Evaluation of Routine Administration of Glycerin Suppositories to Improve Bowel Function in Patients with Uncomplicated Gastroschisis

NCT03355326

Last date of Revision 5/7/2018

Last date of Approval 4/1/2020

Introduction/Background:

Gastroschisis is a congenital defect of the abdominal wall that leads to evisceration of various amounts of the abdominal organs. The mainstay of therapy is restoring continuity of the abdominal wall, either through primary closure or with a synthetic graft when primary closure is not feasible. Closure of the abdominal cavity is confounded by prenatal loss of abdominal domain coupled by resultant swelling of the abdominal viscera due to prenatal exposure to amniotic fluid. Additionally, some patients with gastroschisis have other concomitant abnormalities of the bowel (termed complicated gastroschisis) that require additional surgical intervention. It is well established that bowel function after repair of gastroschisis is impaired due to the aforementioned pathologic processes. Previous studies have shown that the time from surgery to attaining full nutrition through enteral means is a predictor for morbidity in this population. Numerous therapeutic interventions have been proposed to help hasten bowel function and decrease the time to tolerance of total enteral nutrition. A common, but unproven, technique is the use of glycerin suppositories to stimulate bowel function.

Study Procedures:

The purpose of this study will be to determine whether routine use of glycerin suppositories improves bowel function as measured by time to full enteral feeds (primary outcome: defined as enteral feed volume $\geq$120mL/kg/day with appropriate weight gain) in neonates with uncomplicated gastroschisis. Additional secondary outcomes that will be measured include time to first bowel movement, length of hospital stay, infectious complications, days on total parenteral nutrition (TPN), post-operative days on TPN, sequela of long term TPN administration, and post-operative complications.

After obtaining consent, patients will be randomized (utilizing a block technique) into two groups: the treatment group and the control group. Consent and randomization will occur the day of surgery or preceding surgery with the operating surgeon blind to the treatment arm prior to operation. A newly developed study-specific standardized feeding protocol that has been adopted by all pediatric general surgeons at Riley Hospital for Children will be used on all study participants. Signs of feeding intolerance are outlined in the attached feeding protocol. The treatment group will undergo administration of a glycerin suppository beginning the day after abdominal closure and daily until reaching full enteral feeds. Time to first stool (secondary outcome) will also be monitored and recorded. Clinical nursing staff often will report very small bowel movements as “smears”. These will be noted in the study database but will not be considered a first bowel movement. If at any point during treatment the patient develops significant rectal bleeding, suppository administration will be discontinued, and the patient will be removed from the study. The control group will not receive routine glycerin suppositories until full enteral feeds are obtained and will be based upon attending preference thereafter. Weaning of TPN during advancement of enteral feeds will be based upon attending preference. Laboratory values routinely monitored for signs of malnutrition and TPN-induced cholestasis

(secondary outcome) will also be monitored/recorded, these labs are normally drawn in this patient population and no additional labs/blood draws will be required for this study

Inclusion/Exclusion Criteria:

Inclusion criteria:

-Gestational age ≥33 weeks at time of delivery

-Weight >1900g at time of delivery

-Transfer of patient to Riley Hospital for Children prior to any abdominal surgery

Exclusion criteria:

-Neurological Congenital malformations or those known to impair intestinal motility

-Identification of a secondary gastrointestinal abnormality requiring surgical intervention

-Cyanotic heart disease

Power Analysis/Recruitment Period

Assuming the average time to full enteral feeds in the control group will be approximately 21 days with a standard deviation of 3 days and a power (1-β) of 0.8, the study will need to enroll thirty-seven (37) in each study arm to detect a difference of two days between groups (two sided test with an $\alpha = 0.05$). After reaching this enrollment, that data from each group will be analyzed for normality and if found to be normal, student's t-tests will be performed to determine significance for the primary outcome variables. If the resulting data is not normally distributed, Wilcoxon ranked-sum tests will be performed. Data analysis will be completed by Matthew Landman, M.D., M.P.H.

The average number of uncomplicated gastroschisis patients admitted to Riley Hospital for Children is approximately 20 per year. Assuming 80% enrollment (i.e. 44 patients enrolled) with an 85% retention rate to completion (i.e. 37 patients completing the study), the study period will be approximately 5.5 years.

Participant Privacy/Data Safety

All data obtained for use in this study will be abstracted from clinical (medical record) and entered on to a RedCap database built explicitly for this research study. Data entry will occur on the private/encrypted pediatric general surgery research computer, which is available only in the Pediatric General Surgery office within the physical/technical infrastructure of Indiana University Health. Additionally these computers are independently password-protected and all access to the office is

limited to staff only and is continuously supervised. All office doors are locked during non-business hours. Patient names will never be used in the research database in order to help reduce the risk of loss of confidentiality. All physical charts will be reviewed (if needed) in this office and only in this office and delivered immediately back to their respective sites upon completion of review. Paper records will be locked within the pediatric general surgery research office at all times.