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Esophageal disease in pediatrics

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Abstract

The following on esophageal disease in pediatrics contains commentaries on acquisition of neuromuscular maturation; physiology of esophageal peristaltic and sphincteric reflexes; implications for clinical practice; and conditions that predispose to severe gastroesophageal reflux disease (GERD) in children with potential risk for esophageal cancer.

Keywords

embryology; peristalsis; sphincteric reflexes; fetal swallowing; airway protection; Barrett's esophagus; GERD

1. Development of esophageal peristaltic and defensive functions in infants: a synopsis

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Owing to the advances in obstetric and neonatal intensive care practices globally, more infants are now surviving but with aerodigestive concerns. As a result, prevalence of neonatal feeding and airway problems is increasing. Infants born at less than 28 weeks gestation have significant feeding delays, compared with infants born greater than 28 weeks gestation. Evidently, maturation plays a significant role in acquisition of neuromuscular maturation involved with safe oral feeding skills.

In this session, we discussed briefly: (1) embryology of the esophagus, and (2) the physiology of esophageal peristaltic and sphincteric reflexes and esophageal and airway interactions.

Developmental considerations

Fetal swallowing develops by 12 weeks, and development of safe swallowing skills is a process in continuum, modified during postnatal maturation and adaptation, as well as influenced by comorbidities. Swallowing deficits result in those infants that have structural anomalies of gut and polyhydramnios results as amniotic fluid fails to circulate.

Contrasting adult humans, the neonate has nasopharynx and hypopharynx and a relatively large tongue (no oropharynx), the hyoid larynx and epiglottis are in a higher position, and the pharyngeal phase of swallow triggers from the vallecula. Furthermore, the young infant has a shorter esophagus.

Postnatally, rapid development occurs in the first year of life with respect to structure and functions of the esophagus and feeding functions. The lower esophageal sphincter is predominantly intrathoracic in neonates, and the intraabdominal part of the sphincter grows in infancy. Despite these maturational limitations, the human infant has to eat more volume per kilograms of body weight to sustain the growth phase, and yet maintain a safe aerodigestive tract.

Physiology of esophageal peristaltic and sphincteric reflexes

Development of safe swallowing skills is a process in continuum, modified during postnatal maturation and adaptation. The functions of esophagus can be summarized as those involved with:

- (1) aerodigestive safety, responsible for vigilance, coordination, and antireflux defenses;^{1,4,5} and,
- (2) deglutition, responsible for swallowing phases, coordination, and peristaltic propulsion.¹⁻³

The esophagus and airways share similar innervation by the vagus, and interaction of afferent and efferent neuronal pathways modulate sensory–motor function ensuring safe swallowing and airway protection. These modulating mechanisms are aberrant in infants with dysphagia and airway problems.

In developing infants, we have characterized the sensory–motor basis for neonatal esophageal functions.^{4,5} Abrupt bolus as a stimulus activates the esophageal receptors and afferents, resulting in activation of esophageal and airway efferents. Using this approach, we have defined the following reflexes during neonatal maturation: deglutition reflex, pharyngeal reflexive swallow, primary and secondary peristaltic reflexes, upper esophageal contractile reflex, lower esophageal sphincter relaxation reflex, pharyngoglottal closure reflex, and esophagoglottal closure reflex. Furthermore, volume-dependent increment in the recruitment of pharyngeal or esophageal and sphincteric reflexes has been noted, and that maturation improves the sensory–motor characteristics of such reflexes. Such findings suggest that neuronal recruitment improves with maturation, as well as the magnitude and coordination of contractility.

Implications for clinical practice

It is conceivable that deviation in esophageal motility defenses and peristaltic reflexes can occur in conditions such as extreme immaturity, maldevelopment of the foregut, neurological malfunction, or chronic lung disease. Neonatal maturational delays can result in motility disturbances and may form the basis for infant feeding problems. Important neonatal and infant problems related to the esophagus include dysphagia, gastroesophageal reflux disease and aggravation of airway injury due to malfunctions of the swallowing or airway protection mechanisms. Objective evaluation of esophageal motility may provide support for evidence-based management of feeding and airway protection strategies. [This work was supported in part by grant funding from the National Institutes of Health RO1 068158 (Jadcherla)].

2. Pediatric esophageal conditions with a potential risk for esophageal cancer

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Esophageal adenocarcinoma in children is extremely rare, but has been reported.⁶ Most cases have been mainly described in association with BE, which is considered the precursor lesion of esophageal cancer.⁶ BE occurs as a result of chronic and severe GERD. Therefore, in the pediatric population, the chief clinical concern is to prevent children with GERD from developing BE, and to detect those children with GERD that are at risk of developing BE.⁶

Certain underlying disorders that predispose pediatric patients to the most severe and chronic GERD, and its complications, include:

- otherwise healthy with chronic GERD,
- neurologic impairment,
- EA and other malformations,
- chronic lung disease: cystic fibrosis,
- family history and genetic predisposition,
- genetic syndromes: Cornelia de Lange syndrome,
- obesity, and
- other inflammatory problems.

The prevalence of BE in children seems to increase as the severity and chronicity of GERD increase. There are certain underlying disorders that predispose pediatric patients to the most severe and chronic GERD, and its complications. These are shown in Table 1. The exact incidence of BE in otherwise healthy children with GERD is not known. In a recent study that described 6,731 patients who underwent upper endoscopy in 12 pediatric facilities, they found biopsy proven intestinal metaplasia in nine patients (0.133%). Patients with suspected BE were older than patients without BE (median 14.7 vs. 10.1 years; $p = 0.011$), and in logistic regression analyses, both hiatus hernia and older age were independent significant predictors of suspected BE. In another study of children with chronic GERD, esophageal metaplasia was present in some 10% of children with severe chronic GERD, half of whom had goblet cell metaplasia.⁶ Looking at the population of children with GERD that is severe enough to require surgery, BE was found in 11 (7.3%) out of 150 children.

Neurologic impairment is one of the common associated causes that predisposes to severe GERD in children. Studies have mentioned that 10–25% of institutionalized intellectually disabled individuals have symptoms of vomiting, regurgitation, or rumination, and in a recent study of institutionalized individuals, it was found that GERD was more frequent and severe if patients had scoliosis, cerebral palsy, use of anticonvulsant drugs or other benzodiazepines, or who had an IQ < 3. Of those patients that had an endoscopy, BE was found in 18 (14.0%) and peptic strictures in five (3.9%).⁶

Another predisposing condition to severe GERD includes those patients with congenital malformations, in particular esophageal atresia (EA), in which most of the cases of esophageal adenocarcinoma have been described. A recent study that followed children for a mean of 36 years shows a prevalence of BE of 11%.⁷ Therefore, children with EA need to have very close follow-up. Children with other malformations like diaphragmatic hernias are

also at higher risk of developing severe GERD. Children with chronic lung disease, in particular patients with cystic fibrosis, have also been shown to have a higher prevalence of severe GERD and Barrett's BE. It has been suggested that the standardized incidence ratio of esophageal adenocarcinoma in those patients is significantly higher.⁸

The exact role that genetic predisposition plays is not clear. Significant clusterings of reflux symptoms, HH, erosive esophagitis, BE, and esophageal adenocarcinoma occur in families, suggesting some heritability of GERD and its complications. There are, however, well defined genetic syndromes that have been associated with severe GERD and its complications. An example includes Cornelia de Lange syndrome in which BE seems to occur in 10% of those studied, and adenocarcinoma have been described.⁹

The recent obesity epidemic has been associated with an increased incidence of GERD both in adults and children. The impact that it will have in the incidence of BE in the pediatric population is not clear, but it has already been shown in pediatric cross-sectional studies that moderately and extremely obese children are more likely to have a diagnosis of GERD compared with normal weight children (OR 1.16, 95% CI: 1.02–1.32 and 1.32, 95% CI: 1.13–1.56, respectively).¹⁰

The role that other inflammatory conditions play in the development of BE is not clear. Eosinophilic esophagitis (EoE) is an allergy-mediated esophageal inflammation that produces severe esophagitis. BE has not been associated with EoE, but recently the first case reports of BE associated with EoE were published. Given that the incidence of EoE is increasing, long-term follow-up of these patients will be needed to establish if BE will occur more frequently in those patients. Supported by grant NIH K24 DK082792A.

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Concise summaries

- Evidently, maturation plays a significant role in acquisition of neuromuscular maturation involved with safe oral feeding skills.
- Swallowing deficits result in those infants who have structural anomalies of gut, and polyhydramnios results as amniotic fluid fails to circulate. The lower esophageal sphincter is predominantly intrathoracic in neonates, and the intraabdominal part of the sphincter grows in infancy. Despite these maturational limitations, the human infant has to eat more volume per kilograms of body weight to sustain the growth phase.
- Development of safe swallowing skills is a process in continuum, modified during postnatal maturation and adaptation.
- The esophagus and airways share similar innervation by the vagus, and the interaction of afferent and efferent neuronal pathways modulate sensory-motor function to ensure safe swallowing and airway protection.
- Neuronal recruitment improves with maturation, as well as the magnitude and coordination of contractility. Neonatal maturational delays can result in motility disturbances and may form the basis for infant feeding problems.
- Most cases of esophageal adenocarcinoma in children have been described primarily in association with Barrett's esophagus (BE) and, in the pediatric population, the chief clinical concern is to detect those children with GERD that are at risk of developing BE. The exact role that genetic predisposition plays is not clear, but there are, however, well defined genetic syndromes, like Cornelia de Lange syndrome, that have been associated with severe GERD and its complications.
- There are certain underlying disorders that predispose pediatric patients to the most severe and chronic GERD, and its complications. Neurologic impairment is one of the common associated causes that predisposes to severe GERD.
- Another predisposing condition to severe GERD includes patients with congenital malformations, in particular esophageal atresia, in which most of the cases of esophageal adenocarcinoma have been described, thus rendering very close follow-up particularly important. Other inflammatory conditions, like eosinophilic esophagitis, also play a role in the development of BE.