

Byrne et al investigated the role of a concomitant high carbohydrate diet with growth hormone and glutamine [30]. The investigators randomized 41 adults with short bowel syndrome (36 with colons) dependent on parenteral nutrition, to oral glutamine (30g/day) plus growth hormone (0.1 mg/kg), oral glutamine (30g/day) plus growth hormone placebo, and glutamine placebo plus growth hormone (0.1 mg/kg/day) for a period of 4 weeks. The patients were also commenced on an optimal diet, rich in protein (≈20%), low to moderate in fat (≈30%), and high in complex carbohydrates (≈50%). Results revealed the group receiving growth hormone, glutamine, and diet had the greatest reduction of parenteral nutrition volume (7.7 ± 3.2 L/week), parenteral nutrition calories (5751 ± 2082 kcal/week), and parenteral nutrition infusions (4 ± 1 infusions/week). The group receiving growth hormone, glutamine placebo, and diet showed greater reductions in parenteral nutrition volume (5.9 ± 3.8 L/week), parenteral nutrition calories (4338 ± 1858 kcal/week), and parenteral nutrition infusions (3 ± 2 infusions/week), than corresponding reductions in the glutamine and diet group (3.8 ± 2.4 L/week, 2633 ± 1341 kcal/week, and 2 ± 1 infusions/week). The effect was maintained for 3 months in the growth hormone, glutamine and diet group.

In a review of five studies [28-33], including the three outlined above, of human growth hormone and glutamine for patients with short bowel syndrome, Wales PW et al concluded that human growth hormone with or without glutamine appeared to provide benefit in terms of increased weight, lean body mass, energy absorption, and nitrogen absorption [34]. However, the effects were generally short-lived shortly after cessation of therapy, raising the question of the clinical utility of the treatment. The evidence, to date, is inconclusive to recommend this therapy

The role of teduglutide, a GLP-2 analog, was investigated in 83 patients with short bowel syndrome dependent on parenteral support (fluids, electrolytes or nutrients) at least three times a week for a period of at least 12 months prior to the study [35]. Patients were randomized to receive subcutaneous teduglutide 0.10 mg/kg/day (n=32), 0.05 mg/kg/day (n=35), or placebo (n=16) for 24 weeks. Parenteral fluids were decreased at 4 weekly intervals if intestinal fluid absorption (48 hr urine volumes) increased ≥ 10%. Responders were subjects who demonstrated reductions of ≥ 20% in parenteral volumes from baseline at weeks 20 and 24. A graded response score (GRS), which accounted for both intensity and duration of a response at 24 weeks, was introduced as the primary endpoint. Results revealed that using the GRS criteria, teduglutide at a dose of 0.05mg/kg had a significant effect compared to placebo (16/35 vs. 1/16; P< 0.07), whereas at a dose of 1.0mg/kg it did not (8/32 vs 1/16; P=0.16). Plasma citrulline levels were significantly increased in both the teduglutide 0.1mg/kg/day group (16.6 ± 8.3 μmol/l to 32.2 ± 15.4 mol/l; P < 0.0001), and the teduglutide 0.5mg/kg/day group (18.0 ± 10.3 μmol/l to 29.5 ± 16.2 μmol/l; P < 0.0001), but not in the placebo group (22.2 ± 10.6 μmol/l to 24.2 ± 13.6 μmol/l). The authors conclude that teduglutide was safe, well tolerated, intestinotropic with suggested pro-absorptive effects facilitating reduction in parenteral support in patients with short bowel syndrome.

Management of short bowel syndrome

1. Use of proton pump inhibitors to inhibit the excessive gastric secretion
2. Use of antimotilty agents (loperamide, immodium, tinc of opium and codeine) to slow gut transit and increase dwell-time
3. Complex carbohydrates should comprise 50-60% total calories in patients with intact colons.
4. Fats should be restricted in patients with intact colons.
5. Vitamin B12 supplementation in patients who have had ileal resection
6. Cholestyramine should be tried in patients with ileal resection < 100cm and intact colons.
7. Oral rehydration solutions containing at least 90mEq/l of sodium, and the avoidance of dilute (tap) water
8. Supplementation of fat soluble vitamins (A,D,E, and K if colon absent), as well as zinc, selenium, magnesium and calcium
9. Avoidance of simple sugars (monosaccharides and oligosaccharides) due to risk of D-lactic acidosis
10. Parenteral nutrition in those patients in whom fluid and electrolyte balance, and caloric intake cannot be maintained.

Surgical Options

Surgical options include segmental reversal of the small bowel (Biachi procedure), and serial transverse enteroplasty (STEP procedure). Small bowel transplant is considered in patients who have developed life-threatening complications of short bowel syndrome and TPN therapy.

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