Physiotherapy Intervention for Joint Hypermobility in Three Cases with Heritable Connective Tissue Disorders

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ABSTRACT

Background: In joint hypermobility syndromes, chronic pain is the most disabling symptom.

Findings: In our three caricatural cases [Marfan syndrome, Ehlers-Danlos syndrome, and Osteogenesis Imperfecta], we emphasized that it was important to avoid stretching and to train within a controlled range of motion. Submaximal eccentric exercises within a safe range of motion were incorporated to increase the active control of the joint positioning. Each treatment had to be adapted to the individual patient and had to include specific home exercises.

Conclusion: In each case, physiotherapy gave good results in relation to pain, quality of life and stability of rehabilitated joints.

KEY WORDS: Joint hypermobility syndrome, pain, Marfan syndrome, Ehlers-Danlos syndrome, osteogenesis imperfecta

INTRODUCTION

Joint hypermobility involves an increased range of joint motion compared to normal amplitudes in individuals of the same age, sex, and ethnic group (1). General joint hypermobility is common to many diseases. Benign joint hypermobility syndrome [BJHS] affects between five and 10 percent of the Caucasian population, but it also includes rare hereditary dystrophies with abnormal collagen structure or metabolism, such as Ehlers-Danlos syndrome [EDS], Marfan syndrome [MFS], and osteogenesis imperfecta [OI]. Chronic pain is the most frequently reported. There can be multiple origins of the pain: high frequency of subluxations, repeated pathologies of tendons, ligaments, peripheral nerves, soft-tissue contracture, and repeated surgery (2-7).

According to the management of Kerr and Grahame (8) and Ferrell et al. (9) about hypermobility joint syndrome, we treated three young patients affected with MFS, EDS, OI, and severely disabled by chronic pain. Marfan syndrome is a hereditary autosomic dominant disease (10), but in one case out of three, it is a new mutation of the 15q21 gene [FBN1] involving a defect in the synthesis of fibrilline-1 or of another gene [3p25-p24.2; MFS2] that encodes for TGF-β receptor 2 [prevalence 1/5000] (10). The effects are musculoskeletal, cardiac, ocular, pulmonary, dural, and cutaneous (10). Diagnosis is primarily clinical and is confirmed by a genetic analysis of the FBN1 [and MFS2] genes. Ehlers-Danlos syndrome is due to errors involved in type I, III, or V collagen synthesis or to an enzymatic deficit of lysyl hydroxylase or procollagene peptidase accuting in the synthesis of conjunctive tissue [prevalence 1/5000] (5). There are eight different types. The major criteria to detect EDS exist in varying degrees: joint hypermobility and cutaneous hyperextensibility (11). Histological examination can help to detect pathology of conjunctive tissue, but seldom helps to make a precise diagnosis. The detection of specific biochemical abnormality, in the context of a classical, vascular, or other subtype of EDS, is easily detected, as is the detection of the two

alleles of the COL5A1 gene (11). However in the hypermobile form of EDS, the genetic cause is still unknown and electrophoresis of collagen is normal in most cases. The diagnosis of the standard EDS type III is then primarily clinical and could correspond to BJHS (11). Osteogenesis imperfecta is either autosomic dominant or autosomic recessive, and results from an abnormal gene coding for the pro-chain α-1 and α-2 of collagen type I [prevalence 1/20000] (12). There are five forms of various lesions either nonviable or viable (12). Symptomatology is dominated by excessive bone brittleness, frequent fractures, and deformation of the long bones (12). There is also joint hypermobility, blue sclerotics, imperfect dentinogenesis, and deafness. Diagnosis is made clinically, sometimes confirmed through the description of changes of the COL1A1 and COL1A2 genes (12).

CASE REPORTS

Joint hypermobility of each patient was evaluated using the revised Brighton criteria made by Grahame et al. (13) [Appendix 1] and the locomotor aspects [Table 1] were analyzed. Pain experienced was evaluated using a visual analog scale [VAS] and perceptions of quality of life using the Medical Outcome Study Short Form-36 [MOS SF-36] with a comparison to the normative data for the age of 18 years. All three patients underwent an osteodensitometry test [Dexa QDR] in order to evaluate bone mineralization. We used an isokinetic device for muscle strength assessment and reeducation in one case.

Case 1

L.J. was referred to our physical medicine department because of back pain and ulnar tendinopathy. Marfan syndrome was detected at the age of four years. Her father was known to be affected. The disease was also detected later in her younger sister. She presented a marfanoïde habitus with a dorso-lombar compensated scoliosis [35° at the dorsal level, 42° at the lumbar level] and drooping shoulders. Her bone density level was of 0.893 g/cm² for lumbar spine and 0.743 g/cm² for femoral neck, in the normal ranges for her age and sex,

respectively. For several years she complained from polyarthralgy [wrists and shoulders] and had frequent ankle sprains [Table 1]. She suffered from a mitral valve prolapse with effort intolerance but her cardiovascular status was stable. She walked at least 3 kilometers a day. According to the revised Brighton criteria, she presented severe joint hypermobility. Her VAS score was at 8/10 for back pain. Her quality of life assessment was two standard deviations below the mean for “physical health” and “physical role” and between one and two standard deviations for body pain and general health. Her social life was also affected: she didn’t participate at activities for young people, such as dancing, hiking, etc. [Table 2]. She was in her first year of study as an industrial engineer and practiced cello regularly. She could barely attend courses full days because of back pain. She had to restrain cello practice as she developed pain in the tendon of the left extensor carpi ulnaris.

The current problems to be treated were back pain and left extensor carpi tendinopathy. She was re-educated twice a week for two months in our service. She was instructed to correct her drooping shoulders and her hypotonic attitude in front of the mirror. She had to adapt the adequate spine positions when sitting, walking, standing, and sitting on the Bobath ball. She did not do any paravertebral stretching nor lumbar column global self-elongation. She practiced analytical exercises; parts of them were inspired from the Klapp method: strengthening muscles on the convex side of the scoliosis and reinforcement of the abdominal muscles. Pulse and blood pressure were regularly controlled. She was given home exercises to do for at least ten minutes twice a day. For the left extensor carpi tendinopathy, she was given a rigid molded orthosis restricting lateral wrist mobility to be worn when playing the cello. After two months, treatment was interrupted because the symptomatology was improved. The spine was then less painful. Her VAS score had dropped from 8 to 2/10 and her latest MOS SF-36 rating showed an improvement in her physical health and role [Table 2]. She went through her last session of exams at her university without complaining

of spinal pain. A partial correction of her hypotonic attitude and drooping shoulders was obtained. She continues to wear orthoses when playing the cello. After our follow-up she was advised to continue her exercises at home every day.

Case 2

C.L. consulted us for pains in the right elbow and the right wrist [dominant side] after a season of tennis. She presented with a severe clinical form of joint hypermobility, which can correspond to an EDS III. Her bone density level was normal for her age: 1.123 g/cm² for lumbar spine and 1.007 g/cm² for femoral neck. Her revised Brighton score was severe [one major criterion and two minor criteria; Table 1]. She was the product of a twin pregnancy [the twin died in the fourth month of gestation]. Within her family, her grandfather was hyperlax and he died of a cardiovascular pathology. Her mother and one first cousin also suffered from joint hypermobility and her maternal half-brother suffered from scoliosis and has experienced several fractures. C.L had frequent epistaxis [like her mother] and was also myopic. Furthermore, she also suffered of repetitive knee and ankle sprains and subluxations when she was playing soccer and consequently stopped that activity. Her VAS score was 7/10 for right elbow and wrist but her MOS SF-36 results showed no deficit [Table 2]. She was in high school and played tennis regularly.

Physiotherapy [three times a week] consisted of wrist prosupination and flexion extension muscle group reinforcement and proprioceptive training. She had a spontaneous increased range of motion [dorsal flexion at 100° and palmar flexion at 110°] and a defect of control for lower range, at any speed, as evaluated on the isokinetic dynamometer. Thus she was trained to move her wrist at increasing speeds [30°/s [second], 60°/s, 90°/s] within a limited range of motion in flexion and extension. To maximize safety, strengthening exercises were undertaken on an isokinetic dynamometer after an evaluation which showed asymmetrical values at the expense of the right-hand side, at slow [60°/s] and fast [180°/s]

speeds. All the more so since that our purpose was to improve the gesture control, she started a submaximal eccentric program, using slow speeds, very gradually intensified, in a safe range of motion in order to promote protective braking action of the joint (14). C.L. was also given an orthosis restricting the joint range of motion of the wrist when playing tennis. The patient noted a decrease in pain [her VAS score dropped to 1/10] and an increase in the stability of her right arm even when playing tennis as reported by the patient and the objectification of a better control of the positioning of the elbow in space. Isokinetic evaluation highlighted symmetric values and an improvement in maximal torque of 20 to 25 percent in all trained muscles of the right elbow**.** After 18 sessions, the treatment was stopped because of good results. She was also given individualized home exercises: mobilization of the wrist of a precise angular range with or without blinded eyes, and isometric strengthening for several positions of the wrist.

Case 3

V.R. was referred to us for repetitive luxation of the mandible and ankle instability. Additional symptoms were patellar and wrist instability. The clinical diagnosis of OI was made at the age of 11 years. She had a succession of fractures: one of the left and one of the right forearm, one at the level of the foot, and one of the right scaphoid. She also had luxations of the patella, the mandible, and the left wrist. In addition, she developed a pain when abducting her hip even though all imaging examinations were negative. She experienced repeated sprains of the wrists and ankles. She was operated for strabismus at the age of five years and had frequent epistaxis, as well as relatively significant hematoma. Cicatrization was slow, without keloid scar, and was sometimes even atrophic. She had a rather significant level of osteoporosis: 0.658 g/cm² at the lumbar level; normal value at the hip: 0.838 g/cm² [Table 1]. Her maternal grandaunt probably had the same problem of fractures, just like this grandaunt's two daughters, who themselves also present with

osteoporosis. Propensity to epistaxis and hematoma was described in her mother and brother. Her VAS score was evaluated at 8/10 for the pain induced by luxations and her MOS SF-36 results [Table 2] showed a bad general health and limitations with regard to heavy physical activities: running and carrying heavy loads. She was in the first cycle of high school and had bad results in her exams. She had problems of integration and because of her frequent absences. She corresponded to the revised Brighton criteria of joint hypermobility [one major criterion and two minor criteria]. Although the criteria are for patients 16 years of age or older, mandibular luxation and ankle instability are considered pathologic. The duration of unipedal standing was less than 15 seconds before rehabilitation.

Her treatment was successively focused on each of the four current symptoms. Since the fracture risk was high, isokinetic strengthening was avoided and rehabilitation was careful. She received mostly proprioceptive training. She wore a mandible splint at night and was taught to open her mouth without diduction, using the tongue as a stabilizer. She had exercises at home. Ankle and knee instability were reeducated by isometric reinforcement [tibialis anterior, peroneus longus, and vastus medialis] and proprioceptive exercises first on unipedal station, then on an unstable Freeman plate. Electromyostimulation was applied on these muscles with a “computerized muscle pocket exerciser” [COMPEX®]. She also learned to avoid subluxations of the wrist, through proprioceptive exercises similar to those of C.L. She returned to physical training at school owing special arrangements with the educational team. The patient noted a reduction in the subluxations as well as a reduction in the painful sprains [her VAS score has dropped to 2], and her latest MOS SF-36 rating has shown an improvement nearing the normal rating in her general health [Table 2]. She took 1 g of calcium and 400 units of vitamin D per day. Even if intravenous bisphosphonates reduce fracture and decrease pain, we did not prescribe a bisphosphonate therapy. Now the consensus is that in the absence of fracture and with a stable bone status, bisphosphonate injections are

not indicated (12).

DISCUSSION

Our three patients presented rare hereditary disorders of connective tissue with hypermobility syndrome: EDS, MFS, and OI. As already mentioned in such patients, the quality of life is reduced because of chronic pain (2-7).

The literature concerning their management (8,9) does not include randomized controlled studies that would take a rather long time to perform in these rare diseases. Because caution is mandatory for those patients with cardiovascular or fracture risk, cardiologist opinion and bone density measurement could be necessary. However, normal bone density does not exclude a fracture risk related to bone architecture, particularly in these patients.

The three patients were referred at least partially for an acute pain: ulnar tendinopathy [L.J.], wrist sprain [C.L.], and jaw and ankle sprain [V.R.]. Acute problems required an antalgic physiotherapy [i.e. cold packs, electrotherapy], followed by a progressive return to a normal joint range. The patients were fitted with an orthosis for potentially traumatic situations [ulnar for cello, wrist for tennis, and dental splint for temporomandibular instability].

Chronic pain is also a complaint with an impaired quality of life. It is related to gradual ligament and capsular elongation, aggravated by lack of proprioception and muscle weakness; muscle spasms can add pain locally (3,5).

The goal of rehabilitation is thus proprioceptive training, muscle spasms release, and muscle conditionning to protect ligaments and capsula (8,9). The patients must receive a clear description of their disease and the explanations must be rational for adapting adequate attitudes. So after intensive rehabilitation [18 sessions twice a week], careful follow up and coaching would be advisable. The patient needs to keep his motivation and must daily

exercise at home. In our approach, they are asked to call any time if any problem or pain worsening or instability occurs.

Our MFS patient had scoliosis, which gave her pain and posture disorders. The classic conservative treatment of scoliosis consists of stretching, pelvic retroversion, and muscular reinforcement. In this specific case, we avoided stretching. Moreover, in patients with hypermobility, protrusio acetabuli fatigue fracture has been described after vigorous stretching (4). It was very important to carry out muscular reinforcement as part of the treatment (8). However this had to be performed carefully to be in line with the recommendations of the cardiologist. Also, the fitness exercises had to be adapted. We focused on exercises centered on the spine and the abdominal wall. We insisted on the proprioceptive rehabilitation with the Swiss ball. Advices of good posture and control of correct attitude were repetitively given during the sessions (8).

In our EDS patient, the goal was to avoid hypermobility by using the muscles as a protective brake in the control of joint positioning (14). The protective role of muscles mainly results from eccentric conditions. Although the eccentric exercises against manual resistance would be possible, we found some advantages in using an isokinetic dynamometer in terms of safety: the speed control, a fixed range of motion managed by electronic end stop, and the control of the level of developed force [graphic and values on the screen]. Moreover, during exercises, in case of pain and stop of muscular contractions, the isokinetic device is immobilized; the movement is forced on the basis of a minimal tension to develop and not like a “blind” engine. If the patient reaches a level of force higher than the fixed limit, the device stops. However, this type of device is expensive and need adept personnel (15). With regard to the selected method for the follow-up of our patient, only the concentric mode was evaluated. By definition, the goal of the evaluation is to obtain the maximal contraction intensities for each studied muscular group. Given that the developed tensions out of the

eccentric mode are higher than that produced through concentric contractions, and that we decided to avoid any risk resulting from maximal eccentric contractions, particularly in a young subject [brittleness of ossification cores, etc.], we only evaluated the concentric mode. Our purpose was less to perform strengthening exercises than to improve the gesture control by the meaning of submaximal eccentric program. Therefore rehabilitation began using submaximal eccentric exercises at slow speeds, very gradually intensified, in a safe range of motion of the joint (15). Thus isokinetic reeducation can strengthen specific muscles and can also be used for proprioceptive training (14). She did not suffer from luxation/subluxation anymore because she also wore a semi-flexible orthosis during her sports activities.

In the case of the OI patient, prudence was mandatory in order to avoid any fractures. Rehabilitation had to be carried out avoiding high resistance and reinforcement was performed through sub-maximal isometric contractions using electrostimulation. We excluded isokinetic training, preferring proprioception exercises (9). In order to avoid mandibular luxation, the patient wore a mandibular splint at night (2).

CONCLUSION

Joint hypermobility syndrome was associated with cardiac insufficiency in the case of MFS and major osteoporosis in the case of OI. Based on our experience, bone density and cardiovascular evaluation could be mandatory before beginning rehabilitation.

Despite the severe physical conditions of our patients, we reduced their pain level and improved their [physical] health and physical role by using a careful, specifically adapted reeducation program (8). We emphasized that proprioceptive exercises are mandatory (9,14). Submaximal eccentric exercises were implemented to increase the active control of the joint positioning (14,15). Each treatment had to be adapted to the individual patient and had to include specific home exercises and life habits.

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Table 1: Locomotor Profile in our Three Patients

	Case 1 [L.J.]	Case 2 [C.L.]	Case 3 [V.R.]
Age [years]	19	16	13
Height [cm]	182	170	163
Weight [kg]	56	55	62
Beighton score [out of 9]	5	6	4
Involved joints:			
spine	X		
feet	X	X	X
wrist	X	X	X
temporomandibular joint			X
knee			X
Osteopenia - osteoporosis			X
Arachnodactyly	X	X	

Table 2: Medical Outcome Study Short Form-36 Scores for the Ages 18 to 24 Before and After Physiotherapy in the Three Cases

MOS SF-36 ASPECT	Mean value	Case 1 [L.J.]		Case 2 [C.L.]		Case 3 [V.R.]	
		Before	After	Before	After	Before	After
Physical health	92.8 ± 16.8	55**	75*	100	100	90	90
Physical role	91.8 ± 22.6	25**	75*	75	75	25**	50*
Body pain	86.6 ± 17.9	50.7*	75*	100	100	45*	75
General health	72.0 ± 20.1	50*	50	70	100*	45*	65
Vitality	66.4 ± 17.1	60	60	80	80	60	60
Social function	90.2 ± 16.4	50	60	80	80	100	100
Emotional role	82.9 ± 31.1	100	100	100	100	100	100
Mental health	74.8 ± 15.4	64	64	72	72	68	68

MOS-36 = Medical Outcome Study Short Form-36

There is no P value. The scores are considered as abnormal if they are below 2 standard deviations [σ]. Physical health in case 1 and physical role in case 1 and 3 are below 2 σ. These scores are improved after reeducation.

* = >1 σ away from mean, ** >2 σ away from mean

311 **Appendix 1: Revised Brighton Criteria made by Grahame et al. (13)**

Major criteria:

- ✓ A Beighton score of 4 out of 9 or greater
- ✓ Arthralgia for longer than 3 months in four or more joints

Minor criteria:

- ✓ A Beighton score of 1, 2, or 3 out of 9
- ✓ Arthralgia in one to three joints or back pain or spondylosis, spondylolysis/olisthesis
- ✓ Dislocation in more than one joint or in one joint on more than one occasion
- ✓ Three or more soft tissue lesions [e.g. epicondylitis, tenosynovitis, bursitis]
- ✓ Marfanoid habitus
- ✓ Skin: striae or hyperextensibility or thin skin or abnormal scarring
- ✓ Eye signs: drooping eyelids or myopia or antimongoloid slant
- ✓ Varicose vein or hernia or uterine/rectal prolapse
- ✓ Mitral valve prolapse

➔ Hypermobility syndrome if:

2 major criteria

OR 1 major criterion + 2 minor criteria

OR 4 minor criteria

Note: Beighton scale [1 point by positive criteria]

- Passive dorsiflexion of the little finger with 90° [bilaterally]Passive opposition of the thumb to the volar aspect of the forearm [bilaterally]
- Hyperextension of the elbow 10° [bilaterally]
- Recurvatum of the knee 10° [bilaterally]
- Ability to put hands flat on the ground with the legs straight

Total out of 9

312

313