Constipation in Duchenne Muscular Dystrophy: Prevalence, Diagnosis, and Treatment

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Objectives To determine the prevalence and clinical characteristics of constipation among patients with Duchenne muscular dystrophy (DMD).

Study design This cross-sectional prospective study included 120 patients (age range 5-30 years old) with an established diagnosis of DMD. Participants filled out the constipation section of a validated Questionnaire on Pediatric Gastrointestinal Symptoms based on Rome-III Criteria (QPGS-RIII) for the diagnosis of functional constipation as part of a routine clinic visit. We evaluated several potential screening methods for constipation: the Bristol stool form scale, routine physical examination, and fecal load on abdominal radiograph. These methods were compared with the QPGS-RIII in diagnosing functional constipation. Risk factors for the development of functional constipation were determined.

Results Based on the QPGS-RIII, 46.7% of patients with DMD in this cohort were diagnosed with functional constipation. Prevalence was not affected by age or functional status. None of the screening methods tested were sensitive enough to diagnose functional constipation. Among patients with constipation, only 43.6% received specific treatment for constipation and only one-half of these treated patients reported resolution of constipation.

Conclusions This study systematically examined constipation among patients with DMD and provides evidence that constipation among patients with DMD is highly prevalent, underdiagnosed, and undertreated. QPGS-RIII is easy to administer and is an efficient tool to diagnose functional constipation in patients with DMD in a clinic setting. *(J Pediatr 2016;171:183-8)*.

Duchenne muscular dystrophy (DMD) is an X-linked degenerative muscle disorder characterized by progressive weakness affecting skeletal and cardiac muscle. Multidisciplinary supportive care has led to a significant increase in both life expectancy and quality of life of patients with DMD but has revealed a new array of associated medical challenges.[1-3] The involvement of the gastrointestinal (GI) tract is one of the emerging foci of interest in DMD management.[4-6] GI symptoms are diverse and include decreased masticatory performance,[7,8] dysphagia,[9,10] gastric hypomotility,[11] and constipation.

Constipation is a common clinical observation in patients with DMD.[12] In a study of 118 patients that focused on feeding problems and weight gain in DMD, 36% of patients reported constipation.[6] For comparison, the prevalence of constipation in the pediatric and young adult population ranges from 6%-15%.[13-17] Despite its prevalence, clinical characteristics of constipation in patients with DMD have not been systematically investigated.

Our center has provided interdisciplinary care to patients with DMD since 2000. As part of standard care, we have systematically gathered information regarding clinical status, GI symptoms, and nutrition. The aim of this study was to determine the prevalence of functional constipation, to identify possible risk factors, and to evaluate effectiveness of different screening methods to diagnose constipation in a cohort of established patients with DMD. We hypothesized that patients with DMD would have a higher prevalence of constipation than the general population and that prevalence will increase with age and with worsening functional status. We further hypothesized that clinical constipation will be underreported by patients and underdiagnosed by caregivers.

Methods

This prospective cross-sectional study included a cohort of patients with DMD seen at the comprehensive neuromuscular center at Cincinnati Children's Hospital Medical Center between May 2013 and August 2014. Patients were invited to participate in the study during a routine follow-up visit. The study was approved by the local institutional review board.

Inclusion criteria were a diagnosis of DMD based on clinical presentation and verified by lack of dystrophin on muscle biopsy or known dystrophin

BSFS	Bristol stool form scale
DMD	Duchenne muscular dystrophy
GI	Gastrointestinal
QPGS-RIII	Questionnaire on Pediatric Gastrointestinal Symptoms based on Rome-III Criteria

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gene mutation and age >5 years old. There were no exclusion criteria. Written consent/assent to participate in the study was obtained from the parents and/or the patient, based on age and legal power-of-attorney status.

All patients were evaluated for constipation section C (constipation) of the Questionnaire on Pediatric Gastrointestinal Symptoms based on Rome-III Criteria (QPGS-RIII), a diagnostic tool that has been validated in children and is widely accepted for both clinical and research purposes.[18-20] We used the parent-report version for all participants younger than 18 years of age. This questionnaire consists of 11 items regarding frequency and severity of constipation symptoms over the 2 months prior to the visit. Per Rome-III criteria, constipation was diagnosed based on receiving 2 or more positive answers and after ruling out irritable bowel syndrome using section B of the QPGS-RIII questionnaire. Patients over 18 years old used questionnaires for adults, which were scored based on the Rome-III diagnostic criteria for functional GI disorders.[21]

In addition, all patients were evaluated for constipation by: (1) Bristol stool form scale (BSFS): patients or their parents were asked to identify a typical stool form, with stool type-1 or type-2 considered to represent constipation[22,23]; (2) fecal load assessment by a pediatric gastroenterologist, who examined spine radiographs, which were done for clinical monitoring of steroid-induced vertebral fractures, and graded as normal or mildly, moderately, or severely increased; and (3) abdominal examination to determine presence and location of fecal masses, abdominal tenderness, fullness, or other abnormal findings (rectal examination was deferred unless clinically indicated). Additional data included demographics; genetic mutation (if known); Functional Mobility Scale[24]; North Star Ambulatory Assessment (for ambulatory patients)[25,26]; ambulation status (ambulatory vs nonambulatory); medications (glucocorticoid treatment, constipation treatments, other medications); and an estimate of fiber and fluid intake (servings of fruits/vegetables and cups of water/milk per day, respectively). The questionnaire also contained a yes/no question as to whether constipation was a concern at the time of the visit.

Participants were diagnosed as having constipation if they fulfilled Rome-III criteria for functional constipation (based on the QPGS-RIII) or if there was prior documentation of constipation and the patients were treated for constipation at the time of the study.

Data Analyses

Descriptive statistics were used to calculate the prevalence of constipation in this cohort. Logistic regression with backward elimination variable selection was used to determine possible predictors of constipation.

Results

The study enrolled 120 patients with DMD (mean age 13 ± 5.2 years, range 5-30 years). Twenty-five patients were over 18 years old (mean age 21.3 ± 3.3 years). Patient characteristics are described in Table I.

Prevalence of Constipation

The overall prevalence of constipation was 46.7% (56 out of 120). The prevalence among patients younger than 18 years of age was slightly lower than in patients older than 18, although this difference did not reach statistical significance (44.8% vs 52%, $P = .65$). No differences were found when comparing patients below and above 10 years of age ($P = .83$, data not shown). Similarly, the proportion of patients/families that raised concerns regarding constipation on a standard intake questionnaire as well as the proportion of patients who received symptomatic treatment for constipation did not differ between patients younger and older than 18 years of age (Table II).

Risk Factors for Constipation

We evaluated the clinical characteristics of this cohort in an attempt to identify risk factors for the development of constipation. Response rates for all variables were >85%.

Functional status was assessed using the North Star Ambulatory Assessment, the Functional Mobility Scale, and ambulation status (ambulatory vs nonambulatory). We presumed that lack of ambulation may be a contributing factor for constipation, but none of these measures was associated with the presence of constipation ($P = .54$, .68, and 1.0, respectively).

We evaluated calcium supplementation and glucocorticoid treatment as possible risk modifiers. Calcium supplementation could potentially increase the risk of constipation and glucocorticoid treatment could be associated with a decreased risk secondary to improved functional status. Calcium supplementation for those with suboptimal dietary calcium intake was used in 54.9% of patients in this

Table I. Patient characteristics of a cohort of 120 patients with DMD

Patient characteristics	Age <18 y	Age >18 y	Total	*P* value (<18 y vs >18 y)
Number of participants (% of total)	95 (79.2)	25 (20.8)	120	n/a
Age in y (average ± SD)	10.8 ± 2.8	21.3 ± 3.3	12.9 ± 5.2	<.01
Age range in y	5-17	18-30	n/a	n/a
Ambulatory (%)	80 (84.2)	5 (20)	85 (70.8)	<.01
North Star Ambulatory Assessment (average ± SD)	21.6 ± 8.1	n/a	21.3 ± 8.1	-
Functional Mobility Scale	2.33 ± 1.6	5.44 ± 1.87	2.98 ± 2.08	<.01
Steroid treatment (%)	91 (95.7)	21 (84)	112 (91.8)	NS
Calcium supplementation (%)	51 (56)	15 (60)	66 (56.9)	NS

n/a, not applicable; *NS*, not significant.