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Mucous fistula refeeding decreases parenteral nutrition exposure in postsurgical premature neonates☆,☆☆

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ABSTRACT

Background/Purpose: Premature neonates can develop intraabdominal conditions requiring emergent bowel resection and enterostomy. Parenteral nutrition (PN) is often required, but results in cholestasis. Mucous fistula refeeding allows for functional restoration of continuity. We sought to determine the effect of refeeding on nutrition intake, PN dependence, and PN associated hepatotoxicity while evaluating the safety of this practice.
Methods: A retrospective review of neonates who underwent bowel resection and small bowel enterostomy with or without mucous fistula over 2 years was undertaken. Patients who underwent mucous fistula refeeding (RF) were compared to those who did not (OST). Primary outcomes included days from surgery to discontinuation of PN and goal enteral feeds, and total days on PN. Secondary outcomes were related to PN hepatotoxicity.
Results: Thirteen RF and eleven OST were identified. There were no significant differences among markers of critical illness ($p > 0.20$). In the interoperative period, RF patients reached goal enteral feeds earlier than OST patients (median 28 versus 43 days; $p = 0.03$) and were able to have PN discontinued earlier (median 25 versus 41 days; $p = 0.04$). Following anastomosis, the magnitude of effect was more pronounced, with RF patients reaching goal enteral feeds earlier than OST patients (median 7.5 versus 20 days; $p \leq 0.001$) and having PN discontinued sooner (30.5 versus 48 days; $p = 0.001$).
Conclusions: RF neonates reached goal feeds and were able to be weaned from PN sooner than OST patients. A prospective multicenter trial of refeeding is needed to define the benefits and potential side effects of refeeding in a larger patient population in varied care environments.

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Neonates can develop several intraabdominal pathologies that require emergent bowel resection and enterostomy formation. Premature neonates are at even greater risk [1]. These children are at risk for high ostomy fluid losses, electrolyte imbalances, and nutritional deficiencies. Parenteral nutrition (PN) is often needed to supplement patient growth and development. PN administration, however, can result in parenteral nutrition-associated liver disease (PNALD) and can progress to hepatic failure [1–9]. PN administration requires the presence of an indwelling venous catheter, which increases the risk of blood stream infection, sepsis, and thrombosis [4,6,7,10], and increases health costs by $13,000–25,000 per patient-year [11–14].

Neonates who undergo bowel resection and enterostomy formation have 3 distinct phases of care. Phase I entails the initial acute illness with associated bowel perforation or compromise necessitating resection, enterostomy, and possible mucous fistula creation. Phase II includes the interoperative period in which the patient recovers. Enteral nutrition is started at this time, and mucous fistula refeeding may begin, if appropriate. The length of this phase is dependent upon enteral tolerance, whether the patient continues to gain weight appropriately, and if there are signs of persistent PN hepatotoxicity. If there are no concerns, restoration of bowel continuity is delayed until 6 weeks from the initial operation and the patient reaches approximately 2.5 kg of weight. If there are signs of growth failure or PN associated hepatotoxicity, expedited restoration of bowel continuity is preferred as soon as the patient is stable, regardless of weight, in order to mitigate further developmental delay or liver damage if other strategies to prevent these complications have failed. Phase III begins once the patient has undergone restoration of bowel continuity, and includes recovery

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from surgery, initiation of enteral nutrition, weaning of PN, and, ideally, discharge from the hospital on enteral feeds exclusively.

Mucous fistula refeeding involves instillation of proximal ostomy contents, or succus entericus, into a mucous fistula. Succus entericus provides fluid, nutrients, and enterotrophic signals to the distal intestine, all of which are thought to contribute to intestinal maturation and development either directly or systemically through hormonal effects [15–19]. Prior studies have suggested that this technique results in improvement in stoma output [20], fluid absorption [21,22] and weight gain [5,23–29]. However, many question the safety of this technique, citing incidences of hemorrhage [29], metabolic acidosis [27], stomal stenosis [27], intraabdominal fluid collections attributable to mucous fistula cannulation and refeeding [27,29], and death [29]. None of these studies, however, involved a control group to quantify the contribution of refeeding to growth and development, and only a select few employed a consistent protocol for refeeding. This retrospective case–control study sought to elucidate the effect of mucous fistula refeeding in neonates. We hypothesized that neonates who underwent refeeding would have less PN requirements, would be weaned off PN earlier, and suffer less PN associated hepatotoxicity than controls.

1. Materials and methods

1.1. Data source and study population

This is a single center IRB-approved study under protocol IRB00064267 ("Retrospective study to determine the appropriate population and effective strategy for an enteral nutritional method (mucous fistula re-feeding) for infants with previous intestinal resection"). We conducted a retrospective review of neonates who underwent small or large bowel resection and small bowel enterostomy formation with or without mucous fistula creation between July 2012 and July 2014. Neonates with colostomies were excluded as they would be expected to have a different postoperative course and would be at less risk of malabsorptive complications than patients with small bowel enterostomies. Patients who had a mucous fistula and underwent refeeding were placed in the "refeeding" group (RF), and those without a mucous fistula or those with a mucous fistula who did not undergo refeeding were placed in the "ostomy" group (OST). During the period of this retrospective review, the decision to initiate refeeding was based on surgeon preference. The electronic medical record was queried to identify these patients from the Johns Hopkins Neonatal Intensive Care Unit (NICU). Demographic data, operative data, postoperative diagnoses, radiographic information, laboratory values, timing of initiation and termination of parenteral nutrition (PN), timing of enteral nutrition, and complications associated with refeeding were collected. Patients were excluded if there were incomplete data available regarding initiation or termination of enteral or parenteral nutrition as these represent the primary study parameters.

The severity of patient illness was determined by several clinical indicators, including the radiographic presence of intestinal pneumatosis or intraperitoneal free air, vasopressor or corticosteroid administration, blood culture results, and blood product administration. Primary outcomes included total days of parenteral nutrition, days from initial resection/enterostomy to discontinuation of PN, days from initial resection/enterostomy to goal enteral feeds, whether or not the patient was able to be discontinued from PN in the interoperative period, and failure to thrive (FTT) in the interoperative period. FTT was chosen as a surrogate for weight gain as weight gain goals differ among patients based upon age and size. FTT was defined as falling below the 5th percentile or crossing two major percentiles on growth chart for weight according to age. Secondary outcomes included complications related to refeeding and laboratory markers associated with PN toxicity, including maximum AST, ALT, direct bilirubin, and alkaline phosphatase.

1.2. Mucous fistula refeeding technique

We utilize a 6.0 Fr Foley catheter for refeeding. This catheter is initially placed by the attending surgeon after proximal bowel function is confirmed as evidenced by enterostomy production of succus entericus for 24 h. The catheter is manually introduced into the mucous fistula and the balloon is inflated with 0.5 ml of saline. The mucous fistula is observed for signs of vascular compromise for 30 min. Succus entericus is collected from the proximal enterostomy and instilled into the mucous fistula via an electronic feeding pump (Medfusion 3500 syringe pump) at a rate of 1:1 for an additional 24 h before trophic enteral feeding is considered. As the fistula hypertrophies, additional volume is added to the balloon and the mucous fistula is observed as before. If the catheter is dislodged after refeeding has been well tolerated, the pediatric surgery fellow is contacted for immediate replacement.

1.3. Nutrition

All patients receiving nutritional support in the Johns Hopkins NICU are followed by a pediatric registered dietitian. PN is initiated on postoperative day 0 or when a patient is stable postoperatively, and is adjusted daily. Soy based lipids are utilized at our institution. If a patient demonstrates evidence of cholestasis, lipid restriction strategies are implemented. In patients undergoing refeeding, enteral nutrition (EN) is not started until 24 h of refeeding of succus entericus has been tolerated without clinical effects. Enteral feeding is then initiated and standardized guidelines are followed for feeding advancement. Several patients early in the study had enteral feeds initiated prior to refeeding. Mucous fistula feeds were subsequently initiated at trophic rate and advanced to 1:1 over several weeks. Breast milk; donor human milk; and age appropriate formula are used in this order of preference. PN is discontinued when a patient is tolerating approximately 100–120 ml/kg/day of enteral feeds while meeting age appropriate weight gain and growth goals without requiring supplemental parenteral nutrition. Parenteral and enteral feeding regimens were modified as needed for both the RF and OST groups. PN was re-initiated if a patient demonstrated evidence of feeding intolerance or FTT despite modifications to the EN regimen.

1.4. Statistical analysis

Differences between groups were examined through two-sample t-test for normally distributed variables, Wilcoxon rank-sum test for skewed variables, and Fisher's exact tests for categorical variables. Days-to-event outcomes were considered censored for a particular patient if there was no occurrence of the event (e.g., PN discontinuation). In these cases, the outcome was treated as censored at the time of the subsequent event. These days-to-event outcomes were evaluated using survival analysis, and log-rank tests were used to evaluate group differences [30]. Normally distributed variables are reported as mean $\pm$ standard deviation, and non-normally distributed variables as median and interquartile range. All analyses were conducted in Stata version 13.0 [31].

2. Results

2.1. Demographics

From July 2012 through July 2014, 28 neonates were identified who underwent enterostomy formation. Thirteen patients had a mucous fistula created and underwent refeeding (RF group). Fourteen patients underwent ostomy formation without mucous fistula creation, and 1 patient had a mucous fistula created but did not undergo refeeding (OST group). Four OST patients were subsequently excluded; 2 patients with diagnoses of colonic atresia and imperforate anus underwent large bowel resection only and had colostomies created, 1 patient was discharged and later lost to follow-up, and 1 patient with necrotizing