Esophageal pH Monitoring Abnormalities and Gastroesophageal Reflux Disease in Infants With Intestinal Malrotation

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Hypothesis: Infants with rotational abnormalities of the midgut mesentery are at high risk for gastroesophageal reflux disease (GERD) and for sudden infant death (SID) from GERD.

Design: A survey of the prevalence of GERD and the risk factor for SID from GERD in a case series of infants treated for congenital anomalies that include intestinal malrotation. Eighty-one (89%) of the infants studied for GERD had a mean follow-up of 23.2 months (median, 12 months).

Setting: Patients treated in 2 tertiary care centers consisting of a children’s hospital and a university medical center.

Patients: Two hundred eighty-six consecutive infants were treated for congenital anomalies from September 1, 1985, through May 31, 1998. The patients selected for study were 91 infants who had 18- to 24-hour esophageal pH monitoring performed and no prior operation on the stomach or esophagus. The studied infants had intestinal malrotation either alone (n = 55) or associated with a repaired abdominal wall defect (n = 23) or congenital diaphragmatic hernia (n = 13). Of the 91 infants, 34 were asymptomatic at the time of esophageal pH monitoring.

Interventions: Eighteen- to 24-hour esophageal pH monitoring was used to determine the presence of GERD (abnormal pH score ≥ 2 hours postcibal) and the risk factor for SID from GERD (type I or III reflux pattern in combination with a prolonged mean duration of sleep reflux).

Main Outcome Measures: The prevalence of GERD and the risk factor for SID from GERD. The follow-up of GERD was reported as a combination of clinical outcome and subsequent extended esophageal pH monitoring.

Results: Of the 91 infants studied, 80 (88%) had GERD and 26 (29%) had the risk factor for SID from GERD. Of 55 infants with intestinal malrotation alone, 52 (95%) had GERD, and 20 (36%) had the risk factor for SID from GERD. Although GERD was found in 19 (83%) of 23 patients with repaired abdominal wall defects, the prevalence of the risk factor for SID from GERD was significantly lower (13% [3 patients]; P = .03) than in patients with intestinal malrotation alone. The prevalence of GERD in infants with repaired congenital diaphragmatic hernia was significantly lower (69% [9/13]; P = .02) than in infants with intestinal malrotation alone but not for the prevalence of the risk factor for SID from GERD (23% [3/13]; P = .19). Both symptomatic and asymptomatic patients had similar prevalences of GERD (91% [52/57] vs 82% [28/34]; P = .17) and for the risk factor for SID from GERD (31% [18/57] vs 24% [8/34]; P = .28). On follow-up, the prognosis for GERD in infants with intestinal malrotation was better in the infants who were asymptomatic than in those who were symptomatic at the initial extended esophageal pH monitoring.

Conclusions: The prevalence of GERD in infants with intestinal malrotation is high, and the prevalence of the risk factor for SID from GERD is a significant concern. The prevalence of GERD is lower in infants with congenital diaphragmatic hernia. Infants with repaired abdominal wall defects have a lower prevalence of the risk factor for SID from GERD. We recommend careful evaluation and follow-up of infants with intestinal malrotation for problems, such as SID, from GERD.


Rotational abnormalities of the midgut mesentery are a ubiquitous congenital anomaly. Intestinal malrotation is found either alone or in combination with other congenital anomalies such as abdominal wall defects or congenital diaphragmatic hernia. The lack of normal mesenteric fixation leads most often to acute or chronic symptoms from intermittent intestinal obstruction as a consequence of midgut volvulus or internal herniation. These symptoms referable to obstruction are usually relieved successfully by the Ladd operative procedure with or without suture fixation of the midgut mesentery. The Ladd operation appears to be less commonly needed in infants with abdominal wall defects or congenital diaphragmatic her-
PATIENTS AND METHODS

PATIENT POPULATION

From September 1, 1985, to May 31, 1998, a total of 286 consecutive infants with rotational abnormalities of the midgut mesentery were treated at Sunrise Children’s Hospital and the University Medical Center of Southern Nevada, Las Vegas. Ninety-one of these infants were selected for this report because they had no prior operation on the stomach or esophagus and underwent extended esophageal pH monitoring. Informed written consent for the extended esophageal pH studies was obtained from the patients’ parents or legal guardian. Of the patients studied, 55 had intestinal malrotation without an abdominal wall defect or congenital diaphragmatic hernia, 23 had a repaired abdominal wall defect (omphalocele [n = 5] and gastroschisis [n = 18]), and 13 were survivors of a repaired congenital Bochdalek diaphragmatic hernia. Fifty-nine infants (65%) had additional conditions, shown in Table 1. The ages at the time of initial extended esophageal pH monitoring ranged from 2 weeks to 9 months (mean, 2.3 months; median, 2 months). There were 59 boys and 32 girls. Fifty-seven patients (63%) had symptoms suggestive of GERD. These included repeated nonbilius emesis (n = 36), growth retardation (n = 15), recurrent respiratory tract symptoms (n = 23), and irritability (n = 2). Eighteen infants had more than 1 symptom. Thirty-four infants had no symptoms to suggest GERD and were studied because of a perceived increased risk for SID from GERD. Of the 42 symptomatic infants studied with intestinal malrotation alone, 19 were found to have unsuspected and untreated intestinal malrotation at the time of an antireflux operation after GERD had been identified by extended esophageal pH monitoring. Although all symptomatic infants had a barium esophagram and upper gastrointestinal tract series before esophageal pH monitoring, intestinal malrotation was not detected in the 19 infants with intestinal malrotation found at the time of an antireflux operation. In the remaining 23 symptomatic infants, the Ladd operation without intestinal suture fixation was performed before extended esophageal pH monitoring.

EXTENDED ESOPHAGEAL pH MONITORING

Intraesophageal pH monitoring was performed in the distal esophagus for 18 to 24 hours and was evaluated according to a method reported previously. The esophageal pH score more than 2 hours after a meal was used to determine the presence or absence of GERD. A score greater than 64 was thought to be abnormal and indicative of GERD. In patients with GERD, the type I, II, or III pattern of reflux was also determined from the esophageal pH recording. These reflux patterns occur following feedings of apple juice (300 mL/m² of body surface area) and appear as continuous reflux episodes (type I), discontinuous episodes of reflux (type II), or a mixture of continuous and discontinuous occurrences of reflux episodes (type III). The mean duration of acid reflux episodes during sleep more than 2 hours after a feeding (ZMD) was determined. A ZMD was either prolonged (>3.8 minutes) or normal (≤3.8 minutes). The risk factor in the esophageal pH recording that has been associated with SID from GERD is the coexistence of a type I or III reflux pattern and a prolonged ZMD.

PATIENT TREATMENT AND FOLLOW-UP

All patients with GERD documented by extended esophageal pH monitoring were offered treatment of their GERD. Patients with symptoms were offered aggressive treatment with medical antireflux therapy (postural therapy, thickened feedings, and a combination of prokinetic and histamine 2-receptor–blockade medications). An antireflux operation was offered if medical therapy for 6 weeks did not control symptoms or if symptoms were life-threatening. In patients with a prolonged ZMD, medical therapy also included home cardiac and apnea monitoring. Infants with no symptoms of GERD were offered postural therapy as long as they remained asymptomatic. Home cardiac and apnea monitoring was recommended in the treatment of asymptomatic infants with a prolonged ZMD. Follow-up information was available in 64 (89%) of the 72 patients in whom intestinal malrotation was diagnosed before extended esophageal pH monitoring, and in 17 (89%) of the 19 patients in whom intestinal malrotation was diagnosed at an antireflux operation (Table 2).

STATISTICAL ANALYSIS

The prevalence of GERD and the risk factor for SID from GERD were determined. Patient groups were compared using the Fisher exact test. Differences between patient groups were considered to be significant if P<.05.

RESULTS

Of the 91 infants studied with extended esophageal pH monitoring, 80 (88%) had GERD and 26 (29%) had the risk factor for SID from GERD. The prevalence of GERD...
and the risk factor for SID from GERD were not higher in patients with additional conditions (88% [52/59] and 29% [17/59], respectively) than in those without additional conditions (88% [28/32] and 28% [9/32], respectively). Infants with symptoms were not more likely than asymptomatic infants to have a significantly higher prevalence of reflux patterns in the 19 patients who had intestinal malrotation diagnosed at the time of antireflux operation and after GERD had been documented by extended esophageal pH monitoring (type I, 63% [12/19]; type II, 16% [3/19]; and type III, 21% [14/19]).

REPAIRED ABDOMINAL WALL DEFECTS

Nineteen (83%) of the 23 infants with a repaired abdominal wall defect were found to have GERD, and only 3 infants (13%) were found to have the risk factor for SID from GERD. The prevalence of the risk factor for SID from GERD was significantly lower (P = .03) in these infants than in infants with isolated intestinal malrotation. Even though the risk factor for SID from GERD was less prevalent, the prevalence of a prolonged ZMD was 39% (9/23). For symptomatic and asymptomatic patients with repaired abdominal wall defects, the prevalences of GERD (75% [6/8] vs 87% [13/15]; P = .90) and the risk factor for SID from GERD (0% [0/8] vs 20% [3/15]; P = .25) were not significantly different. In the patients with a repaired abdominal wall defect and GERD, the prevalence of each reflux pattern was 47% (9/19) for type I, 42% (8/19) for type II, and 11% (2/19) for type III.

REPAIRED CONGENITAL DIAPHRAGMATIC HERNIA

The prevalence of GERD in infants with repaired congenital diaphragmatic hernia was 69% (9/13). This prevalence was significantly lower (P = .02) than that in infants with isolated intestinal malrotation. The prevalence of the risk factor for SID from GERD in these patients was 23% (3/13). Symptomatic and asymptomatic patients with repaired congenital diaphragmatic hernia had similar prevalences for GERD (71% [5/7] vs 67% [4/6]; P = .78) and the risk factor for SID from GERD (29% [2/7] vs 17% [1/6]; P = .56). In patients with repaired diaphragmatic hernia and GERD, the prevalence of the type I reflux pattern was 89% (8/9) and of the type II reflux pattern was 11% (1/9). No patients were seen with the type III pattern of GERD.

FOLLOW-UP IN ALL PATIENTS WITH INTESTINAL MALROTATION

Even though the presence or absence of symptoms did not have a significant bearing on the prevalence of GERD or the risk factor for SID from GERD, such was not the...
The prevalences of GERD and the risk factor for SID from GERD in infants with intestinal malrotation are much higher than expected. Because GERD has been associated with SIDS, an estimate of the prevalence of GERD and the risk factor for SID from GERD in the general infant population can be made with certain assumptions. The risk of sudden death from GERD was 9.1% in untreated infants with the risk factor, and the risk of SIDS before the avoidance of the prone-flat position was 1.3 per 1000 live births. By assuming that all SIDS deaths occur from having the risk factor for SID from GERD,
then the prevalence of the risk factor for SID from GERD in the infant population would be 1.4%. Because the prevalence of the risk factor for SID from GERD in infants with GERD is 37%,11 the prevalence of GERD in the infant population would be 3.9%. With these assumptions regarding the infant population, the prevalence of GERD would be at least 24 times higher and the prevalence of the risk factor for SID from GERD would be at least 25 times higher in infants with intestinal malrotation alone.

The prevalence of GERD associated with intestinal malrotation is lower in infants with repaired congenital diaphragmatic hernia. This lower prevalence of GERD suggests that factors other than intestinal malrotation are responsible for the observed prevalence. One possible factor may be the high mortality associated with repaired congenital diaphragmatic hernia. Patients with GERD and the risk factor for SID from GERD may be less likely to survive congenital diaphragmatic hernia repair and thereby give the impression that survivors have a lower prevalence of GERD. Although the prevalence of the risk factor for SID from GERD was not significantly lower with repaired congenital diaphragmatic hernia, statistical significance might be achieved with a larger series of infants. A higher prevalence for GERD was expected in infants with intestinal malrotation suggests that these infants usually have a defective gastroesophageal junction that may result from the same conditions that lead to the interference of normal intestinal rotation and fixation during fetal development. Such simultaneous defects in the function of the foregut and anatomy of the midgut do not necessarily result in an anatomic defect of the foregut. This concept is further supported by the gastric emptying abnormalities often seen in patients with intestinal malrotation. Mechanical gastric-outlet obstruction does not appear to be a factor because a high prevalence of GERD persists despite the relief of gastric-outlet obstruction with a successful Ladd operation. The GERD in these patients can also be seen with rapid and slow gastric emptying.6 The factors responsible for the development of the risk for SID from GERD are unknown, but problems with swallowing, esophageal emptying, and gastric acid secretion are likely major components. Unfortunately, the measurement of these factors was not part of this study.

The course of treated infants with GERD and intestinal malrotation depends on the presence or absence of symptoms to suggest GERD. The course in symptomatic infants is similar to that in infants with GERD without intestinal malrotation. Their outcome depends on the reflux pattern type (Table 3).13 In contrast, asymptomatic patients with GERD have a better prognosis than symptomatic patients. Although these infants have a bet-

| Table 3. Course of Treated Gastroesophageal Reflux Disease (GERD) by Age 1 Year According to Reflux Pattern, Symptoms, and Intestinal Malrotation* |
|---------------------------------|---------------------------------|---------------------------------|---------------------------------|
| Reflux Pattern                  | Symptomatic Infants             | Infants With Intestinal Malrotation |
|                                 | Without Intestinal Malrotation and With GERD† | GERD Symptoms (n = 35) | Asymptomatic (n = 29) |
| Type I                          | Antireflux operation needed 50 | 52 | 0 |
|                                 | Fate of GERD in nonoperated-on infants‡ | GERD present 40 | 48 | 63 |
|                                 |                                  | GERD absent 10 | 0 | 37 |
| Type II                         | Antireflux operation needed 10 | 0 | 0 |
|                                 | Fate of GERD in nonoperated-on infants‡ | GERD present 20 | 50 | 50 |
|                                 |                                  | GERD absent 70 | 50 | 100 |
| Type III                        | Antireflux operation needed 50 | 50 | 0 |
|                                 | Fate of GERD in nonoperated-on infants‡ | GERD present 40 | Unknown | 50 |
|                                 |                                  | GERD absent 10 | Unknown | 50 |

* Data are given as percentage of patients.
† From Jolley.12
‡ Results of extended esophageal pH monitoring.

lence of the risk factor for SID from GERD. A shortened intra-abdominal esophagus from increased intra-abdominal pressure following repair of the abdominal wall defect probably does not contribute to the development of GERD because a higher prevalence of the type I or III reflux pattern would be expected because of their association with hiatal hernia.6 The type II reflux pattern is not associated with a hiatal hernia or a decreased lower esophageal sphincter pressure.6

The high prevalence of GERD in infants with intestinal malrotation suggests that these infants usually have a defective gastroesophageal junction that may result from the same conditions that lead to the interference of normal intestinal rotation and fixation during fetal development. Such simultaneous defects in the function of the foregut and anatomy of the midgut do not necessarily result in an anatomic defect of the foregut. This concept is further supported by the gastric emptying abnormalities often seen in patients with intestinal malrotation. Mechanical gastric-outlet obstruction does not appear to be a factor because a high prevalence of GERD persists despite the relief of gastric-outlet obstruction with a successful Ladd operation. The GERD in these patients can also be seen with rapid and slow gastric emptying. The factors responsible for the development of the risk for SID from GERD are unknown, but problems with swallowing, esophageal emptying, and gastric acid secretion are likely major components. Unfortunately, the measurement of these factors was not part of this study.

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Gastroesophageal reflux disease and the risk factor for SID from GERD are highly prevalent in infants with intestinal malrotation. This high prevalence of GERD indicates that infants with intestinal malrotation require careful evaluation and follow-up for problems from GERD.

CONCLUSIONS

Gastroesophageal reflux disease and the risk factor for SID from GERD are highly prevalent in infants with intestinal malrotation. This high prevalence of GERD indicates that infants with intestinal malrotation require careful evaluation and follow-up for problems from GERD.

REFERENCES

12. Kieffer J, Sapin E, Berg A, Beaudoin S, Bargy F, Helardot PG. Gastroesophageal reflux and the risk factor for SID from GERD are highly prevalent in infants with intestinal malrotation, we would have expected at least 2 sudden deaths.

DISCUSSION

Thomas R. Weber, MD, St Louis, Mo: Steve Jolley and his colleagues in Las Vegas have been leaders in bringing science to the confusing and frequently controversial topic of reflux in children. Through the extensive use of pH monitoring, they have been able to identify groups of high-risk patients who benefit from early and aggressive antireflux therapy, including surgical therapy, involving a variety of scenarios. The present study extends these observations to the group of children with intestinal rotational disorders and severe reflux, and they have identified a subgroup who they feel is at great risk for SID from aspiration. The data in this study, although convincing, generate several questions. Why do so many infants and children with intestinal rotational anomalies have such severe reflux? Is it due in part to duodenal obstruction from congenital bands? Or is there abnormal duodenal or gastric peristalsis? Do you have any gastric emptying studies to explain the high incidence of reflux in these patients? Second, you elected to treat nonoperatively several infants whom you have identified as being at high risk for SID. Many pediatric surgeons would consider near SID as an absolute indication for immediate fundoplication. Aren’t you somewhat nervous about treating these high-risk patients medically? This is particularly worrisome in the group of asymptomatic patients in whom you have found continued reflux by pH studies. These are precisely the children who seem to be at greatest risk for near or complete SID episodes.

You obviously used pH monitoring as the gold standard for the detection of reflux in children and have great experience in its application and interpretation. Do you use other diagnostic studies in these patients? How do they correlate with your pH studies? Several patients in your series were found to have intestinal rotation abnormalities at the time of fundoplication. More liberal use of upper gastrointestinal (GI) contrast studies, for example, would probably have identified these anomalies preoperatively, thus eliminating this surprise factor intraoperatively.

Jay S. Grosfeld, MD, Indianapolis, Ind: I get concerned about correlating malrotation and gastroesophageal reflux with the SID syndrome (SIDS). If you wanted to say these conditions are associated with aspiration or the threat of aspiration and death, that is one thing, but the SIDS is different. Especially since the publication of the book by Firstman and Talen, The Death of Innocence, which documents that, unfortunately, many of the infants who were considered to have SIDS were subsequently shown to be suffocated by their parents. The relationship of malrotation to SIDS leaves me cold. I would rather you consider this as a threat for aspiration than suggest that it is a cause of SIDS. Many pediatric specialists do not believe gastroesophageal reflux has anything to do with SIDS. Would you please comment on this? Dr Jolley, does the motility problem in the foregut associated with gastroesophageal reflux extend to the duodenum in patients who have intestinal malrotation? Did some of the patients who were previously operated on for malrotation before the diagnosis of gastroesophageal reflux have a midgut volvulus? Did they require bowel resection? Did they have delayed return of gastric emptying after their last procedure?

Dr Jolley: I do not understand why children with malrotation have a high prevalence of reflux. We do use other modalities to study these patients. All the patients who were symptomatic had an upper GI series and an esophagram, including a small bowel follow-through. In answer to Dr Grosfeld’s question, an x-ray was done to be sure they did not have an obstruction postoperatively. None had the resection of bowel, even though they have had a volvulus, because the bowel was viable and did not need to be resected.

Regarding gastric emptying studies in these patients, we have published this previously and have shown that these patients can have slow gastric emptying, normal gastric empty-
ing, or rapid gastric emptying. There is no pattern of the gastric emptying to suggest that they may have persistent chronic obstruction. It is clear that they do not always have completely normal motility of their stomach.

Why do we treat patients who are at risk for SID medically? This applies only to patients who are asymptomatic. The main reason for treating those patients medically is that we do not know that we should treat them surgically because the limited data that we have on those patients was coupled with the fact that their families discontinued the medical antireflux therapy that they were on. At this point in time, we do not have any evidence that asymptomatic patients at risk for SID will die despite medical antireflux therapy.

The upper GI findings on these patients are typical for nonrotation postoperatively. I can tell you that of the 19 children in whom we were surprised to find intestinal malrotation, all had an upper GI series performed before the antireflux operation, and these were read as normal. Intestinal malrotation was not detected on the upper GI series by either the radiologist or surgeon.

With respect to labeling these patients as SIDS victims, I agree with Dr Grosfeld in that the term “SIDS” has a negative connotation, primarily because it is a catch-all category, and there is no question that there are infants who have been ascribed as SIDS victims who have been the victims of trauma or suffocation at home. We also see patients who are victims of Munchausen by proxy. However, the patients who have reflux and who have died at home have been legitimate SIDS victims. They are victims who have not been the subject of these other factors. The only reason that I can stand up here and say that is that I have been doing esophageal pH monitoring in children for 20 years. We have done close to 3000 esophageal pH studies. In those 20 years and in all those studies, there has not been a single child who has had an autopsy by a pediatric pathologist (who is well trained in the SIDS autopsy) and who was called a SIDS victim who has had any findings on their esophageal pH study other than type I or type III reflux and a prolonged ZMD. This now totals 5 SIDS victims and 4 infants with death from GERD (total of 9 infants). This is probably the most compelling evidence that reflux is a cause of SIDS in these patients, and it is certainly a large portion of what has been called SIDS victims, with other portions being those alluded to by Dr Grosfeld.

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Do Symptoms Predict Cardiac Arrhythmias and Mortality in Patients With Syncope?

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Background: Patients with syncope frequently present with multitude of other symptoms but their significance in predicting morbidity or mortality has not been previously studied.

Objective: To determine if certain symptoms can be used to identify syncope patients at risk for cardiac arrhythmias, mortality, or recurrence of syncope.

Patients and Methods: From August 1987 to February 1991, we prospectively evaluated patients with syncope from outpatient, inpatient, and emergency department services of a university medical center. These patients were interviewed, charts were reviewed, and detailed information on 19 symptoms and comorbidities was obtained. A cause of syncope was assigned using standardized diagnostic criteria. All patients were followed up at 3-month intervals for at least 1 year for recurrence of syncope and mortality. Patients in whom the cause of syncope was determined by medical history and physical examination alone were not included in our analysis.

Results: History and physical examination led to the cause of syncope in 222 of 497 patients enrolled. In the remaining 275 patients, the absence of nausea and vomiting before syncope (odds ratio, 7.1) and electrocardiographic abnormalities (odds ratio, 23.5) were predictors of arrhythmic syncope. Underlying cardiac disease was the only predictor of 1-year mortality. No symptom remained as independent predictor for 1-year mortality or syncope recurrence.

Conclusions: Symptoms, although important in assigning many noncardiac causes, are not useful in risk-stratifying patients whose cause of syncope cannot be identified by other history and physical examination. Triage decisions and management plans should be based on preexisting cardiac disease or electrocardiographic abnormalities, which are important predictors of arrhythmic syncope and mortality. (1999;159:375-380)

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