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A Pilot Study for Evaluation of Hypotonia in Children with Neurofibromatosis Type 1

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Abstract

There are currently no objective criteria to evaluate pediatric hypotonia. The purpose of this pilot study was to identify diagnostic criteria for assessing hypotonia in children with Neurofibromatosis type 1 (NF1). Fifty-five subjects between the ages of 1 and 7 years with a diagnosis of NF1 were evaluated. A physical therapist recorded a subjective tone assessment and objective tone metrics, including ankle dorsiflexion, knee extension, hip abduction, triceps fat percentage, grip strength and head lag during a pull-to-sit test. Multivariate logistic regression analysis showed the presence of head lag paired with increased hip range of motion was a significant predictor of hypotonia. The presence of head lag on a pull-to-sit test paired with increased hip range of motion is an accurate predictor of hypotonia in children with NF1. These objective measures should be prospectively evaluated in other pediatric populations for their ability to predict hypotonia.

Keywords

muscle tone; hypotonia; NF1; head lag; grip strength; hip abduction

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EAS, LEW, ACA, DHG, CMD collected clinical data

ACA, DHG, CMD were involved in direct patient care

EAS and FG performed statistical analysis

EAS, DHG, CMD prepared the manuscript

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Introduction

Children with neurologic diagnoses frequently present with a wide spectrum of muscle tone abnormalities, ranging from high tone (hypertonia) to low tone (hypotonia). In children with hypertonicity, several measures have been developed to objectify the type and severity of hypertonicity, including the Modified Ashworth Scale and the Modified Tardieu Scale.

In contrast, for children with low tone, no standardized assessment tools are available for subjects after infancy and during early childhood. Previous studies have sought to define hypotonia using various methodologies¹, including consensus opinion of physical and occupational therapists² and professional reports of general characteristics of children with hypotonia. While these studies have been useful in developing a candidate set of measures potentially associated with hypotonia, there has not been a study focused on identifying specific correlations between non-invasive, objective clinical measures and the presence of a clinical diagnosis of hypotonia. The frequency of hypotonia and their improvement following therapy³ underscore the need to develop a standardized method of evaluating tone germane to the identification and management of patients with hypotonia.

One of the neurologic conditions in which hypotonia is often reported is the inherited cancer predisposition, neurofibromatosis type 1 (NF1). In this population, previous pilot investigations have revealed that hypotonia correlates with the presence of a brain tumor.⁴ However, in this study, hypotonia was diagnosed using the clinical impression of the treating physician or nurse practitioner, including resistance to passive movement of the extremities and “general global impression” of the amount of tone present. In light of this potential association between brain tumors and hypotonia in children with NF1, this patient population provides an ideal platform to formulate diagnostic criteria for hypotonia. The purpose of this pilot study was to develop a preliminary set of objective criteria for the evaluation of hypotonia in a population of children with NF1 for future application to children with other conditions characterized by low tone.

Methods

Participants

Fifty-eight subjects with diagnoses of NF1 between the ages of 1 and 7 years old enrolled in the study between June 1, 2011 and June 1, 2012. Three subjects were excluded due to having incomplete therapist assessments. Those three subjects did not have a complete data set due to their age and inability to complete all objective measures. Inclusion criteria consisted of a diagnosis of NF1 using National Institutes of Health Consensus Development Conference criteria⁵, age, and ability to participate in the evaluation process. Exclusion included the presence of co-existing tibial pseudarthrosis or dysplasia. Subjects were consented to participate in the study in accordance with an approval Human Studies Protocol at the [Blinded for Review] School of Medicine.

Subjective Assessment of Muscle Tone

Each subject was evaluated by two clinicians, both a physical therapist (C.M.D.) and a physician (D.H.G.) or an advanced practice pediatric nurse practitioner (A.C.A.). Each

clinician was blinded to the impression of the second care provider's impression of the tone. The subjective evaluation by each practitioner included three criteria: (a) the Meryon sign (a test in which the child is lifted by an examiner's hands in the child's axilla and the child slips through the examiner's hands due to shoulder girdle weakness), (b) subjective description of resistance to passive elbow and knee range of motion and (c) subjective description of the muscle quality (either soft, normal, or rigid). From these three subjective observations, a clinical impression of hypotonia or normal tone was made. When both clinicians were in agreement, a diagnosis of hypotonia was rendered.

As the subjects were evaluated as part of their routine NF1 clinical care, the measures had to take less than ten minutes to complete. Given the level of debate surrounding the measurement of hypotonia (the difficulty discriminating between strength, ligament laxity, muscle weakness and increased subcutaneous fat), a wide variety of measures were selected from previous experience, age-matched norms and current published research. A physical therapist with >18 years of experience in pediatric therapy completed all objective measures (C.M.D.). Given the time limitations in the context of a busy outpatient tertiary care clinic, it was not feasible to include a second clinician for range of motion measures.

Objective Assessment for Muscle Tone

Range of motion measurements were performed at the hip and ankle to evaluate muscle length and at the knee to look specifically at ligament integrity. All range of motion measures were performed using established protocols.⁶ Hip abduction was measured with the subject supine using a large goniometer: proximal arm aligned between the anterior superior iliac spines and distal arm aligned with the anterior midline of the femur. Measurements were recorded in degrees away from the midline into hip abduction. Normal hip abduction range of motion is 45 degrees per side, a combined 90 degrees of mobility into abduction. Knee extension/hyperextension range of motion was measured supine: the proximal arm from the greater trochanter to lateral femoral epicondyle and the distal arm aligned with the lateral midline of the fibula to the lateral malleolus. Measures of positive motion at the knee represent knee hyperextension. Normal knee extension is full range, or a measurement of zero degrees.⁶ Ankle dorsiflexion was measured in knee extension: the proximal arm of the goniometer was aligned with the lateral malleolus to the fibular head and the distal arm was parallel to the lateral aspect of the fifth metatarsals. Range was documented in positive degrees from zero, with zero representing neutral dorsiflexion/plantar flexion. A normative value of 20 degrees was used.⁶

A pull-to-sit test was performed to determine the presence or absence of head lag. Subjects were positioned supine on the exam table, and pulled into sit from the wrist/hands. Presence of head lag was noted if the subject did not display the ability to keep their head in line or in front of the shoulders during the maneuver.

Calipers were used to measure the body fat percentage on the right triceps. Subjects less than two years of age were not evaluated for triceps fat percentage. The length of the right humerus along the line of the triceps muscle belly was bisected and a Harpenden Skinfold Caliper was used to obtain a skinfold measure. Taking skinfold measurements allowed for a comparison of the amount of subcutaneous fat between age-matched peers.

Grip strength was quantified using a handheld dynamometer. Subjects less than two years of age were not evaluated for grip strength due to difficulties in obtaining reliable measurements in this age group. Both hands were evaluated using a Jamar Hydraulic Hand Dynamometer. Subjects performed a maximal grasp on a handheld dynamometer adjusted for hand size. Three trials were completed and the average of three trials recorded.

Statistical analysis

A single biostatistician (F.G.) reviewed the data, and evaluated summary statistics for the two cohorts, differences between the two comparison groups, and determined independent objective criteria for the evaluation of low muscle tone, based on multivariate analysis against physical therapist assessment.

Binary logistic regression modeled the relationship between the co-existence of hypotonia and the following independent variables: presence or absence of head lag on a pull-to-sit test (binary), ankle dorsiflexion (continuous), knee extension (continuous), hip abduction (continuous), triceps body fat (continuous), and grip strength (continuous). A forward stepwise selection procedure was used with an alpha of 0.1 for entry. Model explanatory power and fit was assessed using the c-statistic and the Hosmer-Lemeshow lack-of-fit test. An unadjusted alpha level of significance was set at 0.05 for all tests.

Results

Of the 55 eligible subjects, the physical therapist (C.M.D.) identified 22 subjects (40%) exhibiting low tone and 33 (60%) with normal tone. The overall percentage of patients with low tone in this cohort is similar to the percentage found in a previous study.⁴ The demographic characteristics of the hypotonic and normotonic groups were similar (Table 1). All measures, with the exception of average knee range of motion and triceps fat percentage, independently displayed significant correlation with a clinical (subjective) assessment of hypotonia (Table 2).

Significant predictors in the model included presence of head lag (95% Wald CI=0.011-0.310) and average hip abduction (95% Wald CI=1.006-1.216). These findings indicate that subjects with head lag or hip abduction greater than 60 degrees had a 20-fold higher (CI 3.1-127.5) and 1.5-fold higher (CI 2.4-87.9) odds of exhibiting low muscle tone, respectively.

In addition, multivariate regression analysis revealed that the presence of head lag paired with increased hip abduction resulted in the highest correlation with a clinical diagnosis of hypotonia. Moreover, these diagnostic criteria afforded a sensitivity and specificity of 80% and 83%, respectively, relative to the therapist subjective assessment of tone.

Discussion

Assessing disorders of tone is a critical element of the clinical characterization of children with numerous neurological disorders. In this regard, hypotonia is associated with abnormalities of both the central and peripheral nervous systems⁷⁻⁹, and can be a feature of

over five hundred distinct genetic disorders.¹⁰ The prompt recognition of reduced muscle tone, especially in the setting of abnormal laboratory findings (e.g., elevated creatine kinase), dysmorphic facial features, or neurologic abnormalities (e.g., muscle fasciculations), may lead to the correct diagnosis of the underlying condition.

Previous studies have sought to better define subjective criteria for the assessment of hypotonia using therapist consensus opinion. In a survey of 80 therapists, one study found that therapists reported decreased strength, decreased activity tolerance, delayed motor skills development, rounded shoulder posture with leaning onto supports, hypermobile joints, increased flexibility, and poor attention and motivation in association with hypotonia.² In a follow-up study, the same group reported that decreased strength, hypermobile joints, and increased flexibility were the most frequently cited features associated with reduced muscle tone.¹ Importantly, most of the therapists responding to these surveys noted that observation and descriptive findings served as their primary assessment tools. Due to the relative paucity of objective measures to assess low tone in children¹¹, our study focused on the use of clinically measureable and objective findings in an effort to develop criteria to more reliably evaluate tone in children.

Using a variety of objective measures, we found that a persistent head lag, using a simple pull-to-sit test, was useful in identifying low tone in children over the age of one year. Pairing this test with passive hip abduction resulted in excellent specificity and sensitivity for diagnosing hypotonia. Interestingly, this subset of children with NF1 displayed an overall right shift in hip range of motion (increased) compared to the average range of age-matched children.¹² Future studies will be required to determine whether this increased range of motion difference results from muscle weakness, muscle hypotonia or joint laxity.

Several limitations were inherent in this study. Because NF1 is a rare condition with an incidence of 1:2,500 live births and the limitations of the age groups appropriate for accurate evaluation, the total study population was small; however, this population was ideally suited for the establishment of diagnostic criteria with respect to measures of sensitivity and specificity due to the heterogeneity of tone presentations within the cohort of subjects. Using the measurements described in this report, there is suitable sensitivity and specificity for the diagnosis of hypotonia with a high level of confidence in children with NF1. In addition, this study was limited by the use of only one therapist. The inclusion of multiple therapist evaluations would strengthen these preliminary findings by providing inter-rater assessments. However, due to the time constraints in a busy outpatient clinic setting, it was not feasible to have a second therapist involved.

Taken together, the findings reported in this study established the use of two objective measures (head lag, hip abduction) to accurately assess reduced tone in children with NF1. Based on these findings, we advocate its future evaluation and application to other pediatric populations in which hypotonia is a prominent clinical feature.

Conclusion

The presence of head lag on a pull-to-sit test coupled with hip abduction greater than 55 degrees provides a sensitive and specific set of objective criteria for physicians and therapists to rapidly assess pediatric patients for hypotonia. Early identification of patients with low tone could facilitate more prompt identification of at-risk children who would benefit most from therapeutic intervention.

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Table 1

Demographics of the NF1 pediatric patient population.

	Hypotonic N= 22 (%)	Normotonic N= 33 (%)	P value
Mean Age	4.2	4.8	0.184
Male (%)	7 (32)	11 (33)	1.000
Caucasian (%)	20 (91)	24 (73)	0.168
Family History of NF1 (%)	11 (50)	16 (49)	1.000

Table 2

Objective measures of hypotonia in children with NF1.

Measurement	Hypotonic	Normotonic	P value
Ankle range of motion	33.4 (SD=6.1)	25.8 (SD=6.9)	.0002
Hip range of motion	66.3 (SD=7.1)	57.2 (SD=8.2)	.0002
Grip strength	3.7 (SD=1.8)	5.6 (SD=2.3)	.0064
Knee range of motion	+9.1 (SD=4.7)	+5.9 (SD=7.4)	.0694
Triceps fat percentage	10.2 (SD=2.6)	9.9 (SD=2.3)	.7556