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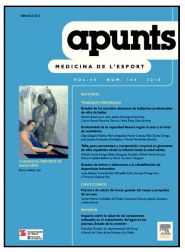

SPECIAL ARTICLE

Inborn errors of metabolism and sports

Mercedes Serrano[a], **M. Antònia Vilaseca**[b] **and Jaume Campistol**[a,*]

[a] *Servei de Neurologia, Unitat de Malalties Metabòliques, Hospital Sant Joan de Déu, Universitat de Barcelona, Barcelona, Spain*
[b] *Servei de Bioquímica, Unitat de Malalties Metabòliques, Hospital Sant Joan de Déu, Universitat de Barcelona, Barcelona, Spain*

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Abstract
Inborn errors of metabolism are a rare and very diverse group of disorders. The majority of them present at paediatric age and have an effect on the child in many spheres of life, often leading to inequalities with other children. To recommend practicing a sport (adapted depending on the condition), like the rest of the children, it is very important, not only from a physical and psychological point of view, but also for their personal and social development. To bring sport nearer to this group of patients is one more manoeuvre for their integration with the other children. However, it is not easy to make general recommendations for such a heterogeneous group of patients. In this article we attempt to make particular recommendations and observations for some of the more common inborn errors of metabolism.

*Author for correspondence.
E-mail address: campistol@hsjdbcn.org (J. Campistol).

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PALABRAS CLAVE
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Errores congénitos del metabolismo y práctica deportiva

Resumen
Los errores congénitos del metabolismo son enfermedades poco frecuentes y muy diferentes entre sí. Muchas de ellas (la mayoría) se presentan en la edad pediátrica y repercuten en diversas esferas de la vida del niño dando lugar, en muchos casos, a situaciones de desigualdad frente a los otros niños. Recomendar la práctica deportiva (práctica deportiva adaptada según el caso), tal y como se hace con el resto de los niños, es importante no sólo desde el punto de vista físico y psíquico sino también para su desarrollo personal y social. Acercar el deporte a este grupo de pacientes constituye una maniobra más para su integración con el resto de los niños. No obstante, no es fácil realizar recomendaciones generales para un grupo de pacientes tan heterogéneo. En este trabajo intentamos realizar unas recomendaciones y observaciones particulares para algunos de los errores congénitos del metabolismo de mayor frecuencia.

Introduction

Inborn errors of metabolism

Inborn errors of metabolism (IEM) are uncommon and are categorised as "rare" or "minority" diseases. They are widely heterogeneous, both in terms of their physiopathology and their clinical manifestations[1-3]. The clinical spectrum ranges from disorders that involve relatively simple treatment (with little disruption to patients' daily lives) to manifestations that cause considerable disability. In some cases, disability associated with IEM can emerge at an early age, in others, the process is slower and disability develops at a later stage.

In general, the diseases cause neurological problems (muscle tone damage, weakness, fatigue, ataxia, epileptic fits, cognitive and behavioural disorders), cardiovascular, renal and digestive difficulties, problems with the development and formation of the skeleton and/or joint mobility. With the exception of those cases in which early diagnosis and treatment allows the patient to live a normal life, inborn errors of metabolism cause disability as they can limit the capacity of the patient to undertake some daily life activities due to their physical and/or psychological effects. The disabilities (physical, psychological, sensorial, intellectual or mental) are of varying degrees of severity.

Disability and sport

As with many chronic paediatric illnesses, children with IEM are at risk of "socio-environmental deprivation" caused by inequality of opportunities for both the child and the parents. This inequality is derived from the disability of the child, defects in the adaptation of the child's surroundings and/or the frequent prolonged hospitalisation periods which are common to IEM patients. There is no doubt that the condition has a negative influence on the education of the child but it is also detrimental to affective development, giving rise to characteristic emotional traits. The cognitive-emotional situation exacerbates the initial environmental deprivation in a cyclical process of negative reinforcement.

Efforts should be made to reduce the impact of the problems faced by IEM patients; hospitalisation must be limited to those periods when it is absolutely necessary and a healthy environment for cognitive development should be created. The child needs to feel satisfaction in educational achievement as this encourages societal integration and generates physical and emotional wellbeing.

Sport and physical exercise (adapted sports, where necessary) are ideal activities for personal and social development[2]. Moreover, sport fosters integration of IEM sufferers with other children and patients. Children with disabilities are able to be involved in sport as a social good that aids integration and social insertion. Sports programmes for IEM patients should be varied (as for all children), flexible and adaptable (as required).

Anyone that suffers a disability has to confront a world that is constructed on the basis of "normal" parameters. Adapted sport can offer a simple and suitable environment for the establishment of realistic, achievable objectives for the improvement of daily life activities. Self-improvement and the strengthening of self-esteem through sport can have both psychological and social benefits for the participant. Sport can teach techniques, rules and social skills that facilitate social integration and help the IEM patient overcome shyness (a common characteristic of those that suffer these illnesses). Furthermore, team sports

Table 1 Groups of inborn errors of metabolism (IEM)

1. The most common IEM intermediate metabolism disorders
1.1. Phenylketonuria
1.2. Homocystinuria
1.3. Urea cycle disorders
1.4. Organic acidurias
1.5. Galactosemia
1.6. Others
2. IEM energy metabolism disorders
2.1. Glyconeogenesis disorders
2.2. Beta-oxidation disorders
2.3. Mitochondrial diseases
3. Complex molecule IEM
3.1. Lysosomal diseases
3.2. Peroxisomal diseases
3.3. Congenital glycosylation disorders
3.4. Glycogenosis

help children to recognise the strengths and weaknesses of their peers and this can ameliorate the stigma of illness and lead to the acceptance of others, and of themselves.

The rules and regulations of sport that must be followed help reinforce the self-discipline that is so necessary for many patients affected by IEM — sufferers often have to follow a strict diet or are subject to close monitoring, regular treatment and clinical control.

As with all children, sport should be introduced gradually, paying careful attention to the preferences (often decided by the group of friends) and abilities of the individual; above all, sport must be enjoyable. Fears will have to be confronted and support must be given, adapting the environment as necessary. With younger patients that suffer motor problems, sports that foster development of balance, agility, stability and coordination should be prioritised.

Discussion

Sport and the different IEM groups

In recent years, there has been a favourable process of growing awareness with regards to rare or minority diseases. Nevertheless, there is a dearth of bibliographic material dealing with sport and IEM patients. Based on 25 years experience, the following section outlines some of the most relevant factors that must be considered when recommending sports activities for patients suffering from the most common types of IEM.

In general, IEM can be classified into three groups, following biochemical and physiopathological criteria (Table 1).

1. The most common inborn errors of metabolism intermediate metabolism disorders

1.1. Phenylketonuria. Nowadays, this condition is usually diagnosed at an early stage and if this is the case, patients that follow a suitable diet can live normal lives. However, late diagnosis can result in cognitive disorders and serious mental retardation.

With groups of patients that have the condition under control, the practice of sport implies no additional risks as long as attention is paid to calorie intake and protein catabolism.

1.2. Homocystinuria. Early diagnosis and treatment of homocystinuria greatly improve prognosis. Sports activities should take into account the subject's cognitive level, movement difficulties, vision (patients commonly suffer myopia and crystalline lens pathologies) and osteopenia (often under treatment). Moderate exercise (avoiding endogenous protein catabolism) is relatively risk free and could stimulate an increase in osseous mass. Some patients may have vascular problems.

1.3. Urea cycle disorders. Common to this group of disorders is clinical toxicity after increased protein metabolism, due to greater ingestion of proteins or higher catabolism of endogenous proteins. When exercising, control of catabolism is vital and this can be achieved with supplementary calorific ingestion before, during and after the session. A method for encouraging mitochondrial activity (essential for the normal functioning of part of the urea cycle) is the biochemically controlled administration of carnitine.

Some urea cycle disorder patients have no significant disabilities (due to early diagnosis and correct treatment), some have cognitive problems (relatively common) and some have motor difficulties (especially those with arginase deficits that often suffer spasticity). Care should be taken to avoid inanition, stress or infection.

1.4. Organic acidurias. In the most common cases (proponic aciduria, methylmalonic aciduria and glutaric aciduria) the previous comments in relation to urea cycle disorders apply. Protein catabolism is damaging so endogenous catabolism should be avoided by means of calorific and carnitine intake.

Clinically, organic aciduria disorders are usually more disabling than urea cycle disorders. They occasionally involve serious problems of movement which can complicate the practice of sport (as happens with dystonia in cases of glutaric aciduria); adapted sport is therefore recommended and swimming is particularly useful for motor improvement.

This type of IEM disorders are characterised by a biotinidase deficit; early diagnosis and treatment can lead to a normal life. Some patients suffer sensorineural hearing loss and this is not detrimental to the practice of sport.

1.5. Galactosemia. In this instance, there are no particular risks involved with the practice of sport; in fact, moderate exercise can foster development of osseous mass. Early diagnosis and treatment can limit patient disability to minor learning difficulties.

1.6. Others. Non-ketotic hyperglycinaemia, creatine brain disorders, IEM of the neurotransmitters and pterins, sulphite oxidase deficiency, etc. In general, these conditions involve significant physical and/or cognitive disabilities. In patients with creatine brain disorders, cognitive difficulties predominate and there is less physical disability (signs of autism, mental retardation, etc.), and in these cases adapted sport is recommended.

2. IEM energy metabolism disorders

IEM include a group of diseases that make it difficult for the muscular tissue to obtain or use energy (glyconeogenesis disorders, beta-oxidation disorders, mitochondrial diseases) and this can affect the practice of sport. However, physical exercise improves patient capacity and aerobic exercise is recommended as long energy supplements are taken.

2.1. Glyconeogenesis disorders. Glycogenosis is normally included in the classification of metabolism disorders of complex molecules. It usually affects intense exercise due to the inability to mobilise glycogen deposits and offer a quick source of glucose. With this group of patients it is important to avoid competition, prolonged inanition and to ensure the supply of exogenous glucose during physical activity.

2.2. Beta-oxidation disorders. Patients have difficulty in obtaining energy from fatty acids when the energy supplied from glucose is insufficient. Prolonged exercise is therefore affected and it is important to ensure a supply of glucose (before, during and after activity) or patients may suffer ketotic hyperglycinemia. Carnitine or middle chain fatty acids are often administered. There should be a careful control of metabolism and the possible cardiovascular complications that can be generated by the illness and contraindicate or limit sport and physical exercise.

2.3. Mitochondrial diseases. These are very serious multisystemic diseases with a wide ranging clinical spectrum that includes a variety of cognitive and physical disabilities. The clinical condition and affected organs of the patient determine the possibilities for sport and physical exercise.

3. *Complex molecule IEM*

3.1. Lysosomal diseases

a) Mucopolysaccharide disease. This affects the nervous system, in some patients there is no cognitive disability but most suffer degenerative skeletal-muscle conditions and organomegalies. Moderate exercise is not contraindicated though personalised adaptation is especially important. In some cases, cognitive problems are so severe that the practice of sport is highly limited.

b) Metachromatic leukodystrophy and neuronal ceroid lipofusinoses. These are degenerative illnesses that result in severe infant disability (depending on the form). Sport is not contraindicated but degeneration quickly limits the possibilities.

3.2. Peroxisomal diseases. These are progressive illnesses that are very serious from the outset, with the exception of late onset disorders such as X-linked adrenoleukodystrophy. There are very limited possibilities for sport with these patients.

3.3. Congenital glycosylation disorders. This is another heterogeneous group of illnesses, the most common of which is phosphomannomutase deficit. In general, patients suffer both cognitive and physical disabilities, often due to associated congenital malformations. Skeletal-muscle anomalies are also common, though adapted sport is possible and beneficial.

3.4. Glycogenosis (See 2.1).

The professional environment

The clinical spectrum of IEM patients is so wide-ranging that it is difficult to make non-personalised recommendations. Many patients simultaneously suffer physical (muscular tone disorders, movement difficulties etc.) and cognitive disabilities, epilepsy and in some cases the vital organs (the heart, liver, kidneys etc.) are also compromised. It is therefore clear that great care must be taken with physical activity and the practice of sport.

The personnel involved in evaluation and control of sport and physical exercise with IEM patients should include: a physiotherapist or rehabilitator (this is standard practice with treatment/follow-up of paediatric patients with disabilities); a nutritionist/dietician (also standard practice); a psychologist (of particular relevance in cases of socialisation problems or introverted personalities) and a sports instructor. Logically, these professionals should work closely with the patient's metabolic illness unit.

Based on the patient's neuromuscular problems, a careful evaluation by the physiotherapist or rehabilitator is essential for advising the patient's doctor and family of the ideal type of exercise or sport. The participation of a sports instructor is vital for adaptation.

In cases of mild intellectual disabilities, the full integration of the patient with non-disabled children is recommended. If social interaction difficulties are suffered by the patient (similar to autism) then the advice of the psychologist must be taken.

The role of the dietician/nutritionist in ensuring that calorific, vitamin and other nutritional needs are satisfied when the patient is involved in sport or other physical exercise is of particular importance for sufferers of IEM that require dietetic treatment.

Experience shows that adapted sports competition has enormous physical and emotional value. Competition with peers stimulates interest, fosters physical wellbeing and social integration.

Conclusions

In many IEM conditions the practice of sport offers innumerable possibilities and benefits for patients, their

families and their environments. The support and direction of a group of professionals that specialise in physical exercise and metabolic illnesses is recommended. The practice of sport can generate significant physical, psychological and emotional rewards. Adapted sport and physical exercise should be fundamental to the treatment and integration of IEM patients.

References

1. Scriver CR, Beaudet AL, Sly WS, Valle D, editors. The metabolic and molecular bases of inherited disease. 8th ed. New York: MacGraw-Hill; 2001.
2. Health and development through physical activity and sport. World Health Organization, WHO/NMH/NPH/PAH/03.2, 2003. Disposable in: http://whqlibdoc.who.int/hq/2003/WHO_NMH_NPH_PAH_03.2.pdf.
3. Sanjurjo P, Baldellou A. Diagnóstico y tratamiento de las enfermedades metabólicas hereditarias. 3rd ed. Madrid: Ergon; 2010.