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Original Article

Hylonome

Physical activity in youth with osteogenesis imperfecta type I

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Abstract

Introduction: Individuals with Osteogenesis Imperfecta (OI) type I often show muscular weakness. However, it is unclear whether muscular weakness is a consequence of physical inactivity or a result of the disease itself. The aim was to assess muscle function in youth with OI type I and evaluate physical activity (PA). **Methods:** Fourteen children with OI type I (mean age [SD]: 12.75 [4.62] years) were compared to 14 age- and gender-matched controls (mean age [SD]: 12.75 [4.59] years). Muscle force and power were determined through mechanography. PA and daily energy expenditure were measured with an accelerometer and a questionnaire. **Results:** Compared to controls, children with OI type I had lower muscle force and power. OI type I children were as active as their healthy counterparts. **Conclusions:** Children and adolescents with OI type I and their healthy counterparts did not reached daily recommendations of PA. Given their muscle function deficit, youth with OI type I would benefit to reach these recommendations to prevent precocious effect of aging on muscles.

Keywords: Osteogenesis Imperfecta, Accelerometer, Mechanography, Muscle Strength, Energy Expenditure

Introduction

Osteogenesis imperfecta (OI) is a rare genetic disorder of increased bone fragility and low bone mass[1]. Other clinical manifestations include short stature, blue sclerae, dentinogenesis imperfecta and hearing loss. The incidence of OI is one in 5000 to 10000 individuals for all types of OI[2]. Several clinically defined types of OI have been described. Severity varies widely, ranging from lethal forms with extremely fragile bones to mild forms with few fractures. The mildest and most prevalent form of OI is type I[3,4]. The majority of patients with OI type I have an identifiable mutation in *COL1A1* or *COL1A2*, the genes that encode the two collagen type I chains α1 and α2[5]. Patients with OI type I typically have recurrent fractures, normal or near normal stature and joint laxity. Individuals with OI type I are generally fully mobile but may experience limitations in overall strength during walking, running and daily living activities[6,7].

Very few studies have evaluated muscle force and power in OI. In one study on 17 children and adolescents with OI type I, hand-held dynamometry found that shoulder abductors, grip, hip flexor and ankle dorsal flexor muscles were weak when compared to references values[8]. Another dynamometry study on 20 children with OI type I concluded that they had non-significant lower ankle plantar flexor force than their 20 age-matched healthy controls[6]. We recently studied dynamic muscle force and power in a group of 54 children and adolescents with OI type I using mechanography[9]. Compared to age- and gender-matched control, these patients had lower force and a tendency towards lower power.

It is unclear whether muscular weakness in OI type I is the consequence of low physical activity or a result of impaired collagen type I synthesis in muscles or tendons. It is conceivable that children and adolescents with OI are less active than healthy peers because of frequent fractures and ensuing immobilization periods[6]. However, to the best of our knowledge, physical activity has not yet been evaluated using objective measurement in children and adolescents with OI type I. The goal of the pres-

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ent study therefore was to assess muscle function and physical activity in children and adolescents with OI type I.

Methods

Study population

Fourteen children and adolescents with a diagnosis of OI type I (mean age [SD]: 12.75 [4.62] years; 9 females) and 14 age- and gender-matched controls (mean age [SD]: 12.75 [4.59] years) took part in this study. All participants were between 6 and 20 years of age.

Participants were eligible to participate in the present study if they were between 6 and 21 years of age. Because mechanography assessment requires substantial cooperation, children under 6 years of age can usually not be assessed. Participants could not participate if they had any fracture or surgery in the lower limb in the 12 months prior to testing or any others musculoskeletal problems.

Patients were recruited at the Shriners Hospital for Children in Montreal during a regular follow-up visit to the outpatients department. Patients were diagnosed with OI type I if they did not have long-bone deformities and no major scoliosis (Cobb angle <30 degrees). Eight participants with OI type I were receiving bisphosphonate treatment at the time of testing. Genetic testing for mutations in *COL1A1* or *COL1A2* had been performed in all patients. In 11 patients, disease-causing mutations were found, whereas 3 patients had negative results.

The control group was comprised of children of employees and general population. This study was approved by the Institutional Review Board of the Faculty of Medicine of McGill University. Informed consent was provided by participants or, in minors, by their parents. Assent was provided by participants aged 7 to 17 years.

Test procedures

After weight and height measurements, muscle function was assessed using mechanography. Instructions were then given to the participants and their parents concerning the two physical activity evaluations (questionnaire and accelerometer). The OI participants and their matched controls were tested in the same season of the year to control for seasonal effects on physical activity[10].

Anthropometric measurements. Height was measured using a Harpenden stadiometer (Holtain, Crymych, UK). Body mass was determined using the Leonardo Mechanograph® GRFP (Novotec Medical Inc, Pforzheim, Germany) for all participants. Height and weight were converted to age- and sex-specific z-scores on the basis of reference data published by the Centers for Disease Control and Prevention[11].

Mechanography. Maximal muscle force and power was determined through mechanography. This objective method has been shown to be reproducible in healthy children and in patients with OI type I[9,12]. Moreover, mechanography provide robust indicators of motor function that are relevant for daily life[13,14]. Leonardo Mechanograph® Ground Reaction Force Plate was used to measure vertical ground reaction forces. The force plate was connected to a laptop computer and force measurements were sampled at a frequency of 800 Hz. Five different tests were performed as described in details elsewhere[12,15]: (a) Multiple two-legged hopping (M2LH), (b) multiple one-legged hopping (M1LH), (c) Single two-legged jump (S2LJ), (d) Heel-rise test (HRT) and (e) Chair-rise test (CRT). Each test was repeated three times and the "best" result was retained as the participant's test result. The definition of "best" result was: highest peak force relative to body weight for a given hop in the multiple one- and two-legged hopping ("force tests"); highest peak power per body mass during the take-off phase of a single two-legged jump, during the first rise of the heel-rise test and for the second rise of the chair-rise test ("power tests")[12].

Physical activity measurements. Physical activity in children is typically intermittent and characterized by rapid changes from rest to physical activity of vigorous intensities[16]. It is important that the measuring tool reflect the sporadic nature of physical activity of children. Accelerometers are widely used to assess the volume and the distribution of physical intensity in different type of population[17-19] because there are lightweights, not a burden for the participant and they reliably reflect the intensity and the volume of physical activity in children[20]. Questionnaires can be used to complement accelerometers and provide a more detailed portrait of physical activity[21,22]. Physical activities were measured using an accelerometer[23] and the Bouchard Diary[24]. The GT3X+ accelerometer (Actigraph™, LLC, Pensacola, FL, USA) was used to measure the volume and the distribution of physical activity. The GT3X+ is a small (4.6 cm x 3.3 cm x 1.5 cm) and lightweight (19 g) triaxial accelerometer designed to detect acceleration up to 6 G's with a frequency ranging between 30 to 100 Hz. The accelerometer was placed directly on the skin on the right hip of the participants through an elastic belt. The participant had to remove the device for sleeping and aquatic activities. Participants were instructed to wear the device from the time they woke up until the time they went to bed for a period of seven consecutive days[25]. The data were recorded at a frequency of 60 Hz. Participants with four or more valid days of accelerometer wear-time were included in the analysis. A valid day was defined as ten or more hours of wear-time. Non wear-time was defined as at least 60 consecutive minutes of zero counts. A maximum of two minutes with counts ranging from 0 to 100 were allowed in the non wear-time[26]. Counts represent a quantitative measure of activity over time[27]. Physical activity was determined separately for the days of the week and the weekend because children's activity varies greatly between week-days and weekend-days[28]. Physical activity was categorized in three groups: Sedentary (0-99 counts per minute), Light (100-2199 counts per minute), Moderate to Vigorous (more than 2200 counts per minute)[17,28]. The volume of physical activity i.e. the average number of minutes in moderate to vigorous physical activity, the distribution of physical activity, i.e the percentage of time spent in each category of intensity and the average number of step per minute was also determined for each participant. The variables were normal-

	OI	Controls	*P*
Gender (male/female)	5/9	5/9	
Age (yr)	12.72 (4.57)	12.75 (4.62)	0.98
Weight (kg)	42.43 (18.14)	48.41 (19.86)	0.08
Weight (z-score)	-0.48 (1.53)	0.41 (0.58)	0.06
Height (m)	1.45 (0.23)	1.53 (0.24)	0.003
Height (z-score)	-0.77 (1.37)	0.38 (0.85)	0.01
BMI ($kg*m^{-2}$)	18.97 (3.93)	19.74 (3.16)	0.51

Osteogenesis imperfecta (OI).
Results are given as mean (SD).
The P value indicates the significance of the difference between patients with OI type I and controls.

Table 1. Anthropometric data.

	OI	Controls	*P*
Force tests (Peak Force per Body Weight)			
Multiple two-legged hopping	4.08 (0.53)	5.05 (0.69)	< 0.001
Multiple one-legged hopping right leg*	2.64 (0.27)	3.23 (0.34)	< 0.001
Multiple one-legged hopping left leg*	2.57 (0.31)	3.20 (0.43)	< 0.001
Power tests (Peak Power per Body Mass)			
Single two-legged jump	38.8 (7.8)	42.7 (10.9)	0.04
Heel-rise test	5.3 (1.2)	6.4 (2.0)	0.01
Chair-rise test†	10.3 (4.3)	13.2 (3.2)	0.03

Osteogenesis imperfecta (OI).
Results are given as mean (SD).
The P value indicates the significance of the difference between patients with OI type I and controls.
**Two participants in the OI group were unable to generate enough force to perform the test.*
†*Two participants in the OI group had invalid results.*

Table 2. Results of mechanography.

ized according to the amount of time the accelerometer was worn because participants did not wear the device the same amount of time.

In addition, energy expenditure during physical activity was assessed using the Bouchard diary. This questionnaire is a valid and reliable measure of energy expenditure[24,29]. The questionnaire consists of 96 15-min blocks per day (24h). Participants were asked to record their activity on a scale of intensity levels (1 to 9, 1 being the lowest and 9 the highest) for the same 7 days that the accelerometer was worn. Participants were asked to fill up the questionnaire with the help of one of their parents. For each participant, the days corresponding to valid days with the accelerometer were retained for analysis of the questionnaire. The average of the week days and the weekend was used to assess the daily energy expenditure[28]. Total daily energy expenditure was calculated as the amount of time spent in each period multiplied by the correspondent Metabolic Equivalent of Task[24].

A follow-up by phone was done at the first, the fourth and the seventh day to insure that the questionnaire and the accelerometer were properly utilized. A prepaid envelope was given for the return of the device and the questionnaire.

Statistical analysis

Results are presented as mean (SD) and a P value <0.05 was considered significant. Shapiro-Wilk tests were used to assess the normal distribution of the variables, if the variable was normally distributed; a paired t-test was used to compare the two groups and if the variable was not normally distributed; a Wilcoxon test was used. All calculations were performed using PASW 18® (SPSS Inc., Chicago, IL, USA).

Results

The analysis was performed on 14 participants with OI type I and on 14 controls. As expected, OI type I patients were shorter than controls, and tended to have lower body mass (Table 1).

Two participants in the OI group were unable to generate enough force to perform the multiple one-legged hopping tests

	OI	Controls	*P*
Steps per min			
Week	10.73 (3.0)	11.77 (4.1)	0.31
Week-end*	8.85 (5.9)	9.09 (3.3)	0.90
Daily steps			
Week	8760.03 (2220.6)	9463.66 (2782.0)	0.34
Week-end*	6864.58 (4377.1)	7057.54 (2586.6)	0.78
Physical Activity			
Sedentary (%)			
Week	55.51 (15.1)	56.11 (16.7)	0.83
Week-end*	55.74 (15.4)	57.32 (14.2)	0.89
Light (%)			
Week	40.09 (13.7)	38.58 (15.7)	0.56
Week-end*	40.27 (11.7)	39.42 (12.8)	0.98
Moderate to Vigorous (%)			
Week	4.40 (3.0)	5.31 (2.5)	0.31
Week-end*	3.26 (2.0)	3.99 (5.3)	0.71
Moderate to vigourous (min)			
Week	37.77 (23.3)	44.16 (19.5)	0.31
Week-end*	30.19 (38.7)	27.31 (15.4)	0.79
Bouchard diary			
MET			
Week	160.87 (20.8)	172.64 (27.7)	0.21
Week-end*	163.76 (43.8)	169.73 (31.4)	0.73

Osteogenesis imperfecta (OI).
Results are given as mean (SD).
The P value indicates the significance of the difference between patients with OI type I and controls.
**One participant in the OI group had no valid data for the week-end days.*

Table 3. Results of GT3X+ and Bouchard's questionnaire.

on the right and left foot, and two participants in the OI group had invalid results for the chair-rise test. The OI type I group had significantly lower peak force per body weight and lower peak power per body mass in each of five tests (Table 2). More specifically, patients with OI type I generated 19%, 18% and 20% less force per body weight than controls for the multiple two-legged hopping, multiple one-legged hopping right and multiple one-legged hopping left respectively. In the three power tests, they generated 9%, 17% and 22% lower power per body mass than controls for the single two-legged jump, heel-rise test and chair-rise test respectively.

The number of steps per minute, the volume and the distribution of physical activity measured from the accelerometer data were very similar between the OI and control groups for both weekdays and weekend days (Table 3). During the week, participants with OI type I spent an average of 37.77 minutes per day in moderate to vigorous activity as compared to 44.16 minutes per day for the age-matched controls. During the weekend, participants with OI spent slightly more time (30.19 minutes) in moderate to vigorous activity than the control group (27.31 minutes). Estimated daily energy expenditure as derived from the Bouchard questionnaire data was similar between the two groups (see Table 3).

Discussion

The goal of the present study was to assess the muscle function and physical activity in children and adolescents with OI type I. As expected, patients with OI type I generated less force per body weight and less muscle power than their healthy counterpart. These results are similar to previous studies[8,9]. Pubertal status was not determined, but as OI type I does not affect sexual maturation, matching participants by age and gender can be expected to lead to two groups with similar maturity status.

Surprisingly, children and adolescents with OI type I actually were as active as their healthy counterparts. The volume of physical activity, the distribution of physical activity, the time in sedentary activity, the number of steps and the estimate daily energy expenditure reported for the two groups were similar during the week and on weekends. It is important to note that these results only concern patients with OI type I. OI type I is the mildest of all OI types[1] and it is therefore possible that patients with other types of OI and lower functional abilities are less active than their healthy counterpart.

The American College of Sports Medicine as well as other health organizations recommend that healthy children should participate in a minimum of 60 minutes of moderate to intense

physical activity daily[30]. In the present study, the two groups did not reach these recommendations. Furthermore, it has been shown that children with OI type I and IV can improve their isometric force with appropriate training[31]. Physical activity incorporating strengthening exercises could possibly be an interesting approach for improving muscle function in children and adolescents with OI type I. As OI type I patients generate less power per body mass than healthy children, a higher volume of moderate to vigorous physical activity could provide a greater benefit for this population. Physical activity can be performed at low cost, is self-sustaining and is an opportunity for children with OI type I to play an active role in their treatment.

Regarding study limitations, the external validity of our data is limited by the nature of our sample. For example, patients with other OI types and with lower functional abilities may be less active than the patients we studied here. Thus, the results of this study are sample specific and can be generalized only to the OI type I patients. Moreover, the small sample size statistically limits the interpretation of our data. However, as OI type I is a rare genetic disease and by taking into account the heaviness of our protocol, the number of participants included in this study provide results that demands to be considered. Future studies should address these limitations.

Conclusion

To our knowledge, this is the first study assessing physical activity in children and adolescents with OI type I. Our results demonstrated that youth with OI type I were as active as healthy counterparts although they did not reach daily recommendations of physical activity. The difference in muscle function and the similarities in the volume of physical activity between the two groups suggest that hypoactive lifestyle is not the primary cause of muscle weakness in children and adolescents with OI type I. However, a higher volume of physical activity could prevent adverse effect of aging on muscle function observed in OI patients type I.

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