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Connective tissue disorder—a new subgroup of boys with slow transit constipation?

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Abstract

Purpose: Slow transit constipation (STC) is a form of chronic constipation, with delayed colonic passage of stool. Possible etiologies include reduced neurotransmitter levels, reduced interstitial cells of Cajal density, or a disorder of connective tissue (CT) synthesis. A common CT disorder is generalized joint hypermobility (GJH). This study aimed to investigate whether there was a greater prevalence of GJH among patients with STC than controls.

Methods: Children (aged 7-17) diagnosed with STC by radio/nuclear transit study were recruited from outpatient clinics. Controls (no history of constipation) were recruited from outpatient clinics and a scout jamboree. Hypermobility was assessed using the Beighton score (4 or more = hypermobile). This project received ethical approval by the human research ethics committee.

Results: Thirty-nine STC subjects and 41 controls were measured. Of 39 STC subjects, 15 (38%) were hypermobile, compared to 8 (20%) of 41 controls ($P = .06$). Analyzed by gender, 10 (38%) of 26 STC males and 1 (4%) of 23 control males were hypermobile ($P < .01$).

Conclusions: These results show that GJH is higher in STC children, particularly males, suggesting that a disorder of CT synthesis plays a role in the etiology of STC. Further research is required to ascertain the nature of any relationship and how this knowledge may aid our understanding and treatment of STC.

Constipation is a serious childhood condition; its reported prevalence varying from 0.3% to 28% [1,2] and being more prevalent in boys [3]. Organic causes account for a small percentage of patients with chronic constipation, which can be classified into the following 3 categories based on the site of slowing: normal transit constipation, slow transit constipation (STC), and disorders of defecation with retention in the rectum [4]. Slow transit constipation is

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characterized by delayed transit throughout the colon in contrast to functional fecal retention in the rectum. Slow transit constipation has recently been demonstrated in children [5], and its exact cause is not known. Genetic links, dysfunctional enteric nerves, decreased levels of substance P (an excitatory neurotransmitter), reduced numbers of interstitial cells of Cajal, and disorders of connective tissue synthesis have all been implicated in its etiology. Our study arose from a clinical observation that some children with STC appeared to have joint hypermobility.

Generalized joint hypermobility (GJH) is a relatively benign condition with excessive laxity of multiple joints resulting in a greater than normal range of motion because of a disorder of collagen synthesis [6]. It has a genetic component, linked to deficiency in the tenascin-X gene [7]. It is similar, although less severe, than other hereditary disorders of connective tissue such as Marfan syndrome, Ehlers-Danlos syndrome, and osteogenesis imperfecta. Generalized joint hypermobility should not be confused with the benign joint hypermobility syndrome (BJHS), a condition of hypermobile joints with musculoskeletal symptoms [8]. The prevalence of GJH varies from 10% to 25% between different populations and is influenced by ethnicity, sex, and age [9-14]. Since GJH was first recognized, a number of systems have been used to diagnose it clinically. The most common scoring system is the Beighton score [15]. There have been a number of reports that have found an association between GJH and autonomic dysfunction [16], and GJH and constipation [17-19].

Our hypothesis was that children with STC would have a higher prevalence of GJH than children without STC. Therefore, the aim of this study was to compare the prevalence of GJH in children with STC and in age-matched and gender-matched control subjects.

1. Methods

This was a cross-sectional study that determined the prevalence of GJH, in 2 populations—control children and children with STC. Thirty-nine STC subjects were recruited from medical and surgical clinics within the Royal Children's Hospital (Melbourne, Australia). They were aged 7 to 17, with chronic constipation more than 2 years duration, and diagnosed with STC by radionuclear transit study [20]. They had previously undergone blood and endocrine tests to rule out metabolic or hormonal disorders and had no identified anatomical defects that could cause constipation. Control children were aged 7 to 17 years with no history of constipation requiring medical treatment. Forty-one control children were recruited from the Australian Scout Jamboree and normal children or siblings attending other outpatient clinics. Before examination, children and their parents gave informed consent to proceed. Each child's date of birth was recorded. Height and weight were measured to calculate body mass index (BMI). Subjects were then examined to determine joint mobility, using the Beighton score [15]. The following maneuvers are used in calculating the Beighton score: passive dorsiflexion of each fifth metacarpophalangeal joint to more than 90°, passive apposition of each thumb to the volar aspect of the forearm, hyperextension of each elbow to more than 10°, hyperextension of each knee to more than 10°, and place hands flat on the floor while knees extended in standing. Results for each maneuver were recorded, giving a score out of 9. Subjects scoring more than 4 were classed as hypermobile.

The human research ethics committee granted ethics approval for this study (project no. 23040B).

Results were analyzed using Stata Statistical Software (StataCorp LP, College Station, TX) and GraphPad Prism (GraphPad Software, San Diego, CA).

2. Results

2.1. Subject characteristics

Eighty subjects (49 males and 31 females) were examined for GJH. The average age of the subjects was 12.0 (range, 7.4-17.7; SD, 2.6). The average BMI was 19.5 (SD, 3.3). Thirty-nine subjects were diagnosed with STC based on radionuclear transit study. There was no significant difference in age, gender, or BMI between the STC (n = 39) and control groups (n = 41) (Table 1).

2.2. Prevalence of GJH

The prevalence of GJH was higher in children with STC (38%) than control children (20%) ($P = .06$; χ^2 test) (odds ratio [OR], 2.578; 95% confidence interval [CI], 0.942-7.053). Overall, 39% of females and 22% males had GJH. This was not statistically different ($P = .12$) (Table 2).

Using a Beighton score 4 or more, 10/26 males and 5/13 females with STC were identified to have GJH. So were 1/23 male and 7/18 female control children.

No relationship was found between BMI and GJH.

Table 1 Subject characteristics

Group	n	Age (range [SD])	BMI (SD)
Overall	80	12.0 (7.4-17.7 [2.6])	19.5 (3.3)
Control	41	12.0 (8.0-17.6 [2.6])	19.2 (3.1)
Male	23	12.3 (8.0-17.6 [2.6])	18.1 (2.5)
Female	18	12.0 (8.2-17.6 [2.6])	20.6 (3.2)
STC	39	12.0 (7.4-17.7 [2.7])	19.8 (3.5)
Male	26	11.9 (7.4-17.7 [2.9])	19.5 (3.6)
Female	13	12.3 (9.8-16.4 [2.5])	20.4 (3.3)

Slow transit constipation and control subject characteristics.