of NEC and discover potential therapeutic targets. However, the penetrance of disease in these models is variable. It has been shown that a maltodextrin-based formula induces NEC-like injury in preterm piglets. Our goal was to determine if maltodextrin induces intestinal injury in newborn mice as a first step to develop a reliable and reproducible NEC animal model.

Methods: C57BL/6 mice 5–7 d old were fed by gavage with a commercially available infant formula containing predominantly maltodextrin (70% maltodextrin/30% lactose; $n = 32$) or a commercially available formula with lactose as the main carbohydrate source (infant formula or puppy milk replacer; $n = 27$), 5 times daily. Additionally, the mice were exposed to hypoxia (5% O_2, 95% N_2) for 10 min, twice daily for 4 consecutive days. Animals were euthanized when clinical symptoms of NEC (abdominal distension, lethargy) were observed or were killed at the conclusion of the enteral nutrition at day 5. The small and large intestines were removed, fixed with 4% paraformaldehyde or 10% formalin, and paraffin-embedded sections were stained with hematoxylin and eosin.

Results: Mice in the maltodextrin-containing diet group had a higher degree of mortality than did mice in the lactose-containing diet group (56% compared with 26%, $P = 0.019$). Of the mice who survived the 4-d protocol, those fed a maltodextrin-containing diet also had a higher incidence of intestinal injury than did those fed the lactose-containing diet (85.7% compared with 0%, $P = 0.0001$). The higher incidence of intestinal injury and mortality in the maltodextrin group coincided with a decline in body weight at the time the animals were killed (–0.12 g compared with +0.38 g). Intraluminal distension in the small intestine and cecum was evident on gross examination. The histology revealed blunted villi in the distal small intestine, suggesting an NEC-like injury.

Conclusions: In newborn mice, maltodextrin-containing formula leads to weight loss, high incidence of intestinal injury, and increased mortality compared with lactose-containing formula.

Funding Sources

Charles H and Judy Hood Family Infant Health Research Program NIH R01 DK104346.

Novel Long-Acting Glucagon-Like Peptide-2 Analog Enhances Intestinal Adaptation and Growth in Neonatal Piglet Model of Short Bowel Syndrome with Ileal Resection (OR10-05)

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Objectives: Glucagon-like peptide-2 (GLP-2) is a trophic factor released from enteroendocrine cells in the ileum. Loss of ileum is common in neonatal short bowel syndrome (SBS), requiring long-term parenteral nutrition (PN). In neonatal piglets, we have shown that ileal resection is associated with limited intestinal adaptation and reduced endogenous GLP-2 secretion. Furthermore, continuous intravenous treatment with native recombinant GLP-2 improved histologic adaptation and reduced days on PN. No notable growth in intestinal length was observed. In this study we examine the effects on intestinal adaptation and growth of a novel long-acting subcutaneous GLP-2 analog, FE203799 (FE), in neonatal SBS piglets with ileal resection.

Methods: Neonatal piglets aged 2–5 d were randomly allocated to saline control ($n = 9$) or FE treatment ($n = 8$). All piglets underwent 75% intestinal resection with resection of ileum and jejunocolic anastomosis. PN and partial enteral nutrition started on postoperative days 0 and 2, respectively. Saline and FE treatment were administered subcutaneously on days 0 and 4 (5 mg $\cdot$ kg^{-1} $\cdot$ dose^{-1}). On day 7, terminal laparotomy was performed, small intestinal length and weight measured, and tissue collected for jejunal histology (villous height, crypt depth).

Results: On day 7, saline- and FE-treated piglets were healthy and had gained equivalent weight (3.70 $\pm$ 0.32 and 3.47 $\pm$ 0.22 kg, respectively; $P = 0.10$). Compared with saline-treated piglets, FE-treated piglets exhibited growth in intestinal length (percentage of change) (+12.8% $\pm$ 8.1% compared with –6.1% $\pm$ 7.6%; $P < 0.001$), greater small intestinal wet weight (g) (29.4 $\pm$ 4.5 compared with 22.7 $\pm$ 1.8 g; $P = 0.001$), and larger villus height (0.1 mm) (8.63 $\pm$ 1.73 compared with 6.56 $\pm$ 1.32; $P = 0.015$). Crypt depth was not significantly different between groups (0.1 mm) (1.74 $\pm$ 0.65 compared with 1.42 $\pm$ 0.11; $P = 0.16$).

Conclusions: The subcutaneous GLP-2 analog FE203799 enhanced intestinal adaptation in a neonatal model of SBS with ileal resection. Compared with our prior experience with continuous intravenous GLP-2 in the same piglet model, the increase in intestinal length noted with FE treatment has important clinical implications for treating neonatal SBS. Furthermore, this GLP-2 treatment can be given once or twice weekly, which is advantageous over administration as daily injection or continuous therapy.

Funding Sources

Funded by GlyPharma Therapeutic.

Supplementation with the Leucine Metabolite β-Hydroxy-β-Methylbutyrate Activates mTORC1 in Skeletal Muscle of the Neonate via a Rag-Independent Process (OR10-06)

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Objective: Our studies in a piglet model of the human neonate have demonstrated that supplementation with leucine, or its metabolite β-hydroxy-β-methylbutyrate (HMB), enhances protein synthesis in skeletal muscle by stimulating mammalian target of rapamycin 1 (mTORC1)–dependent translation initiation. Recent studies have identified signaling components that may be involved in leucine-induced mTORC1 activation; however, the mechanism by which HMB activates mTORC1 is unclear. The aim of this study was to investigate potential mechanisms involved in HMB-induced mTORC1 activation through amino acid–sensing components in the skeletal muscle of neonates.

Methods: Piglets (5–7 d old, $n = 7$–9/group) were studied after an overnight fast (F) or were fed for 24 h with one of the following diets: *1*) low-protein diet [8.3 g protein $\cdot$ kg body weight (BW) $^{-1}$ $\cdot$ d^{-1}] without HMB (LP); *2*) LP + 4 μM HMB $\cdot$ kg BW^{-1} $\cdot$ d^{-1} (HMB4); *3*) LP + 40 μM HMB $\cdot$ kg BW^{-1} $\cdot$ d^{-1} (HMB40); *4*) LP + 80 μM HMB$\cdot$ kg BW^{-1} $\cdot$ d^{-1} (HMB80); or *5*) high-protein diet (18.0 g protein$\cdot$ kg BW^{-1} $\cdot$ d^{-1}) without HMB (HP). Upstream signaling components relevant to mTORC1 activation in longissimus dorsi muscle were measured.