ABSTRACT

BACKGROUND: Interpretation of pediatric electromyography interpretation in myopathic disorders is technically challenging. We assessed our electromyographic experience with respect to sensitivity and specificity in pediatric myopathy.

METHODS: We did a retrospective chart review of patients ≤18 years between 2009 and 2013. Two hundred twenty-four electromyographic studies were reviewed with the following referral diagnoses: myopathy, muscle weakness, neuromuscular disorders, myositis, myalgia, myoglobinuria, myasthenia, myotonia, cramps, periodic paralysis, hypotonia, and developmental delay. Only children who had an electromyography and muscle biopsy were included for analysis. Patients with neurogenic electromyography and neuromuscular junction disorders were excluded. Myopathic electromyography was defined as short duration, low amplitude, polyphasic motor unit potentials with rapid recruitment.

RESULTS: Seventy-two patients were included (age range, 6 months-18 years). The following observations were made: group A: myopathic electromyography or pathognomonic of muscle disease and biopsy or genetically confirmed myopathy (32 cases); group B: myopathic electromyography but biopsy normal or nondiagnostic (12 cases); group C: normal electromyography but biopsy normal or nondiagnostic (25 cases). The most common diagnoses were congenital myopathy (seven cases), metabolic myopathy (six cases), muscular dystrophy (six cases), genetically confirmed myopathy (five cases), myopathy, undefined (five cases), and inflammatory myopathy (four cases).

CONCLUSIONS: Pediatric electromyography was 91% sensitive and 67% specific in myopathic disorders. The metabolic myopathies were commonly missed by electromyography.

Keywords: electromyography, children, muscle biopsy, myopathy

Introduction

Electromyography (EMG) and nerve conduction studies (NCS) play a pivotal role in the evaluation of patients with neuromuscular disorders. EMG helps in localizing the lesion within the peripheral nervous system, determines disease severity, and may identify the proper muscle to biopsy. However, pediatric EMG is not only fraught with technical difficulties and poor tolerance but also relies heavily on the skill of the examiner. Pediatric EMG is effective in diagnosing various disorders of the peripheral nervous system. Earlier studies have consistently revealed EMG to be more effective in diagnosing neurogenic disorders than myopathic disorders at an early age. Subsequent studies found a higher yield in identifying myopathic disorders in older children. In two of these latter studies, myopathic disorders only represented a subset of the children studied.

Historically, muscle biopsy has represented the gold standard in the diagnosis of myopathy. Muscle tissue can be characterized by its histology, ultrastructural features, and by performing biochemical analysis and immunocytochemical stains. Muscle biopsy also provides tissue for genetic analysis. However, in recent years major advances in the genetic basis of neuromuscular diseases have occurred. The genetic basis of numerous neuromuscular disorders...
increasingly known, and many of the genetic mutations can be commercially tested. Some of the neuromuscular disorders (e.g., spinal muscular atrophy or Duchenne muscular dystrophy [DMD]) are increasingly diagnosed by molecular genetic testing without preceding ancillary tests such as EMG or muscle biopsy.

As a result, the contemporary practice of neuromuscular disorders and the application of EMG have evolved in the pediatric population with present populations differing from those previously reported.

In the present study, we performed a retrospective analysis to determine the diagnostic yield of pediatric EMG in myopathic disorders from a single tertiary care center in this modern era. We determined the sensitivity and specificity of the EMG findings in regards to the presence or the absence of a clearly defined muscle disease with the gold standard of diagnosis represented by the muscle biopsy or pathognomonic genetic testing.

Materials and Methods

The institutional review board of the Mayo Clinic, Rochester, Minnesota, approved the study protocol. We retrospectively searched the database to identify children (≤18 years of age) who underwent EMG at our electrophysiology laboratory over a 5-year period (2009-2013). These children were evaluated and referred by either a pediatric neurologist or neuromuscular specialist at the Mayo Clinic. We reviewed the EMG findings of each patient with the following referral diagnoses to identify potential cases of myopathy: myopathy, muscle weakness, neuromuscular disorders, myositis, myalgia, myoglobinuria, myasthenia, myotonia, cramps, periodic paralysis, hypotonia, and developmental delay. We correlated the EMG findings to the muscle biopsy and confirmatory genetic tests when available.

Motor and sensory NCS were performed according to the standard techniques using surface electrodes and were interpreted with regard to age-specific controls. Skin temperature was kept >32°C, and the extremities were warmed if required. As per our laboratory’s protocol, at least one motor and one sensory nerve were examined in an upper and lower limb. Needle EMG studies were performed with standard concentric needle electrodes. Needle EMG studies were performed either by the staff physicians with board certification in electrodiagnostic medicine or by the EMG fellows under the staff physician’s direct supervision. Muscles were sampled at the discretion of the electromyographer according to the clinical context and included at least one muscle in upper and lower extremities. Myopathic EMG was defined as low amplitude, short duration, polyphasic motor unit potentials often with rapid recruitment. Motor unit potentials were analyzed semi-quantitatively and graded on an ordinal scale using previously published normative data in children and infants. We also recorded the presence of spontaneous discharges on needle EMG in the form of fibrillation potentials, fasciculations, myotonic discharges, and complex repetitive discharges.

Conscious sedation was routinely used for children ≤10 years of age to ensure adequate quality and tolerance of the study. Sedation was used in older children at the discretion of the referring physician or at the request of the patient’s guardians. Conscious sedation was achieved by a combination of one or more of the following agents: ketamine, midazolam, and propofol under supervision of the pediatric anesthesiologists.

Children underwent muscle biopsy if the clinical suspicion of myopathy was high regardless of the EMG results. Open muscle biopsies were performed under general anesthesia by the surgeons. The muscles chosen for biopsy were guided by the clinical examination or the EMG findings. The muscle biopsies were interpreted by our muscle pathologists. Hematoxylin and eosin, trichrome, Nicotinamide adenine dinucleotide dehydrogenase, succinate dehydrogenase, cytochrome c oxidase, pH 4.3, 4.6, and 9.4 preincubated and toluidine blue—developed Adenosine triphosphatase, acid phosphatase, myophosphorylase, Periodic acid-Schiff, oil red O, nonspecific esterase, and Congo red stained frozen sections were routinely examined. Special immunocytochemical stains were performed according to the clinical context and routine biopsy findings. A muscle biopsy was considered myopathic if there were definite necrotic and regenerating fibers or when there were two or more of the following characteristics: increased internal nuclei, fiber size variation, increased endomysial connective tissue elements, and specific structural or histochemical abnormalities or inflammatory changes. Genetic testing was performed to further characterize the myopathy based on the clinical phenotype and muscle biopsy findings. In one patient in group A, the diagnosis was obtained by the genetic testing alone based on the clinical phenotype (selenoprotein-1 myopathy [SEPN1]).

Patients were classified based on the EMG and muscle biopsy or genetic findings into the following groups: group A: myopathic EMG and biopsy or genetically confirmed myopathy; group B: myopathic EMG and biopsy normal or nondiagnostic; group C: normal EMG but biopsy or genetically confirmed myopathy; and group D: normal EMG and biopsy normal or non-diagnostics. A definitive diagnosis of myopathy was made if there was a genetically confirmed myopathy or EMG was pathognomonic of a muscle disease in the absence of a diagnostic muscle biopsy (for example in two children with diffuse myotonic discharges without myopathic motor unit potentials suggestive of myotonia congenita). We excluded from our study children with neurogenic EMG findings and those with electrophysiologic findings characteristic of neuromuscular junction disorders.

Statistical analysis

We calculated the diagnostic yield of the EMG in detecting muscle disorders in children by using descriptive statistics. We calculated sensitivity, specificity, and the positive likelihood ratio of EMG in predicting a muscle disease when compared with the gold standard of muscle biopsy or genetic testing.

Results

We identified 224 children with suspected myopathy based on the referral diagnoses. We included 69 children in the analysis who had undergone both an EMG and a muscle biopsy. Three additional children were also included that did not undergo muscle biopsy, but the definitive diagnosis of myopathy was confirmed by either genetic testing or by pathognomonic EMG findings (Table 1). This resulted in a total of 72 individuals who were included in the final analysis.

We reviewed the medical records of those 72 individuals in detail to determine the clinical features, muscle biopsy reports, genetic test results, and final diagnoses. In almost all children, four or more muscles were sampled (fewer than four muscles were sampled in only four cases). EMG was 91% sensitive (32 of 35) and 68% specific (25 of 37) in regards to final diagnosis of definitive myopathy. If the EMG demonstrated myopathy, the positive likelihood ratio

| TABLE 1. Children With Electromyography (EMG) and Muscle Biopsy |
|----------------------|----------------------|----------------------|
| EMG                  | Final Diagnosis of Definitive Myopathy |
| Muscle Biopsy (+)    | Muscle Biopsy (−)    |
| Myopathic (+)        | Group A (32)         | Group B (12)         |
| Normal (−)           | Group C (3)          | Group D (25)         |

- Three children did not have muscle biopsy in group A (one had genetically confirmed muscle disease and other two had characteristic EMG and clinical findings suggestive of myotonia congenita).
- One child had nonspecific muscle biopsy but revealed reduced complex I and II on histochemical analysis of the electron transport chain in muscle tissue.
suggests that it is 2.8 times more likely that a definitive myopathy would be identified (Table 2).

**Group A, myopathic EMG and myopathy by biopsy or genetic testing**

There were 32 children in this group. Most children (18 or 56%) were between 3 and 10 years of age. All children in this group had myopathic EMG except two who had diffuse myotonic discharges without myopathic motor unit potentials. Among patients with myopathic EMG, rapid recruitment pattern was noted in 18 (56%). Fibrillation potentials were present in 16 patients (50%), and seven had myotonic discharges (22%). Creatine kinase (CK) was elevated (>300 IU/L) in 16 children (50%). The muscle biopsies were available in 29 children, one was diagnosed with SEPN1 based on genetic testing and two were diagnosed with myotonia congenita based on EMG and clinical findings (Table 3).

These were the final diagnoses in 32 children: congenital myopathy in seven children (22%), including centronuclear myopathy (three children), multiminicore disease (one child), congenital fiber type disproportion (one child), and undefined (two children); genetically confirmed myopathy in five children (16%), including collagen VI myopathy (three children), SEPN1 myopathy (one child), and lamin A/C myopathy (one child); inflammatory myopathy in four children (12.5%); metabolic myopathy in three children (9%), including McArdle disease (one child), mitochondrial myopathy (one child), and mucolipidosis type II (one child); muscular dystrophy, undefined genetic type in six children (19%); myopathy, undefined type in four children (12.5%); myotonia congenita in two children (6%); and vacuolar myopathy, undefined type in one child (3%).

**Group B, myopathic EMG but no myopathy on biopsy or genetic testing**

This group comprised 12 children. Most of the children in this group were older with seven of the 12 children aged 11-18 years. All had myopathic EMG. A rapid recruitment pattern was noted in six of them (50%). None had spontaneous discharges in the form of fibrillations or myotonia. CK was elevated in only one patient. The muscle biopsy was either normal or nondiagnostic of myopathy in all of them. None of the patients in this group had a final clinical diagnosis of myopathy.

**Group C, normal EMG but myopathy by biopsy or genetic testing**

This group had three children. None of them had myopathic EMG or any spontaneous discharges. Two of them had carnitine palmitoyltransferase II (CPT2) deficiency. One of the CPT2 cases had recurrent rhabdomyolysis; both had normal CK at baseline. Muscle biopsy of both CPT2 cases revealed mild increased lipid droplets in type I fibers. The final case in this group was diagnosed with a mitochondrial disorder. CK in this case was normal, and the muscle biopsy was nondiagnostic. The final diagnosis of the latter case was confirmed by biochemical testing including quantitative western blood analysis of subunit proteins demonstrating a decrease in complexes I and II, and oxidative phosphorylation supercoiled analysis revealed multiple abnormalities (Table 3).

**Group D, normal EMG and no myopathy on biopsy or genetic testing**

There were 25 patients in this group who had normal EMG. The muscle biopsy was either normal or nondiagnostic of myopathy in all of them. None of the patients in this group had a final clinical diagnosis of myopathy.

**Discussion**

EMG is an important ancillary investigation in the evaluation of neuromuscular diseases. EMG is particularly important in muscle disorders because it guides subsequent testing and diagnostic procedures. EMG, unlike the muscle biopsy, allows widespread sampling of the muscle tissue. Muscles revealing moderate EMG changes are ideal targets for biopsy rather than those that are normal or severely affected. It is therefore important that the sensitivity of EMG is maximized even at the expense of some specificity when identifying the proper muscle to biopsy. In this retrospective study, we investigated the diagnostic accuracy of EMG in children with myopathic disorders. Our results revealed that EMG was very sensitive (91%) in detecting myopathic disorders in children. If the EMG was myopathic, the likelihood that the evaluation would lead to a definitive diagnosis was 2.8 times higher than a normal EMG.

Previous studies evaluating the accuracy of EMG relative to the final diagnosis in children included neurogenic, myopathic, and neuromuscular junction disorders. Our study was unique in that we compared the diagnostic utility of the EMG findings in patients with a definitive diagnosis of myopathy only, thus avoiding the confounding bias by including other peripheral neuromuscular disorders.

The earlier studies have revealed a high concordance rate of EMG with neurogenic disorders (88% to 93%) but a low concordance rate with myopathic disorders (31% to 50%) in very young children. More recent studies over a wider age range of pediatric patients have revealed a higher rate of correlation in myopathic disorders. Hellmann et al. included 49 patients with myopathic disorders (two of them had myasthenia) and reported an EMG concordance rate of 80%. Rabei et al. included 11 patients with...
myopathy in their study; EMG was concordant in three of four children >2 years of age (75%). Chang et al.3 noted sensitivity of conventional needle EMG in diagnosing myopathic disorders to be 96%, which is comparable with our study.

The etiological diagnoses of definitive myopathies (congenital myopathy, genetically confirmed myopathy, inflammatory myopathy, metabolic myopathy, myotonia congenita, and muscular dystrophy) were established in a higher proportion of our cases compared with the previously published series. Two previous studies reported a higher proportion of patients with DMD (25% to 50%).8,9 However, because of widespread availability of the genetic tests for DMD, clinicians rarely request EMG in cases with suspected DMD in children any longer, and none of our patients had DMD.

Congenital myopathy was the most common diagnosis in our population, and all of them had myopathic EMG. This is in contrast to the previous studies, which revealed a poor yield of EMG in diagnosing congenital myopathy. In our study, EMG had the greatest difficulty in identifying metabolic myopathies. Our study included six children with metabolic myopathy, and three of them had a normal EMG (false negatives) with normal CK. If one has a high degree of suspicion for metabolic myopathy, biopsy should be performed even after the setting of a normal EMG. Muscle biopsy, biochemical analysis, and genetic testing of the muscle tissue yielded definitive diagnoses in all our metabolic myopathies with a negative EMG.

Our study had 12 false positive myopathies by EMG as defined by our gold standard. Among the patients with a myopathic EMG but negative biopsy and genetic testing, a strong clinical suspicion for a muscle disorder was still present in seven patients. A muscle biopsy may be non-diagnostic in the setting of a myopathy because of sampling error or patchy distribution of the myopathy. Genetic testing was inconclusive in our patients who were tested. As these myopathies are genetically diverse, one cannot rule out every possible genetic mutation. We anticipate that we may be able to identify additional myopathies in future with the availability of additional genetic tests, which would further increase the sensitivity of the EMG in myopathy.

Spontaneous electrical discharges in EMG play an important role in characterizing neuromuscular disorders. These have not been categorically reported in the prior studies in children. Fibrillations in neurogenic disorders suggest active denervation. In myopathic disorders, fibrillations suggest partial denervation of the muscle fibers by necrosis, inflammation, or fiber splitting.1 The identification of fibrillation potentials in patients with a myopathic EMG provides an etiological clue to the clinician. Their presence suggests a myopathy with fiber necrosis, inflammation, fiber splitting, or vacuolization on muscle biopsy. In our study, fibrillations were always present in children with inflammatory myopathies and in a high proportion of cases with dystrophic muscle biopsies.

Myotonic discharges are characteristic, but rare waveforms encountered in pediatric EMG. They comprised prolonged trains of spontaneously firing single muscle fiber action potentials, with waxing and waning amplitudes and frequencies giving them a characteristic sound.1,16 When present, they provide valuable clues to the diagnosis of muscle disorders. They may be associated with clinical myotonia, perceived by the patient as stiffness and elicited at the bedside as action or percussion myotonia. In myotonia congenita, patients may have difficulty initiating movement but usually improves after mild exertion (“warm-up phenomenon”). Paramyotonia (i.e., paradoxical myotonia) on the other hand is worsened by repeated muscle contraction, prolonged exertion, and exposure to cold temperatures.11 Diffuse myotonic discharges without myopathic motor unit potentials are the hallmark of channelopathies:

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**TABLE 3.**

Characteristics of Children in Groups A, B, and C

<table>
<thead>
<tr>
<th>Groups</th>
<th>Number</th>
<th>Fibrillations</th>
<th>Myotonic Discharges</th>
<th>Elevated CK (&gt;300 IU/L)</th>
<th>Final Diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group A (n = 32)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;2 yr</td>
<td>3</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>Congenital myopathy (1) and myopathy, undefined (2)</td>
</tr>
<tr>
<td>3-10 yr</td>
<td>18</td>
<td>10 (one with complex repetitive discharges)</td>
<td>6</td>
<td>7</td>
<td>Congenital myopathy (6), collagen VI myopathy (3), lamin A/C-myopathy (1), inflammatory myopathy (2), myotonia congenita (1), myopathy, undefined (1), muscular dystrophy, undefined (1), metabolic myopathy (2), and vacuolar myopathy, undefined (1)</td>
</tr>
<tr>
<td>11-18 yr</td>
<td>11</td>
<td>5</td>
<td>1</td>
<td>8</td>
<td>SEPN1 myopathy (1), inflammatory myopathy (2), myotonia congenita (1), myopathy, undefined (1), muscular dystrophy, undefined (5), and metabolic myopathy (1)</td>
</tr>
<tr>
<td>Group B (n = 12)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;2 yr</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>None</td>
</tr>
<tr>
<td>3-10 yr</td>
<td>5</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>Congenital myopathy, undefined (1), myopathy, undefined (1), and unclear diagnosis (3)</td>
</tr>
<tr>
<td>11-18 yr</td>
<td>7</td>
<td>5</td>
<td>0</td>
<td>1</td>
<td>Myopathy, undefined (2), focal myopathy (1), possible metabolic myopathy (2), unclear diagnosis (2)</td>
</tr>
<tr>
<td>Group C (n = 3)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;2 yr</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>1</td>
<td>Metabolic myopathy—mitochondrial (1)</td>
</tr>
<tr>
<td>3-10 yr</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>None</td>
</tr>
<tr>
<td>11-18 yr</td>
<td>2</td>
<td>0</td>
<td>0</td>
<td>2</td>
<td>Metabolic myopathy—CPT2 deficiency (2)</td>
</tr>
</tbody>
</table>

Abbreviations:

CK = Creatine kinase
CPT2 = Carnitine palmitoyltransferase II
nondystrophic myotonia (myotonia congenita, paramyotonia, and sodium channel myotonia) and hyperkalemic periodic paralysis. Conversely, myotonic discharges are more frequently associated with myopathic motor unit potentials in various myopathies: muscular dystrophies, myotonic dystrophy type I and II, myofibrillar myopathies, metabolic myopathies (glycogen storage disorders in particular acid maltase deficiency), inflammatory myopathies, drug-induced myopathies (chloroquine, colchicine, and statins), or endocrine myopathies (hypothyroidism).

In our study, seven children had myotonic discharges. Two had diffuse myotonic discharges without myopathic motor unit potentials. These two patients had myotonia on examination and were diagnosed with myotonia congenita. The other five children did not demonstrate clinical myotonia and all had less abundant myotonic discharges on their EMG with concomitant myopathic motor unit potentials. All of them had primary myopathies including congenital myopathy (three children), inflammatory myopathy (one child), and muscular dystrophy (one child).

EMG and NCS are technically challenging to perform in young children and require considerable experience of the neurophysiologist. Sometimes, it may be difficult to perform a satisfactory and adequate study in an awake or struggling infant. At our institution, we routinely perform conscious sedation in children <10 years of age for almost 20 years. In nearly all cases, we are able to get an adequate EMG study when performed under these controlled settings. The quality of the recorded waveforms has markedly improved over the era when we performed EMG without sedation (personal observation, E.J.S.). The point of conscious sedation in performing EMG and NCS has not been specifically addressed in the previous studies.

The limitations of our study include the retrospective design and the referral bias inherent to a tertiary care center. Additionally, our study has a small percentage of children <2 years of age. Although we perform semi-quantitative analysis of the motor unit potentials in all cases, we could not reliably quantitate the false positive or negative rates for myopathic recordings in the youngest children because of the small number of cases in this population. Finally, being a tertiary center with an expertise in myopathy, we cannot disregard the possibility of confirmation bias in interpreting EMG studies in these children.

EMG continues to play a pivotal role in the diagnosis of neuromuscular disorders in childhood. Breakthroughs in neuromuscular genetics have led to a changing paradigm in the utilization of pediatric EMG. In particular, the role of EMG has diminished in the assessment of the common neuromuscular disorders of childhood such as DMD and spinal muscular atrophy. Our study revealed that EMG is very sensitive in detecting myopathic disorders in children. Spontaneous electrical activities, particularly myotonic discharges, provide important etiological clues to the diagnosis. Although we have not systematically analyzed the role of conscious sedation in performing EMG in children, based on our experience, we believe conscious sedation in young children improves the quality of the study, providing reliable findings in nearly all cases. Future studies need to be performed to address this issue specifically, particularly in the youngest age groups. Metabolic myopathies should be considered and further workup warranted in the appropriate clinical setting even if EMG is negative.

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