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EFNS GUIDELINES/CME ARTICLE

EFNS guideline on diagnosis and management of limb girdle muscular dystrophies

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The limb girdle muscular dystrophies (LGMD) are termed as such as they share the characteristic feature of muscle weakness predominantly affecting the shoulder and pelvic girdles; their classification has been completely revised in recent years because of elucidation of many of the underlying genetic and protein alterations in the various subtypes. An array of diagnostic measures is possible but with varying ease of use and availability. Several aspects of muscle cell function appear to be involved in the causation of muscle pathology. These cellular variations may confer some specific clinical features thus permitting recognition of the LGMD subtype and hence directing appropriate levels of monitoring and intervention. Despite an extensive literature on the individual limb girdle dystrophies, these publications may be impenetrable for the general neurologist in this increasingly complex field. The proposed guidelines suggest an approach to the diagnosis and monitoring of the limb girdle dystrophies in a manner accessible to general neurologists.

Introduction

Objectives

To provide guidelines for the best practice management of the limb girdle muscular dystrophies (LGMD) based on the current state of clinical and scientific knowledge in the published literature.

Background

LGMD was first described as a clinical entity in 1954 by Walton and Natrass [1]. However it was not until the 1990s that linkage studies and the identification of the group of proteins associated with dystrophin at the sarcolemma began to demonstrate the heterogeneity of LGMD. Classification of LGMD was established through workshops held at the European Neuromuscular Centre (ENMC). The most recent classification is shown in Table 1 [2]. LGMD are grouped into two sections, autosomal dominant (1) or recessive (2), and further subdivided into subtypes, each of which is known by a designated suffix allocated in chronological order of gene identification. As the genes and proteins involved in these disorders are identified, this locus based approach is being superseded by a classification based on the underlying genetic defect.

With molecular clarification has come the increasing realization that it is possible in some instances to recognize characteristic patterns of disease through thorough clinical assessment. Areas of particular importance are the involvement of the cardiac and respiratory systems but other features such as the presence of muscle hypertrophy, contractures and scapular winging may also be of diagnostic help. Prognosis for LGMD is not uniform and thus timely intervention through early identification of potential complications may improve survival.

An array of diagnostic measures is possible but with varying ease of use and availability; mutation analysis for some genes is a huge undertaking and analysis of expressed proteins may be complex. Nevertheless many causative mutations have been identified and it has been possible to work towards genotype–phenotype correlations. Genetic analysis has also extended the phenotypic range in several of the subtypes, with some genes producing hugely variable clinical features in affected individuals.

Search strategy

The following search protocols were employed with relevant keywords: MEDLINE for original papers and

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This is a Continuing Medical Education article, and can be found with corresponding questions on the Internet at http://www.efns.org/content.php?pid=132. Certificates for correctly answering the questions will be issued by the EFNS.

Table 1 105th European Neuromuscular Centre workshop classification (from Ref. 2)

Disease	Mode of inheritance	Gene location	Gene symbol (gene product)
Limb-girdle MD, dominant	AD	5q22–q34	LGMD1A (= MYOT) (myotilin)
	AD (AR)	1q11–21	LGMD1B (= LMNA) (lamin A/C)
	AD (AR)	3p25	LGMD1C (= CAV3) (caveolin-3[a])
	AD	6q23	LGMD1D (CMD1F)
	AD	7q	LGMD1E
Limb-girdle MD, recessive	AR	15q15.1–q21.1	LGMD2A (= CAPN3) (calpain 3)
	AR	2p13	LGMD2B (= DYSF) (dysferlin)
	AR	13q12	LGMD2C (= SGCG) (γ-sarcoglycan)
	AR	17q12–q21.33	LGMD2D (= SGCA) (α-sarcoglycan)
	AR	4q12	LGMD2E (= SGCB) (β-sarcoglycan)
	AR	5q33–q34	LGMD2F (= SGCD) (δ-sarcoglycan)
	AR	17q11–q12	LGMD2G (= TCAP) (telethonin)
	AR	9q31–q34.1	LGMD2H (= TRIM32)
	AR	19q13.3	LGMD2I (= FKRP) (fukutin related protein)
	AR	2q	LGMD2J (= TTN) (titin)
	AR	9q34	LGMD2K (=POMT1)
	AR	9q31	LGMD2L (=FCMD) (fukutin)
	AR	11p13	LGMD2M
	AR	19q13	LGMD2N (=POMT2)

[a]Rare recessive cases have been described for 1B and 1C.

review articles (1985–2005); Cochrane database (http://www.cochrane.org/index0.htm); American Academy of Neurology (AAN) and European Federation of Neurological Sciences (EFNS) practice parameters or management guidelines (http://www.aan.com/professionals/practice/guideline/index.cfm; http://www.efns.org/); EMBASE, patient organizations (http://www.muscular-dystrophy.org; http://www.mdausa.org; http://www.mda.org.au); previous guidelines (http://www.inahta.org/inahta_web/index.asp; http://www.york.ac.uk/inst/crd/darehp.htm; http://www.g-i-n.net/index.cfm?fuseaction=membersarea).

Method for reaching consensus

The results of the literature review were evaluated by members of the task force; only those studies specific to LGMD or the subtypes have been included. Older studies pre-1985 include cases of 'limb girdle dystrophy' but without accurate molecular diagnosis it is not possible to extract reliable data from these and so they have been excluded. All the evidence was categorized as class IV [3].

Results

The LGMD are relatively recent in their identification and clarification and efforts are ongoing with further genes and proteins expected to be found. In addition, the conditions are individually rare, some with only a few families identified. To date, no substantial randomized controlled trials of management of genetically defined LGMD have been published. However as each condition has become better understood, the phenotypic features of each have become apparent through case reports and cohort studies and it is possible to recommend both general and specific good practice points [3] for the management of the LGMD based on this knowledge.

Expert consensus recommendations for management of LGMD

Aspects of care – diagnosis

Clinical assessment

General principles. Thorough clinical assessment provides the basis for directing further investigation. Neonatal course, timing of developmental motor milestones and ability to rise from the floor/presence of Gowers' manoeuvre may all be of relevance. The ability to run, hop and jump and sporting ability may be significantly affected in childhood or may be normal until even middle age. The age of onset may vary both between and within subtypes and even between patients with the same mutation.

By definition, LGMD have in common a predilection for involvement of the proximal musculature in the shoulder and pelvic girdles but these may be differentially affected, particularly in the early stages, and involvement of distal muscles may also occur. Rate of progression of the muscle weakness may not be linear. Features such as spinal rigidity, scoliosis and limb contractures should be sought. Hypertrophy, usually of

Table 2 Predominant clinical features for the more frequently occurring LGMD

Disease	Age of onset[1]	Weakness[2]	CK level[3]	Muscle hypertrophy[4]	Contractures[5]	Special features[6]	Respiratory[7]	Cardiac[8]
LGMD1A	c,d	Proximal/distal	A	No	No	Dysarthria	No	Yes
LGMD1B	a,b	Proximal/distal	A	No	Yes		Yes	Yes A, CM
LGMD1C	a–d	Proximal/distal	B/C	Some cases	No	PIRCs, RMD	No	No
LGMD2A	a–c	Proximal	B/C	Some cases	Yes		No	No
LGMD2B	b,c	Proximal/distal	C	No	No		No	No
LGMB2C-F	a,b	Proximal	B/C	Yes	Secondary		Yes	Yes CM
LGMD2I	a–d	Proximal	B/C	Yes	No		Yes	Yes CM

[1]Range of age of onset in majority of patients: a, age <10 years; b, 10–20 years; c, 20–40 years; d, age >40 years.
[2]Pattern of distribution of weakness in limb muscles.
[3]Range of creatine kinase (CK) level at diagnosis: A, normal or mildly elevated at $<5\times$ upper limit of normal; B, 5–10$\times$ upper limit of normal; C, $>10\times$ upper limit of normal.
[4]Presence of muscle hypertrophy in limb muscles may occur.
[5]Presence of early fixed joint contractures may occur.
[6]Percussion-induced rapid muscle contractions (PIRCs); Rippling muscle disease (RMD).
[7]Presence of frequent respiratory complications.
[8]Presence of frequent cardiac complications: A, arrhythmia; CM, cardiomyopathy.

calf muscles but also of other limb muscles and even the tongue, may be present. Family history may suggest an autosomal dominant inheritance or consanguinity.

Although it is not possible to provide an absolute prediction of the clinical pattern, Table 2 outlines the presence or absence of typical features in each LGMD to give a guide to the underlying diagnosis [4–6]. Exceptions to the commonly recognized patterns can occur and the table should be seen as a guide only. It is also important to point out that for mutations in some of these genes, there is clinical heterogeneity. Specific examples of this include myotilin mutations (responsible for the rare LGMD1A and myofibrillar myopathy), caveolin-3 mutations (reported with a range of presentations including hyperCKaemia, LGMD1C and rippling muscle disease) and lamin A/C mutations, which are probably the most clinically variable of all, and have been reported in at least seven distinct diseases, in some of which muscle involvement may be minimal or absent. The variability in presentation for all of these conditions means that different family members, or indeed the same individual, may present with one or more manifestations of mutation in a particular gene.

Specific clinical pointers/indicators. In contrast to the congenital muscular dystrophies and myopathies, the only LGMD which may result in neonatal hypotonia is LGMD1B (lamin A/C). None of the LGMD has been described in association with neonatal contractures. Those conditions which are most likely to present in early childhood are LGMD1B, 1C (caveolin-3 deficiency), the sarcoglycanopathies, LGMD2A (calpain deficiency) and some cases of LGMD2I. All of the LGMD may result in a lifelong decreased sporting ability. This is less probably in LGMD2B (dysferlin deficiency) which in many patients is associated with a normal sporting ability until an abrupt onset of difficulty, occasionally preceded by a transient painful swelling of calf muscles.

Age of onset is relatively well-defined for some conditions: the mean age of onset for LGMD2A is in the early teens and in LGMD2B is 20 ± 5 years [4]; however for others a much wider age range is found, such as in LGMD1C where age of onset may be from early childhood to the 8th decade depending on the phenotype [7]. LGMD2C-F are also variable in their onset and progression; some patients (typically especially β- and δ-sarcoglycanopathies) may be as severely affected as patients with Duchenne muscular dystrophy (DMD) whereas others are still ambulant into their 40s. Alpha-sarcoglycanopathy (LGMD2D) tends to be the mildest of the sarcoglycanopathies [8].

Most LGMD by definition involve predominantly proximal musculature, certainly once the full phenotype has evolved, but potential diagnostic difficulty could arise in, for example, the presence of only distal muscle involvement in the early stages of the Miyoshi type of dysferlin deficiency (although the characteristic gastrocnemius weakness is helpful) or in some patients with LGMD1B or 1C. An example of another useful discriminator is the relative preservation of hip abductor muscles in LGMD2A [9,10] and striking involvement of the posterior thigh muscles as shown on muscle MRI [11]. Scapular winging is most characteristically seen in LGMD2A and 2C-F.

Associated features such as muscle hypertrophy may be observed quite frequently in LGMD1C, 2C-F

and 2I (Fukutin related protein, FKRP). Calf hypertrophy is most common but other limb muscles may also be involved as may the tongue. The calf hypertrophy present in LGMD2I (in addition to the cardiac and respiratory involvement) resembles the Becker phenotype and has led to misdiagnosis of patients in the past. Macroglossia is seen in LGMD2C-F and 2I on occasion. Focal muscle atrophy is most typical of LGMD2A.

Contractures are most common in LGMD1B where they may occur in childhood or develop over the course of the condition, representing an overlap with the autosomal dominant Emery-Dreifuss muscular dystrophy phenotype also caused by mutations in lamin A/C. Contractures may be also be seen in LGMD2A but tend to be milder. Spinal rigidity is often a feature in LGMD1B and occasionally in LGMD2A [9]. Scoliosis is most often seen in LGMD2C-F, particularly once wheelchair dependence occurs. Specific indicators include the reported dysarthria in the rare LGMD1A (myotilin) patients. On the other hand, phenotypic variation within the same family as well as overlapping phenotypes are well-recognized; a mutation in a single LGMD gene such as caveolin-3 may produce one or more of a number of manifestations such as rippling muscles and percussion induced repetitive contractions. This also occurs in the laminopathies where some members of the family may have partial lipodystrophy or peripheral neuropathy in addition to their muscle weakness, whereas other members do not and indeed other patients may have pure cardiac disease.

Intellectual impairment and facial weakness are not characteristically seen. A malignant hyperthermia reaction to general anaesthesia has been reported only in two patients from the Hutterite population who have mutations in FKRP (rather than TRIM32).

Geographical location of cases may also be helpful. LGMD2G (telethonin) has so far only been described in Brazilian patients. LGMD2H (TRIM32) is a relatively mild form seen in some areas of Canada with onset in the second or third decade and slow progression; most patients were still ambulant into their 50s [12]. LGMD2J (titin) was described in Finnish patients initially.

Cardiac involvement is very common in LGMD1B, 2C-F and 2I whereas significant disease is infrequent in LGMD1C, 2A and 2B. Cardiac complications may take the form of dysrhythmias or hypertrophic or dilated cardiomyopathy. Patients may be affected by both a dysrythmia and cardiomyopathy, especially in LGMD1B. Respiratory muscle weakness does not necessarily accompany cardiac impairment; it is seen most often in LGMD2C-F and in 2I but tends to be insignificant in 2A and 2B. Symptoms of nocturnal hypoventilation may herald the development of significant respiratory muscle weakness and need for intervention.

Investigation

Serum creatine kinase (CK) is a simple and useful investigation provided that non-muscle conditions are excluded first. The degree of elevation may be helpful in differentiating broadly between diagnoses; typically, it may be normal or only mildly raised in conditions such as LGMD1A and 1B, moderately raised (5–10× upper limit of normal) in LGMD1C, 2A, 2C-F and 2I and grossly raised ($>10\times$) in LGMD2B.

Neurophysiology studies are of little value in refining a diagnosis of LGMD. Nerve conduction studies can exclude a neuropathy if this causes diagnostic doubt in the early stages of presentation. Electromyography usually shows myopathic features in patients with any type of LGMD with no ability to further specify the diagnosis. Laminopathy patients may additionally or exclusively have a peripheral neuropathy.

Muscle imaging with computed tomography or magnetic resonance imaging is used increasingly to determine patterns of muscle involvement. No large studies of the LGMD have been published but case reports and small series suggest characteristic patterns in some conditions. The most consistent examples are LGMD2A which selectively involves hip extensors and adductors [11], involvement of the glutei in α-sarcoglycanopathy [8] and LGMD2J where loss of the thigh muscles and involvement of tibialis anterior is present [13].

Muscle biopsy site(s) may be guided using imaging results. They will probably yield the most useful information if they are undertaken on a clinically affected muscle but preferably not one that is 'end-stage'. No studies compare open versus needle biopsies, although with the increasing number of immunohistochemical and immunoblotting procedures were possible, it is important to obtain sufficient tissue to allow meaningful interpretation.

Muscle tissue should be analysed firstly with standard histological techniques. All LGMD show dystrophic features with variation in fibre size, increased numbers of central nuclei and endomysial fibrosis. Inflammatory infiltrates are seen most commonly in dysferlin deficiency. Thus there is the potential for diagnostic confusion and patients may have received a previous diagnosis of polymyositis. Rimmed vacuoles and *Z*-line streaming may be seen in myotilin deficiency. Table 3 summarizes typical findings in each condition.

Immunohistochemistry and immunoblotting should be undertaken in a laboratory with sufficient expertise in both the performance and interpretation of these techniques. Immunohistochemical staining with a panel

Table 3 Characteristic muscle biopsy findings in LGMD

Disease	Protein	Histological features	Immunohistochemistry: Primary changes	Secondary changes
LGMD1A	Myotilin	Dystrophic, inflammatory Infiltrate, rimmed vacuoles	Myotilin normal, DGC intact	↓ Lamininγ1
LGMD1B	Lamin A/C	Dystrophic	Lamin A/C usually normal	↓ Lamininβ1
LGMD1C	Caveolin-3	Myopathic or dystrophic	↓ Caveolin-3 labelling	↓ Dysferlin
LGMD2A	Calpain-3	Dystrophic	Absent, partial deficiency or normal	Calpain-3 degradation
LGMD2B	Dysferlin	Dystrophic, inflammatory	↓ Dysferlin	↓ Calpain-3 in half
LGMD2C	γ-sarcoglycan	Dystrophic	↓ γ-sarcoglycan	↓ other SG, dystrophin
LGMD2D	α-sarcoglycan	Dystrophic	↓ α-sarcoglycan	↓ other SG, dystrophin
LGMD2E	β-sarcoglycan	Dystrophic	↓ β-sarcoglycan	Severe↓ other SG, dystrophin
LGMD2F	δ-sarcoglycan	Dystrophic	↓ δ-sarcoglycan	Severe↓ other SG, dystrophin
LGMD2G	Telethonin	Dystrophic, rimmed vacuoles	Loss of telethonin labelling	
LGMD2H	TRIM32	Myopathic, sarcotubular		
LGMD2I, 2K, 2L and 2N	FKRP	Dystrophic	Often normal	↓ lamininα2 and αDG
LGMD2J	Titin	Myopathic, dystrophic, rimmed Vacuoles	↓ Titin	↓ Calpain-3

DGC, dystrophin-glycoprotein complex; αDG alpha-dystroglycan; SG sarcoglycans; EM, electron microscopy; ↓, reduced level.

of antibodies ideally including all four anti-sarcoglycan antibodies may show one or more abnormalities. Demonstration of normal dystrophin staining is important (although there may be a mild secondary reduction in sarcoglycan deficiency). Quantitative analysis of proteins by Western blotting may be an additional useful technique for elucidating primary and secondary protein abnormalities [14,15].

Primary changes on immunoanalysis may be clear and direct analysis specifically towards the underlying genetic defect, such as caveolin-3 reduction in LGMD1C. In other diseases, because of the interdependence of the sarcolemmal and associated proteins, disruption of one member of the complex or pathway may result in the concomitant loss of interacting proteins. This is particularly prominent in disorders of the dystrophin-associated complex, where there may be reduction in all or many of the complex members, and secondary calpain-3 reduction is seen in half of dysferlin deficiency patients and in patients with LGMD2J. These *secondary* changes may lead to diagnostic difficulty, particularly when direct assay for the primary defect is difficult.

In other situations, secondary changes may be the only clue to the underlying disorder. For example, in LGMD1B lamin A/C labelling is usually normal but there is frequently a secondary reduction in laminin-β1 in adult patients. In LGMD2I, secondary reduction of laminin-α2 on immunolabelling was detected in most cases [16] and reduction in α-dystroglycan may also be seen. Similar changes are seen in the rarer conditions LGMD2K, 2L and 2N reflecting the common pathological feature in this group of loss of glycosylation of alpha dystroglycan [17]. A summary of commonly observed primary and secondary changes is shown in Table 3.

Immunoblotting has been the accepted test required for the diagnosis of LGMD2A [18]. However there is variability in the quantity and function of calpain-3 protein detected on immunoblots, even for those patients in whom a calpain mutation is proven [19] and thus emphasis may shift to earlier analysis of the calpain-3 gene [20].

One group has developed a blood-based assay for dysferlin expression in monocytes, showing that this correlates with skeletal muscle expression. This potentially avoids the need for muscle biopsy although is not in mainstream use at present [21].

DNA analysis directed to provide confirmation of mutation in the affected gene(s) is the gold standard of diagnosis, and necessary to be able to offer carrier or pre-symptomatic testing to other family members. This is more straightforward in some forms of LGMD than others, depending to a large extent on whether or not there are commonly detected mutations or if mutations in different families tend to be unique. For example, the FKRP 'common mutation' C826A in LGMD2I can be detected readily in a diagnostic laboratory whereas some of the other causative genes are large, e.g. dysferlin (55 exons), and screening for mutations a formidable task. Thus mutation analysis in these genes is at present available only in selected laboratories. Mutation detection for the rarer types of LGMD may only be available on a research basis.

Good practice points. Careful clinical assessment of factors such as the pattern of muscle involvement, associated features and family history should suggest probably diagnosi(e)s in a patient with LGMD. Confirmation of this should be achieved through the selective use of predominantly laboratory-based investigations, some of which are highly special expertised and should only be undertaken in a laboratory with appropriate expertise. In some conditions this may be relatively straightforward but in others verification of the underlying mutation presently remains in the realm of the research laboratory. In the UK, patients may be referred for assessment to the centre for limb girdle muscular dystrophy (n.scag@ncl.ac.uk) funded by the National Specialist Commissioning Advisory Group.

Assessment and monitoring of adjunctive aspects

Respiratory management. Respiratory muscle weakness resulting in symptomatic hypoventilation and respiratory failure is found in a few of the LGMD, most frequently in LGMD2I [16] and the sarcoglycanopathies. In LGMD2I and occasionally in the sarcoglycanopathies, respiratory failure may arise whilst the patient is still ambulant [2,16].

There are no recommendations specific to the LGMD but extrapolation from the monitoring and investigation of respiratory involvement in other neuromuscular conditions is helpful. Awareness of symptoms of respiratory insufficiency such as frequent chest infections, morning headache and daytime somnolence is important. Measurements of sitting and supine if $<80\%$ FVC may be made in the outpatient clinic. Overnight pulse oximetry is recommended if the FVC is $<60\%$. Annual influenza vaccination and prompt treatment of respiratory infections are suggested. Liaison with a respiratory physician with experience in the management of neuromuscular disorders is essential to ensure optimal timing of intervention with nocturnal home ventilation.

Cardiac management. The important issue of cardiac complications in LGMD as well as in other muscle conditions was considered at the 107th ENMC Workshop [22]. Cardiac involvement may manifest as a conduction defect and/or cardiomyopathy. In laminopathies, arrhythmias such as atrioventricular block, atrial paralysis and atrial fibrillation/flutter occur in the majority of patients by age 30 years and permanent pacing is required. However, even with permanent pacing, a recent paper cites a sudden death rate of 46% in lamin A/C mutation carriers and therefore recommends an implantable defibrillator [23]. Dilated cardiomyopathy arises in a third of laminopathy patients and is usually severe. Arrhthymias and hypertrophic or dilated cardiomyopathy are present in approximately 20% of sarcoglycanopathy patients. One-third of LGMD 2I patients have a cardiomyopathy which is symptomatic. The remaining LGMD do not characteristically show significant cardiac compromise.

Thus the ability to define precisely the underlying genetic defect allows a tailored approach to monitoring through better anticipation of the onset and progression of cardiac aspects. Monitoring and treatment of LGMD1B, 2C-F and 2I patients require close cardiological supervision. ECG and echocardiography are suggested as the standard initial investigations. In the absence of dedicated studies, treatment of heart failure is undertaken on general principles with early use of angiotensin-converting enzyme inhibitors. Anticoagulation may need consideration in patients with atrial fibrillation or standstill. For patients with particularly severe cardiac failure but relatively well-preserved respiratory function consideration of cardiac transplantation may be appropriate.

Good practice points. Although serial monitoring of basic measurements of respiratory and cardiac function is attainable in the neurology outpatient setting, patients with a LGMD subtype known to place them at additional risk of cardiorespiratory complications ideally should be managed in conjunction with a respiratory physician and/or cardiologist. Intervention in the form of nocturnal ventilatory assistance for respiratory failure and with permanent pacing and/or management of cardiomyopathy may be life saving. The need to monitor for and treat complications as appropriate also applies to those patients in whom the underlying diagnosis is unknown as it follows that the attendant risk of cardiorespiratory complications is also unknown, but that general principles of management will apply.

Physical management. There are no papers relating specifically to LGMD and physiotherapy, exercise or orthotic use. The application of general principles is probably appropriate, as reviewed in Eagle [24]. Prevention of contracture development through stretching and splinting orthoses is important in maximizing functional ability. Release of functionally limiting contractures (especially of the Achilles tendons) may be necessary especially in LGMD1B, LGMD2A, in childhood onset sarcoglycanopathy or LGMD2I. Scoliosis in LGMD occurs mainly after wheelchair dependence and attention should be paid to seating. The role of exercise is controversial but basic guidelines as for other types of muscular dystrophy would encourage

gentle exercise within comfortable limits and the avoidance of prolonged immobility.

Genetic counselling
Many patients seek medical advice because of concern for themselves, relatives or descendants. Delineation of the LGMD subtype allows knowledge of its autosomal dominant or recessive inheritance pattern to inform genetic counselling appropriately. Confirmation of the diagnosis in LGMD2I patients in particular has led to altered advice in some as previously they had been thought to be affected by Becker muscular dystrophy, an X-linked condition.

Drug treatment. There are no established drug treatments for the LGMD. Six patients with sarcoglycan-deficient muscular dystrophy took part in a double-blind, placebo-controlled crossover trial of creatine monohydrate. Thirty patients with other conditions were included. The mean improvement of 3% in muscle strength over the 8-week trial period was found to be significant but modest [25]. There are no relevant studies on the use of co-enzyme Q10 (ubiquinone).

Corticosteroids have an established role in DMD boys [26]; on this basis they have been used empirically in some patients with LGMD2C-F with reported improvement [27,28]. As these conditions are so much rarer than DMD, it will not be possible to perform adequate treatment trials without collaboration amongst multiple neuromuscular centres. Anti-inflammatory drugs have been suggested to suppress the inflammation seen in LGMD2B muscles. Trials in the animal model of LGMD2B are proposed and there is a randomized clinical trial underway in Germany.

Suggested date for revision of guidelines

Because of the rate of advance in this group of conditions, it is suggested that these guidelines are reviewed after 2 years.

Conflict of interests

None declared.

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