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Electrical stimulation as part of rehabilitation therapy in patients with haemophilia.

Estimulación eléctrica como parte de la terapia de rehabilitación en pacientes con hemofilia

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Abstract

Haemophilia is a disease that increases the risk of spontaneous bleeding. The spontaneous bleeding would appear into muscles of joints and soft tissues leading an arthropathy. To prevent recurrent bleeding and haemophilic arthropathy a prophylactic treatment has to be administered together with physical rehabilitation. In developing countries with low access to prophylaxis treatment, the level of sports done by haemophilic children is low, even though it has been recognised the importance of sports and some form of physical activity. Also in general in these countries, treatment of haemophilia does not meet the standards of developed ones.

KEYWORDS: Haemophilia; Arthropathy; Physiotherapy.

Resumen

La hemofilia es una enfermedad que aumenta el riesgo de hemorragia espontánea. El sangrado espontáneo puede ocurrir en los músculos de las articulaciones y en los tejidos blandos que conducen a artropatía. Para prevenir el sangrado recurrente y la artropatía hemofílica, debe administrarse un tratamiento profiláctico junto con la rehabilitación física. En los países en vías de desarrollo con bajo acceso al tratamiento de profilaxis, el nivel de deportes practicados por niños hemofílicos es bajo, aunque se ha reconocido la importancia de los deportes y alguna forma de actividad física. En general, en estos países, el tratamiento de la hemofilia no cumple con los estándares de los industrializados.

PALABRAS CLAVE: Hemofilia; artropatía; fisioterapia.

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INTRODUCTION

Haemophilia is a bleeding inherited disease with an X-linked recessive pattern, that it will be clinically observed only in males.[1] This disease is due to absence or deficiency of blood coagulation factor VIII in haemophilia A and deficiency of coagulation factor IX in the haemophilia B.[2]

According some reports published including the report of the World Federation of Hemophilia (WFH)[3] the estimated prevalence of the disease is about 1 in 10,000 people worldwide for the haemophilia A and 1 in 50,000 for the haemophilia B.[4,5] In Mexico, the Mexican Federation of Hemophilia reported 5,522 patients registered in 2016.[5]

Clinical manifestations

The clinical manifestation of haemophilia A and B is spontaneous and recurrent bleeding. If bleeding appears intracraneally, in the neck space o it is gastrointestinal it may be life-threatening.[6] The severity of symptoms depends on the level of deficit of the clotting factor and based on that, haemophilia is classified as mild >5%-40%, moderate: 1%-5% and severe < 1%.[1,7] Other factors that can cause bleeding in haemophilic patients are traumatism, daily physical activity and sports.[1,8]

In early ages, haemophilia produces bleedings predominantly into joints,[6,7] but they could also appear in muscles and soft tissues.[6] In children, mean age of having hemarthrosis is at 2-5 years and would be caused by minor trauma or even spontaneously.[9] When bleeding episodes occur recurrently in the same joint can lead to haemophilic arhtropathy, chronic synovitis and muscular contractures and haematomas,[4,9,10] which, in turn, lead to decreased mobility and loss of walking ability and early use of a wheelchair. The joints most frequently affected are knees, ankles and elbows.[1,9,11] Although the bleeding pattern varies among patients, in general 10 to 15 hemarthrosis occur per year.[1]

Intramuscular haemorrhages are also common in children with haemophilia[1] and if they appeared in a major muscle would produce anaemia. Haemorrhages inside the forearm and leg may cause compartment syndrome, which is an obvious risk for the limb.[9]

Diagnosis

Key aspects for the diagnosis are the clinical history (including familiar history and inhered factors), characteristics of haemorrhage, physical exam and laboratory tests.[1]

When a diagnosis of haemophilia is suspected, laboratory screening test can be done.[1] The best test to know levels of FVIII and FIX is the activated partial thromboplastin time (aPTT).[1] The definitive diagnosis of haemophilia and its classification are performed by measuring the functional level of FVIII or FIX for HA or HB, respectively. Most patients have < 30% of the factor function.[1]

Complications of haemophilia

One of the most important complications in haemophilic patients is joint bleeding which would cause arthropathy.[2,11] To manage, early diagnosis, adequate treatment, physiotherapy and avoidance of re-bleeding are crucial.[11] The clinical manifestations include warm, swollen and pain in the joint affected, and patient adopt an antialgic position which causes deformities.[11]

Non-invasive imaging techniques as radiographs and ultrasound can be used. Ultrasound is indicated in early stages of disease to detect joint alterations and muscle hematoma.[9] Nevertheless, the gold standard image technique for the

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diagnosis is magnetic resonance imaging (MRI) although its use is limited by the difficulty of the technique and accessibility problems.[9,11]

When hemarthrosis occurs repeatedly or the disease is poorly controlled, secondary synovitis appear, which should be treated as early and aggressively as possible.[11] Diagnosis could be confirmed by ultrasound for the knee or MRI for elbow and ankle. In some cases a synevectomy is needed to delay the onset of arthropathy.[11]

Another complication is muscular hematoma, which is associated with direct trauma. Most cases of muscular hematoma resolved spontaneously.[11] Clinically, it is manifested as pain and functional impairment.[9] Muscle bruising could produce muscular atrophy and compartment syndrome.[9]

Some scales are available to evaluated physical function in children with haemophilia. WHF recommend the Gilbert score for clinical evaluation but it is not very sensitive in children at early disease.[9]

The Childhood Health Assessment Questionnaire (CHAQ)[12] and the revised CHAQ with 38 questions describing the ability to perform daily activities that could be affected by joint limitation[12] are also widely used. However CHAQ was not developed specifically for haemophilic patients.[12]

Recently it has been introduced the Haemophilia Joint Health Score (HJHS),[9] which is a more sensitive version of the Gilbert score.[12] In a review published by Stephensen et al,[13] 14 clinician-assessed outcomes measures were identified to evaluated physical function in these children and the authors found that the HJHS is the recommended measure due to its good internal consistency.[13]

There is evidence that increasing risk of bleeding is associated with physical activity, especially if it is a high impact activity and it has been performed one hour before bleeding starts. However, the relative increased bleeding risk associated with physical activity is mild and the absolute increased risk is small.[7] On the other hand, prophylactic clotting factor seems to have a greater absolute effect on bleeding risk than physical activity.[7,14]

Treatment

The gold standard in the current management of haemophilia is based on the replacement of the missing or deficient factor.[1] As a general rule the dose of FVIII has to be administered every 8-12 h and FIX every 12-24 h.[1] There are to treatment forms: prophylaxis or preventive treatment and on demand treatment.

Usually the prophylaxis is done with FVIII at dose of 10-15U/kg/d or 20-40IU/kg every second day or three times weekly in haemophilia A or twice weekly in haemophilia B,[14] and the objective is to maintain a FVIII concentration (FVIII:C) >1% of normal levels.[14]

The efficacy of prophylaxis to prevent bleeding and arthropaty in children has been stated in some studies.[11,15] However it has been found that there are big differences in treatment accessibility between developed and developing countries, and even within the same country, with these differences being determinant for the clinical evolution of joint bleeding.[1,16] It is remarkable that only 30% of patients worldwide receive the appropriated treatment for haemophilia,[1] probably due to high cost of this medication.[1]

On demand treatment consists of an intravenous administration of 2 to 30 units of FVIII/kg when bleeding occurs until symptoms diminish.[11,17]

Primary prophylaxis is a regular treatment during 45 weeks of the year[14] and its objective is to avoid joint damage.[1] The goal of secondary prophylaxis is to delay the arthropaty and it is administered as a regular treatment started after two or more bleedings and during 45 weeks after joint disease has appeared.[1,14] Some evidence suggest that prophylaxis is able to prevent recurrent joint bleeding[18,19] and it is recommended for children.[8,18]

The main complication of treatment is the development of inhibitory antibodies against external coagulation factors.[14] To avoid this, medications with high safety and efficacy standards are currently available to improve the management of these patients, known as bypass agents,[1] such activated prothrombin complex concentrates (APCC, factor eight inhibitor bypassing activity-FEIBA) and recombinant activated factor VII (rFVIIa, NovoSeven).[14] Both agents have demonstrated their efficacy and safety in decreasing the frequency of bleeding.[20] But the high cost of this medications is the responsible for the low level of prophylaxis implementation worldwide.[18,21]

Physical activity

In the past decades, the advice for haemophilic children were to avoid sports or just doing non-impact activities such swimming and walking,[7] but at the same time an increase of obesity and chronic joint disease was observed in those children due to inactivity.[11,16,22] Also these children may have a higher risk for reduced bone density.[23] As a result of new and safe molecules of FVIII and FIX, with long half-lives,[14,24] the current tendency is to advise children to being more active and to increase their sports level[16] in order to prevent obesity and metabolic disorders and to improve muscular integrity, cardiovascular health and psychosocial abilities.[16,23,25,26] albeit they have to avoid impact activities.[7] A number of studies have observed a relationship between low-physical activity and reduced lumbar bone mass in haemophilic patients.[23,26] A study published by Broderick et al in 2013 stated that Australian children with haemophilia dedicate near 8 hours per week to physical activity (including 3.8 h in vigorous activity) and 25 h per day to small-screen entertainment, with this level of activity being not in accordance with the Australian guidelines, which recommend at least one hour daily of moderate to vigorous physical activity and no more than two hours per day of small-screen time.[16] Recommendations of WFH and the evidence published stated a consensus on the needed to encouraged children to practice some sport in order to improve their general well-being.[24]

Physical rehabilitation

Rehabilitation and replacement therapy seems to be the best approach in the conservative management of haemophilic patients in order to protect the musculoskeletal system against repeated bleeding and reduce their morbidity rates and improve their quality of life.[9] Pharmacologic treatment is not enough to prevent and treat musculoskeletal bleeding, even more if patients have a sedentary lifestyle.[24] Haemophilic patient needs complementary treatments as rehabilitation and physiotherapy together with physical exercise and sport to improve their musculoskeletal health.[24]

In developing countries where the use of prophylaxis is not widespread, physical activity and sport should also be encouraged.[24] In those countries treatment of bleeding episodes is usually rest and cold, and when clinical episode is over performing a simple exercise program to restore mobility and strength is recommended.[24] This recommendation also applies for patients with circulating inhibitors.[9,24]

To treat hemarthrosis, the first treatment is replacement therapy. If this therapy could be

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administered during the first 2 hours after the onset, the amount of bleeding will be limited.[9,27] After 24 hours, if bleeding has stopped, isometric exercise could be started together with passive mobilisation of knee. To alleviate pain pulsatile ultrasound and electro stimulation can be used.

Electrostimulation

Looking for methods of muscle strengthening with no risk increase for patients with risk of muscular bleeding, Gomis et al published the results of their study aimed to assess the effects of electrical stimulation program over a 8 weeks on muscle trophism in haemophilic arthropathy and confirm the efficacy of this technique improving muscular strength due to hypertrophy produced by electrical stimulation.[2]

Among the different currents used for electrical stimulation, the Kotz currents are the most frequently used for strengthening, due to its ability to obtain changes in muscular mass and strength. It has been observed that these currents relieve articular pain.[28]

When electrical stimulation is applied in tissues, a transformation occurs from electrical energy to thermic energy which leads vasodilatation and improvement of throphism. The aims of electrical stimulation in haemophilic patients with hemarthrosis are analgesia, to accelerate reabsorption of hematoma and to help in strengthening muscles.

Some studies have been published evaluating electrical stimulation in patients with haemophilia.[2,10] One of this, previously mentioned, included 15 patients with severe haemophilia and 15 healthy volunteers as a control group with no intervention. Results in haemophilic patients showed significant increase in muscle diameter, isometric force and electromyography activity of the biceps brachii while there were not significant changes in control group.[2]

Another study, the first one testing this technique in haemophilia, included 10 patients with haemophilia A. A total of 18 sessions of electrical stimulation were applied to the quadriceps of patients, and results were compared with healthy volunteers. After treatment, haemophilic patients had a strength gain of 13.8% in the stimulated leg. The authors concluded that electrical stimulation help to increase strength and trophism, it is not dangerous for patients and it can be used as a therapy in haemophilia.[10]

Haemophilia in Mexico

Access to treatment is the main challenge by the majority of people with haemophilia in the world, and Mexico is no an exception.[21]

The Haemophilia Federation of Mexico (FHRM) estimates that among the 6,000 people who suffer from it in the country, only 30% receive adequate medical treatment.[1-8] In Mexico, children suffer between 10 and 37 bleeding episodes per year, and they are treated with 530 to 817 UI/kg/year of factor.[21] In general, in developing countries, treatment of haemophilia does not meet the standards of developed countries,[1] which implies a high level of disabling locomotor complications, transfusion infections, and shortening of life expectancy.[1]

As it has been stated prophylaxis treatment preserves musculoeskeletal health, and early prophylaxis decreases the risk of developing inhibitors in untreated patients.[1] Even though, some barriers to its widespread use have been identified as cost, lack of education of patients and their family members, lack of personnel specialized in haemophilia, and intravenous administration.[1,21] On the other hand, the cost of prophylaxis may be balanced by days gained at work or at school, less hospitalizations, less orthopaedic surgery and better quality of life.[29]

REFERENCES

1. García-Chávez J, Majluf-Cruz A. Hemofilia. Gac Méd Méx 2013;149:308-21.
2. Gomis M, González L-M, Querol F, Gallach JE, Toca-Herrera J-L. Effects of electrical stimulation on muscle trophism in patients with hemophilic arthropathy. Arch Phys Med Rehabil 2009;90:1924-30.
3. WFH. Guidelines for the management of haemophilia. Available in https://www.wfh.org/en/page.aspx?pid=646 Last access feb-2017.
4. González LM, Querol F, Gallach JE, Gomis M, Aznar VA. Force fluctuations during the Maximum Isometric Voluntary Contraction of the quadriceps femoris in haemophilic patients. Haemophilia 2007 Jan;13(1):65-70.
5. Federación de Hemofilia de la República Mexicana, A.C. Reporte de hemofilia en México. 2014. Available in http://www.hemofilia.org.mx/web16/biblioteca/ Last access feb-17.
6. Kenet G, Chambost H, Male C, Lambert T, Halimeh S, Chernova T, et al. Long-acting recombinant fusion protein linking coagulation factor IX with albumin (rIX-FP) in children. Results of a phase 3 trial. Thromb Haemost 2016 Sep 27;116(4):659-68.
7. Broderick CR, Herbert RD, Latimer J, Barnes C, Curtin JA, Mathieu E, Monagle P, Brown SA. Association Between physical activity and risk of bleeding in children with hemophilia. JAMA 2012;308(14):1452-1459.
8. Diagnóstico y tratamiento de Hemofilia Pediátrica México. Secretaría de Salud,2009. Actualización 2012. Disponible en www.cenetec.salud.gob.mnx/interior/gcp.htlm Último acceso feb-2017.
9. De la Corte-Rodriguez H, Rodriguez-Merchan EC. The role of physical medicine and rehabilitation in haemophiliac patients. Blood Coagul Fibrinolysis 2013;24(1): 1-9.
10. Querol F, Gallach JE, Toca-Herrera JL, Gomis M, Gonzalez LM. Surface electrical stimulation of the quadriceps femoris in patients affected by haemophilia A. Haemophilia 2006 Nov;12(6):629-32.
11. Rodriguez-Merchan EC. Prevention of the musculoskeletal complications of hemophilia. Adv Prev Med 2012;(2012):1-8.
12. Groen W, Van der Net J, Bos K, Abad A, Bergstrom BM, Blanchette VS, et al. Joint health and functional ability in children with haemophilia who receive intensive replacement therapy. Haemophilia 2011;17:783-790.
13. Stephensen D, Drechsler WI, Scott OM. Outcome measures monitoring physical function in children with haemophilia: a systematic review. Haemophilia 2014;20:306-321.
14. Giordano P, Franchini M, Lassandro G, Faienza MF, Valente R, Molinari AC. Issues in pediatric haemophilia care. Italian J Pediatrics 2013;39:24.
15. Gringeri A, Lundin B, von Mackensen S, Mantovani L, Mannucci PM. A randomized clinical trial of prophylaxis in children with hemophilia A (the ESPRIT Study). J Thromb Haemost 2011;9(4):700-710.
16. Broderick CR, Herbert RD, Latimer J, Van Doorn N. Patterns of physical activity in children with haemophilia. Haemophilia 2013;19:59-64.
17. Rodriguez-Merchan EC, Jimenez-Yuste V, Aznar JA, et al. Joint protection in haemophilia. Haemophilia 2011;17(Suppl. 2):1-23.
18. Feldman BM, Funk S, Lundin B, Doria AS, et al. Musculoskeletal measurement tools from the International Prophylaxis Study Group (IPSG) Haemophilia 2008;14(Suppl. 3):162-169.
19. Blanchette VS, Manco-Johnson M, Santagostino E, Ljung R. Optimizing factor prophylaxis for the haemophilia population: where do we stand? Haemophilia 2004;10(Suppl 4):97-104.
20. Carcao M, Lambert T. Prophylaxis in haemophilia with inhibitors: update from international experience. Haemophilia 2010 Mar;16 Suppl 2:16-23.
21. Tlacuilo-Parra A, Villela-Rodriguez J, Garibaldi-Covarrubias R, Soto-Padilla J, Orozco-Alcala J. Functional independence score in hemophilia: a cross-sectional study assessment of Mexican children. Pediatr Blood Cancer 2010 Mar;54(3):394-7.
22. Khawaji M, Astermark J, Akesson K, Berntorp E. Physical activity and joint function in adults with severe haemophilia on long-term prophylaxis. Blood Coagul Fibrinolysis 2011;22(1):50-55.
23. Tlacuilo-Parra A, Morales-Zambrano R, Tostado-Rabago N, Esparza-Flores MA, Lopez-Guido B, Orozco-Alcala J. Inactivity is a risk factor for low bone mineral density among haemophilic children. Br J Haematol 2008 Mar;140(5):562-7.
24. Querol F, Pérez-Alenda S, Gallach JE, Devís-Devís J, Valencia-Peris A, González Moreno L. Hemofilia: ejercicio y deporte. Apunts Med Esport 2011;46(169):29-39.
25. Engelbert RHH, Plantinga M, Van der Net J, et al. Aerobic capacity in children with hemophilia. J Pediatr 2008;152:833-8.
26. Barnes C, Wong P, Egan B, et al. Reduced bone density among children with severe hemophilia. Pediatrics 2004;114:e177-81.
27. DiMichele D. Hemophilia. New approach to an old disease. Pediatr Clin North Am 1996;43:709-736.
28. Niedźwiedzka B, Wróbel P, Trabka R. The impact of muscle training by Kotz phasal currents on increased strength and mass of the medial head of the quadriceps muscle of the thigh in patients with degenerative disease of the femoropatellar joint. Ortop Traumatol Rehabil. 2002 Apr 30;4(2):218-21.
29. Hay CR. Prophylaxis in adults with haemophilia. Haemophilia 2007 Sep;13 Suppl 2:10-5.

https://doi.org/10.24245/rhematol.v20i2.3106