Journal of Pediatric Surgery (2009) **44**, 251–256

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Journal of Pediatric Surgery

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Development of a standardized definition for Hirschsprung's-associated enterocolitis: a Delphi analysis

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Received 5 October 2008; accepted 7 October 2008

Key words:
Hirschsprung's disease;
Aganglionosis;
Enterocolitis;
Pull-through surgery

Abstract

Purpose: The reported incidence of Hirschsprung's-associated enterocolitis (HAEC) is extremely variable. A standardized definition would permit comparison of different studies and provide an interpretable outcome measure for future prospective studies in patients with Hirschsprung's disease.

Methods: The Delphi method is a technique for achieving consensus among a panel of experts. A list of 38 potential criteria from the history, physical examination, radiologic studies, and pathologic specimens was made available to pediatric surgeons and gastroenterologists who have contributed to the literature on Hirschsprung's disease. Each expert ranked the diagnostic importance of each item using a Likert scale. In subsequent surveys, the same process was used, but the means and SDs from previous rounds were included as a way of influencing the experts toward consensus. Cronbach's α was used after each round to measure variability among the experts. Once consensus was reached, an overall "HAEC score" was developed by assigning a value of 1 or 2 to each item that was considered important by the expert panel. The score was then validated by circulating 10 clinical cases to the panel and asking if each represented HAEC or not.

Results: Twenty-seven experts completed the survey. Cronbach's α increased from 0.93 after the first round to 0.97 after the second. Criteria receiving the highest scores were diarrhea, explosive stools, abdominal distension, and radiologic evidence of bowel obstruction or mucosal edema. Eighteen items were included in the score. During the validation process, the score agreed with the experts in 9 of the 10 case scenarios.

Conclusion: The most important clinical diagnostic criteria for HAEC were identified from a larger pool of potential diagnostic items through a consensus approach using the Delphi method. A score was developed and validated and can now be used as a standardized and reproducible outcome measure for future studies in children with Hirschsprung's disease.

Presented at the 39th annual meeting of the American Pediatric Surgical Association, Phoenix, AZ, May 27-June 1, 2008.

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0022-3468/$ – see front matter © 2009 Elsevier Inc. All rights reserved.
doi:10.1016/j.jpedsurg.2008.10.052

Despite advances in the diagnosis and management of Hirschsprung's disease, Hirschsprung's-associated enterocolitis (HAEC) remains a significant cause of morbidity and mortality and the most common cause of death in infants and children with Hirschsprung's disease [1-3]. Hirschsprung's-associated enterocolitis can occur at any time, including before diagnosis of Hirschsprung's disease and after definitive pull-through procedure.

Numerous theories have been proposed regarding the pathophysiology of HAEC. Bill and Chapman [4] first suggested that HAEC develops from partial mechanical obstruction leading to mucosal ischemia and bacterial invasion of the dilated ganglionic segment. It was hypothesized that a hypersensitivity to bacterial antigens that occurs in Hirschsprung's disease influences the development of HAEC. Other authors have suggested that children with Hirschsprung's disease are more likely to develop infections with *Clostridium difficile* [5,6]. However, the organism is not universally present in children with Hirschsprung's disease [7]. Several authors have suggested that HAEC results from a loss of normal mucosal immune defense [8,9]. These studies examined the role of intestinal immunocytes in developing HAEC and proposed that there is a defect in the release of immunoglobulins in the aganglionic colon. Other studies have revealed that children with Hirschsprung's disease demonstrate a deficiency in transfer of secretory IgA across the gastrointestinal mucosal cells [10,11]. Mucin production has also been found to be significantly reduced in patients with Hirschsprung's disease, resulting in a decrease in epithelial barrier function, which could potentially promote the development of HAEC [12].

Many risk factors for the development of HAEC have been identified. Delay in the diagnosis of Hirschsprung's disease can lead to increased risk for developing enterocolitis [3,5]. Hirschsprung's-associated enterocolitis seems to be more common in children with longer segment disease [3,13-15]. There is also evidence that children who develop HAEC are more likely to have recurrent episodes [5,16,17] and that intestinal neuronal dysplasia is a risk factor for the development of HAEC [16,18]. Postoperative complications and presence of anastomotic stricture and development of intestinal obstruction may also be associated with enterocolitis [19,20]. Other factors reported to be associated with HAEC include female sex, trisomy 21, and presence of other associated congenital anomalies [3,5].

The incidence of preoperative HAEC is 15% to 50% and postoperative enterocolitis occurs in 2% to 33% of patients [3,5,21-23]. Thus, the reported incidence of HAEC varies markedly between surgical groups. It appears that differing definitions of HAEC have led to this significant variation in the incidence of HAEC in published series [3,22,24]. The clinical presentation of HAEC ranges widely from mild abdominal distension to impending shock. Children can present with fever, diarrhea, and abdominal distension [25]. Some children may have explosive diarrhea, vomiting, rectal bleeding, and lethargy, whereas others may present with loose stools and perianal excoriation. Such nonspecific symptoms can easily be overlooked and misdiagnosed as gastroenteritis, leading to either a missed diagnosis or delay in diagnosis. Several authors suggested HAEC is limited to the ganglionic segment [26], whereas other authors demonstrated that the histologic features of HAEC affect both ganglionic and aganglionic segments [16]. Lack of a clear definition for HAEC has made it extremely difficult to evaluate the literature and compare surgical interventions and management strategies in which HAEC is a significant outcome measure.

The purpose of this study was to develop a standardized definition of HAEC, which can be used as an outcome measure by surgeons reporting the results of the surgical treatment of Hirschsprung's disease and by investigators studying strategies for the prevention and treatment of HAEC.

1. Methods

The Delphi method was used to achieve consensus among a panel of experts regarding standardized criteria for the diagnosis of HAEC. A list of 38 potential criteria involving history, physical examination, radiologic studies, and pathologic findings was established by the authors based on published reports. Forty-four international pediatric surgeons and gastroenterologists who have contributed to the literature on Hirschsprung's disease were invited to participate. Each participant was given secure access to a Web-based survey containing the list of 38 criteria for diagnosis of HAEC (Table 1). Each expert rated the diagnostic importance of each item using a Likert scale from 1 (completely unimportant) to 5 (extremely important). Experts were also asked to provide suggestions for other criteria that may be used for diagnosis of HAEC. In subsequent rounds, the same process was repeated while revealing the mean and SDs from the previous rounds to encourage the experts to reassess their initial judgments and establish consensus on the most important criteria.

The iterations were repeated until consensus among the expert panel was achieved by statistical analysis. Cronbach's α correlation coefficient was calculated using SPSS (SPSS, Chicago, Ill) after each round to measure consensus within panelist group. This test estimates the internal reliability for a group of multiple covariates that have been ranked in a scale fashion [27]. A Cronbach's α of .8 was considered to have good internal reliability. In subsequent rounds, the increased value of the Cronbach's α indicated consensus. Once there was consensus on the most important items, an overall "HAEC score" was developed by assigning a value of 1 or 2 to each item.

A series of 10 clinical cases was developed by the authors, attempting to represent the full range of likelihood for the diagnosis of HAEC. To validate the HAEC score, the clinical