

A COMPARISON OF THE TROPHIC EFFECTS OF TWO GLUCAGON LIKE PEPTIDE 2 ANALOGUES STUDIED IN NEONATAL PIGLETS WITH SHORT BOWEL SYNDROME WITHOUT ILEUM

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Introduction: Given increasing survival of neonates with short bowel syndrome (SBS) a priority should be to improve patient quality of life and reduce costs of care. Both can be achieved by promoting autonomy from parenteral nutrition (PN). Trophic treatments that enhance innate adaptation have the potential to achieve that outcome. A long acting glucagon like peptide-2 (GLP-2) analogue (Teduglutide) has been approved for use in adults with SBS, decreasing total PN fluid volumes. Recently studied in children, this treatment decreased both PN fluid volume and energy requirements. We previously studied a longer acting GLP-2 analogue (Apraglutide) and confirmed trophic benefit. The purpose of this study was to directly compare the trophic effects of Teduglutide to Apraglutide in neonatal piglets with SBS.

Methods: Neonatal piglets 3-5 days old were randomized to the following treatments: daily saline (CON; n=8), daily Teduglutide (TED: 0.05mg/kg/dose; n=8) or twice weekly Apraglutide (APRA 5mg/kg/dose; n=8). All piglet had 75% distal small intestinal resection, including entire ileum and part of cecum, with a jejunocolic anastomosis. All treatments were given by subcutaneous injection. Piglets were maintained for 7 days on 100% of nutrient requirements by PN and given trophic enteral nutrition (20% requirements). On day 7, terminal laparotomy was performed, the small intestine weighed and measured and jejunal tissue collected for a veterinary histopathologist, blinded to treatments, to measure villus height and crypt depth. Data is presented as mean (SD); comparisons use one-way ANOVA with post hoc tukey (* indicates different to control).

Results: On trial, all piglets were healthy and gained equivalent weight (kg) [CON: 1.3 (0.3), TED: 1.3 (0.2), APRA: 1.2 (0.2); p=0.82]. Both treatments increased total small bowel weight (g) [CON: 25.1 (4.1), TED: 27.9 (3.5), APRA*: 33.1 (6.2); p=0.008] and length (cm) [CON: +0.7 (6.8), TED: +14.4 (6.6), APRA*: +20.8 (12.6); p=0.001]. Compared to saline and Teduglutide, the Apraglutide treatment significantly increased villus height (μm) [CON: 0.65 (0.01), TED: 0.58 (0.01), APRA*: 0.90 (0.01); p=0.001]. Neither treatment was associated with differences in crypt depth (μm) [CON: 0.17 (0.03), TED: 0.16 (0.02), APRA: 0.15 (0.01); p=0.008].

Conclusion: In neonatal piglets without ileum, which as we have previously shown have limited potential for innate adaptation or linear intestinal growth, treatment with trophic factors increased small intestinal weight and linear growth. Treatment with Apraglutide was associated with greater histological adaptation. As Apraglutide treatment has a lower dose frequency and, based on this data, appears to exhibit potentially greater trophic benefits than the currently available GLP-2 analogue, further studies in the pediatric population of Apraglutide are warranted.