Nuclear transit studies of patients with intractable chronic constipation reveal a subgroup with rapid proximal colonic transit

Yee Ian Yika,c,d, Timothy M. Cainb, Coral F. Tudballb, David J. Cookb, Bridget R. Southwella, John M. Hutsona,b,c,⁎

a F Douglas Stephens Surgical Research and Gut Motility Laboratories, Murdoch Children's Research Institute, Melbourne, Australia
b Royal Children’s Hospital, Melbourne, Australia
c Department of Paediatrics, University of Melbourne, Australia
d University of Malaya, Kuala Lumpur, Malaysia

Received 5 August 2010; revised 12 February 2011; accepted 16 February 2011

Key words:
Nuclear transit study; Rapid proximal colonic transit; Food intolerance; Allergy; Children

Abstract

Aims/Background: Nuclear transit studies (NTS) allow us to follow transit through the stomach and the small and large intestines. We identified children with chronic constipation with rapid proximal colonic transit and characterized their clinical features.

Methods: We reviewed NTS from 1998 to 2009 to identify patients with chronic constipation and rapid proximal colonic transit, defined as greater than 25% of tracer beyond hepatic flexure at 6 hour and/or greater than 25% of tracer beyond end of descending colon at 24 hour. This was correlated with clinical symptoms and outcome from patient records.

Results: Five hundred twenty children with chronic constipation underwent investigation by NTS, and 64 (12%) were identified with rapid proximal colonic transit. The clinical history, symptoms, and outcome in 55 of 64 available for analysis frequently showed family history of allergy (10.9%) and symptoms associated with food allergy/intolerance: abdominal pain (80%), anal fissure (27.3%), and other allergic symptoms (43.6%). Eighteen children were treated with dietary exclusion, with resolution of symptoms in 9 (50%).

Conclusions: Some children with intractable chronic constipation have rapid proximal colonic transit, have symptoms consistent with possible food allergy/intolerance, and may respond to dietary exclusion. The NTS can identify these patients with rapid proximal transit that may be secondary to food intolerance.

© 2011 Elsevier Inc. All rights reserved.

Chronic constipation is a common problem in children [1], and in recent years, more causes have been revealed as more sophisticated tests such as rectal biopsy, gastrointestinal transit study, and anorectal manometry have allowed us to better understand its underlying pathophysiology.
However, in most cases the underlying mechanisms of chronic constipation still remain unknown.

Radiologic investigations have been used increasingly to classify the subtypes of chronic constipation. Transit studies using plastic markers and x-rays are able to identify patients with slow colonic transit readily [2,3]. Nuclear transit study (NTS) has the added advantage of identifying patients with slow colonic transit and/or fecal retention and describing their gastric emptying and small bowel motility [4-6]. The NTS is a physiologic study of the gastrointestinal motility with low-radiation dose (calculated radiation exposure comparable with 2 abdominal radiographs), helping in the investigation and targeting the causes of chronic constipation in children and in planning its management appropriately [7,8].

This retrospective study was prompted by the recognition of rapid transit in the proximal colon in a patient with intractable chronic constipation (not responding to multiple different laxative therapies, behavioral therapy, and toilet-training program and with symptoms for more than 2 years) that was shown to be associated with food allergy. We wondered if this was an isolated case or an indication of a more fundamental association between motility and response to luminal contents. We, therefore, performed a retrospective review of our NTS database of more than 600 studies and found a surprising number of patients with rapid proximal colonic transit, which has not been studied and reported previously in children. Only one prior report by Romanczuk and Samojedny [9] found prolonged colonic transit in children with food-allergy-related constipation. In this study, we were able to identify a new subgroup of children with chronic constipation, which, on NTS, was found to have rapid transit through the proximal colon associated with anorectal retention.

1. Methods

Nuclear transit studies have been in common use at our institute, a tertiary referral center, to investigate children with intractable chronic constipation (defined as chronic constipation not responding to maximal laxative therapy, behavioral therapy, and toilet-training program with duration of symptoms of >2 years) since 1997. After cessation of laxative treatment for 5 days beforehand, children drank milk containing either technetium Tc 99m colloid (pre-2000) or Gallium citrate (post-2000) at a dose calculated to be equivalent to 2 standard abdominal radiographs as previously described [8,10]. Six regions of interest were identified: 1, small bowel; 2, ascending colon; 3, transverse colon; 4, descending colon; 5, rectosigmoid colon; and 6, evacuation into toilet. Images were taken between 0 to 2 hours (at 0, 0.5, 1, and 2 hours), then at 6, 24, 30, and 48 hours. Normal transit rates were determined from adult data and plastic marker studies.

The NTS is a noninvasive radionuclear imaging technique, which simply involves the ingestion of a radiotracer and serial images captured using a γ camera. The calculated radiation dose is equivalent to 2 abdominal x-rays. The NTS was first started to identify the patterns of colonic transit in children with intractable chronic constipation [8,10]. This study is reserved for children with intractable chronic constipation (medical treatment–resistant group). All these children had been treated with dietary change, laxatives, and behavioral therapy by their respective treating physicians. Children with chronic constipation who improved with medical treatment or with palpable fecaloma were not subjected to an NTS. The algorithm adopted in the management of children with chronic constipation at our hospital is shown in Fig. 1.

The data from all NTS were transferred from the nuclear medicine department and stored in an electronic database in the surgical research unit, with ethical approval from the institutional ethics committee (no. 30059A).

All NTS from 1998 to 2009 (>600 studies in 520 children) were reviewed retrospectively (by YIY) to identify children with chronic constipation who had rapid proximal colonic transit, which was defined as greater than 25% of tracer beyond hepatic flexure at 6 hour and/or greater than 25% of tracer beyond end of descending colon at 24 hour (Fig. 2). All studies with apparent rapid proximal transit were then reviewed independently by JMH to confirm the diagnostic criteria.

The NTS findings were correlated with clinical symptoms (ie, abdominal pain, anal fissure, other allergic symptoms, eg, eczema, asthma, and family history of allergy) and outcome (clinical improvement of constipation at follow-up) from detailed examination of the patient’s records. Other laboratory investigations included endoscopy, contrast enema, rectal biopsy, anorectal manometry, skin prick testing, or serology marker for food allergy. The NTS were not repeated.

2. Results

During the period of the study (1998 to 2009), a total of 520 children with intractable chronic constipation not responding to good medical treatment underwent investigation by NTS. In this retrospective review, 64 (12%) of 520 were identified with rapid proximal colonic transit as defined in the Methods section (see Fig. 2).

Review of clinical history, symptoms, and outcome in 55 of 64 children that were available for analysis showed family history of allergy (10.9%) and a high rate of symptoms associated with possible food allergy/intolerance: abdominal pain (80%), anal fissure (27.3%), and other allergic symptoms (43.6%) (Table 1).

Eighteen of the 64 children (who were identified after the index case) were treated with dietary exclusion (usually
cow’s milk [CM] and/or wheat protein) with resolution of symptoms in 9 (50%) within 6 to 12 months. Four children showed no clinical improvement after dietary exclusion (one child has cystic fibrosis, one with normal pressure hydrocephalus, one has impaired rectal sensation on anorectal manometry, and one with short coccyx on sacral x-rays). Another 5 children who were treated by dietary exclusion have no documentation of clinical symptoms or were lost to follow-up.

In the other group of 37 patients who were not treated with dietary exclusion, only 4 improved with toilet training and laxative therapy. Twenty-nine of these children were continued on laxatives, 2 children had had sigmoid colectomy, and one child had had appendicostomy for antegrade colonic enemas. Four children have no further records of continuing treatment.

Rectal biopsies were performed in 18 children, with one child demonstrating mild eosinophilia. There were 3 children subjected to skin prick testing, all were negative; one child had a positive serology marker for food allergy (non–immunoglobulin E [IgE] for CM allergy); 4 had barium enema, all normal; 5 had upper endoscopy, 2 had colonoscopy: all normal; 5 had celiac screen, all negative; 2 had anorectal manometry with anismus present; and 2 had magnetic resonance imaging, which showed no abnormality in one child and the other child had a spinal canal lipoma with sacral agenesis. There was very low concordance rate with food allergy/intolerance in the current patient population from the tests performed.

3. Discussion

In this study, a subgroup of children with intractable chronic constipation was identified with rapid proximal
colonic transit on NTS. This was unexpected and quite different from the children we had previously identified with slow proximal colonic transit, causing “slow-transit constipation.” In addition, they did not just have holdup in the rectosigmoid colon secondary to anorectal retention associated with aberrant toileting behavior. The precise cause is yet to be determined with certainty, but the associated symptoms and response to treatment were suggestive of food allergy and/or intolerance. Food allergies are commonly encountered conditions affecting up to 8% of children younger than 10 years [11]. Constipation related to food intolerance has been increasingly reported [12-19], and the underlying pathophysiology of this entity is under study. Constipation has been identified as one of the most common gastrointestinal disorders in patients with atopic dermatitis and food allergy [11,20]. In 1963, Davidson et al [21] reported that constipation in pediatric patients considerably improved when treatment included the exclusion of CM and its derivatives from the diet. Subsequently, the association between CM protein and chronic constipation was reported by Buisseret [22] with 2 further case reports indicating that constipation might be the only clinical manifestation of CM protein intolerance (CMPI) [13,14]. During the 1990s, work from Carroccio et al [18] indicated a clear relationship between CMPI and chronic constipation in children unresponsive to laxative treatment [19] and showed that an exclusion diet was able to correct the constipation. The frequency of constipation owing to CMPI ranges between 28% and 70% [15-17]. Shah et al [16] conducted a prospective study in children and found that a clinical history with symptoms of allergy were highly associated with intractable constipation, suggesting the possibility of food intolerance as the underlying cause. In addition, the occurrence of perianal lesion (ie, anal fissure) in children with chronic constipation diagnosed with food allergy is well reported and studied [23-25]. We observed the occurrence of anal fissure in one third of our patient group.

The correlation of rapid proximal colonic transit with clinical history and symptoms of allergy in one child directed our attention to investigate food intolerance/allergy as a possible contributing cause to intractable constipation. We found 18 children with rapid transit in the proximal colon who were treated with dietary exclusion and that 9 children (50%) responded positively to the treatment. Another 37 children with rapid proximal transit were not treated with dietary exclusion. Eighty percent of these children (n = 55) had abdominal pain, and 40% had other allergic symptoms, so it is possible that food intolerance/allergy was a contributing cause of constipation in these children as well. These children were only identified retrospectively, so dietary exclusion treatment was not given to all. Only 4 (10%) of 37 improved compared with 50% of those given dietary exclusion. A better response with dietary exclusion suggests this could be an underlying cause contributing to the rapid proximal colonic transit and constipation. Although the link is weak, it is worth considering dietary exclusion and testing this association in future treatment and studies. A prospective study is necessary to confirm or refute this association.

This retrospective review showed rapid proximal colonic transit and anorectal holdup in 64 (12%) of 520 children with intractable chronic constipation (not responding to different laxative therapies, behavioral therapy, and toilet-training program) undergoing NTS. Rapid proximal colonic transit could be produced by the underlying malabsorption caused by intestinal mucosal inflammation, with “osmotic diarrhea” flushing the passage of feces through the proximal colon. Only one previous report by Romanczuk and Samoje’dny [9] using plastic markers demonstrated slow total and segmental colonic transit in children with food intolerance/allergy–related constipation. Shah et al [16] used radio-opaque pellets to study the intestinal transit of children with atopy.
and found that the delay in fecal passage was a consequence of stool retention in the rectum and not of a generalized motility disorder. In the current study, the children have anorectal retention or holdup phenomenon, with anal fissure in one third, possibly caused by the cell-mediated immunologic reaction of food intolerance. Although rectal biopsy was suggested to be a good screening test by Carroccio et al [18], in our series, it was a poor screening test for food intolerance/allergy–related constipation with only one case of eosinophilia. The concordance rate for other investigations performed was very poor in identifying food intolerance/allergy as the cause of constipation.

The criteria of rapid colonic transit put forward by us are of necessity, completely arbitrary, and based on our understanding and accumulated experience of normal and slow colonic transit in investigating children with chronic constipation using NTS. We hope, however, that with time, we will be able to refine the criteria and establish whether there is an association of rapid proximal colonic transit with food intolerance/allergy. We also hope that more NTS done outside our institute could investigate similar findings to establish universal criteria for rapid colonic transit.

In our institution, the NTS has an increasingly important role in investigating children with chronic constipation and has aided in the management of this chronic debilitating condition. Children with normal proximal colonic transit and anorectal retention usually respond to standard medical therapies using laxatives, toileting program, behavioral modifications, and biofeedback therapy [26,27]. Slow colonic transit characterizing slow-transit constipation is more difficult to treat because they do not respond to standard medical therapies [28-30], but recent studies with transcutaneous electrical stimulation using interferential current offer hope by improving colonic transit and quality of life [31-33].

In conclusion, at our institute, NTS is helpful to identify not only children with intrinsic slow colonic transit but also rapid proximal colonic transit that is likely secondary to food intolerance. The fact that 50% of children tested responded to dietary exclusion points to food intolerance/allergy as the most probable cause leading to chronic constipation in children with rapid proximal colonic transit. Future studies treating those with rapid proximal colonic transit with dietary exclusion or testing for food intolerance are needed to determine if this association is consistent and widespread.

References


