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Results of a prospective pilot trial on mobility after whole body vibration in children and adolescents with osteogenesis imperfecta

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Objective: To evaluate the effect of whole body vibration on the mobility of long-term immobilized children and adolescents with a severe form of osteogenesis imperfecta. Osteogenesis imperfecta is a hereditary primary bone disorder with a prevalence from 1 in 10 000 to 1 in 20 000 births. Most of these children are suffering from long-term immobilization after recurrent fractures. Due to the immobilization they are affected by loss of muscle (sarcopenia) and secondary loss of bone mass.
Subjects: Whole body vibration was applied to eight children and adolescents (osteogenesis imperfecta type 3, $N=5$; osteogenesis imperfecta type 4, $N=3$) over a period of six months.
Interventions and results: Whole body vibration was applied by a vibrating platform (Galileo Systems) constructed on a tilting-table. Success of treatment was assessed by measuring alterations of the tilting-angle and evaluating the mobility (Brief Assessment of Motor Function). All individuals were characterized by improved muscle force documented by an increased tilting-angle (median = 35 degrees) or by an increase in ground reaction force (median at start = 30.0 [N/kg] (14.48–134.21); median after six months = 146.0 [N/kg] (42.46–245.25).
Conclusions: Whole body vibration may be a promising approach to improve mobility in children and adolescents severely affected with osteogenesis imperfecta.

Introduction

Osteogenesis imperfecta, also known as brittle bone disease, is a hereditary disease involving collagen type 1 deficiency. Its incidence is between 1:15 000 and 1:25 000. All described gene defects associated with osteogenesis imperfecta lead to a reduced stability of the musculoskeletal system and to muscular hypotony in most patients.[1] Clinical symptoms are brittleness of bones, especially of extremities and the vertebrae, a reduced muscular tonus, reduced body length, grey sclera and dentinogenesis imperfecta in some individuals.[2] Severely affected children with osteogenesis imperfecta are mostly dependent on a wheelchair and have reduced mobility. The reduced mobility is a consequence of frequent fractures of the extremities and the immobilization after surgery. There are no neurological deficits in these patients.

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The treatment is based on three important pillars: bone surgery,[3,4] bisphosphonates[5,6] and physiotherapy.[7] The importance of surgical procedures is already well described to correct deformities. Bisphosphonates are administered to improve bone mass and vertebral morphometry. There are only a few reports on the importance of physiotherapy and the related functional outcome in children and adolescent with osteogenesis imperfecta.[8,9] This is somehow surprising because the improvement of mobility and independence should be the endpoint of all therapeutic procedures in these patients.

A close relationship between muscle force and bone strength has been described previously and the consequences of reduced mobility on the musculoskeletal system have been shown in immobilization studies.[10]

Different methods of whole body vibration have been used for many years to increase muscle force in adults in special fields.[11,12] It is used in athletes to increase their performance and in cosmonauts to prepare them for space missions.[13,14]

Recently whole body vibration has been used to improve impaired biomechanical function of the musculoskeletal system in motor-impaired adults.[15]

The therapeutic principle is based on the activation of proprioceptive spinal circuits. The proprioceptive organs in muscles and tendons detect a change of the body position by a change of their length and induce a contraction of the antagonist stabilizing the system due to the spinal reflex. This reflex can be used for a therapeutic approach using a vibration system to induce the change of body position and to activate the muscular system. Lower frequencies decrease the muscular tonus in contrast to higher frequencies, which increase the muscular tonus.[16] In detail, whole body vibration improves inter- and intramuscular coordination, inducing high-frequency muscular contractions of agonists and antagonists in the neuromuscular system.

The application of vibrations increased bone formation and metabolism in skeletal muscles and skin.[17,18] Interestingly, whole body vibration is thought to prevent the loss of bone and muscle mass in immobilized adults.[19] Different types of whole body vibration systems have been used in the rehabilitation in adults in recent years. Ward *et al.* applied high-frequency vibration with low amplitude to motor-impaired children with cerebral palsy. They measured an improvement of trabecular bone density in these children.[20] The aim of our study is to determine the functional effects of whole body vibration on muscle force and mobility in severely motor-impaired children with osteogenesis imperfecta.

Subjects and methods

In Table 1 important parameters are summarized describing the characteristics and treatment of the eight patients participating in the trial.

Table 1 Important characteristics at start of whole body vibration and incidence of fractures during the two years before whole body vibration and during the six-month training period

Patient number	Sex	Age (years)	OI type	Bisphos phonates	Telescopic rod in femur and tibia	Constant physical therapy	Fractures during 2 years before WBV	Fractures during 6-month training
1	F	4.9	III	Yes	No	Yes		0
2	F	7.7	IV	Yes	No	Yes	4	1
3	F	9.2	III	Yes	Bilateral	Yes	3	0
4	F	9.4	IV	Yes	Bilateral	No	1	0
5	M	9.9	III	Yes	Bilateral	Yes	0	0
6	M	14.9	III	Yes	Bilateral	No	4	1
7	M	8.8	III	Yes	Bilateral	Yes	2	0
8	F	9.5	IV	Yes	Bilateral	Yes	2	0

OI, osteogenesis imperfecta; WBV, whole body vibration.

The incidence of fractures during the last two years before whole body vibration and during the six months of training is reported.

In the present study we used the Cologne Standing and Walking Trainer System Galileo to improve muscle function in children with osteogenesis imperfecta. This is a modified tilt-table combined with the 'Galileo' whole body vibration system (Figure 1). The patient lies on his or her back with the feet placed on the vibrating platform during training. At the beginning of the six-month training period the patients start with a tilt angle of 10 degrees. Over the training period the table was tilted towards the vertical depending on the individual functional status of the patient. The aim was to turn the patients 10 degrees further towards the vertical every 2–3 weeks.

The patients were asked to exercise during the vibration, bending and straightening their knees. The angle in the knees should vary between 10 and 45 degrees during training. The patients should always try to press their feet as hard as possible against the platform during the vibration training.

The Galileo system is a whole body vibration system using a side alternating platform. One foot of the patient is elevated slightly while the other foot is lowered consecutively during vibration. This induces musculospinal reflexes and activates the muscles. The amplitude of the vibration varies from 0 mm exactly at the axis of the platform to 1 cm at the edge, depending on the position of the patient's feet on the platform.

The frequency of the vibration can be controlled and can be adapted to the patient's physical ability.

We calculated the ground reaction force to measure the improvement of muscle force during the treatment. The ground reaction force (F) depends on the angle of the tilt-table, the body weight of the patient and includes gravity [$F =$ (acceleration of gravity $\times$ body mass) $\times$ sin(tilt-angle)]. As the patient becomes more vertical the applied force to the platform increases. Therefore, higher muscular force is needed to keep the patient in an upright position. The tilting-angle thus determines the applied force. Mobility of the patients was characterized with the Brief Assessment of Motor Function (BAMF).[21] This is a validated test to assess a wide range of mobility in patients regardless of age, pubertal status and physical training status.

The therapeutic programme was conducted over a period of six months. Patients and their parents were instructed in the use of the Cologne Standing and Walking Trainer System Galileo by a physiotherapist before the training equipment was installed at home. The programme comprised two daily therapy sessions with three cycles each.[22] Table 2 describes the configuration

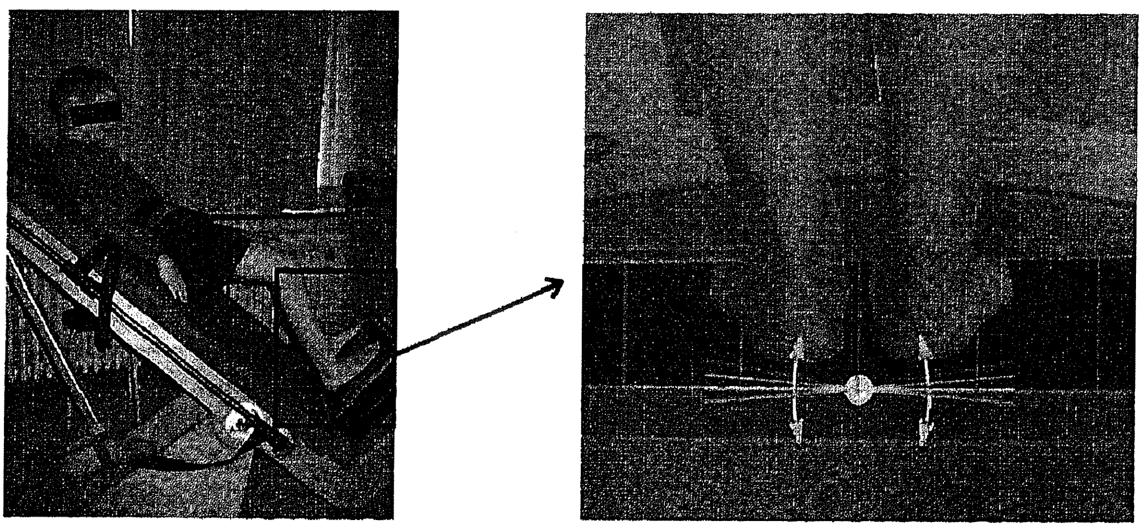

Figure 1 The Cologne Standing and Walking Trainer System Galileo.

Table 2 Exercise programme for whole body vibration in patients affected with osteogenesis imperfecta and configuration at start of training period

Tilting-angle (degrees)	10	3 minutes break	10	3 minutes break	10
Frequency (Hz)	15–20		20–25		20–25
Time period of applied WBV	3 minutes		3 minutes		3 minutes
Amplitude of vibration	1 (1–2 mm)		1 (1–2 mm)		1 (1–2 mm)

WBV, whole body vibration.

of the equipment at the start of the programme. The tilting-angle and the frequency were adapted and increased in relation to the increase in the patient's physical ability. Tilting-angle and BAMF were measured at the start of whole body vibration (M0), after three months (M3) and after six months (M6) of training. Additional therapies (e.g. drug administration such as bisphosphonates and physiotherapy) which had been started over one year previously were continued during whole body vibration.

Differences for analysed variables were calculated by two-tailed paired t-tests. Simple linear correlations were calculated for the association between ground reaction and BAMF score. Statistical differences were ascribed to be significant at $P<0.05$. All statistical procedures were performed by the use of PC Statistics 4.0 (Hoffmann-Software, Giessen, Germany). The study was approved by the ethics committee of the university of Cologne, Germany, and informed consent was obtained from legal guardians.

Results

Tilting-angles at start of therapy (M0) were significantly lower than tilting-angles after three (M3) and six months (M6) of therapy (paired t-tests, two-tailed, $P=0.014$ and $P=0.0048$, respectively). Tilting-angles were not significantly different between M3 and M6 ($P=0.08$, $\beta=0.6$). The calculated ground reaction force (F) at M0 was significantly lower than F (M3) and F (M6) (paired t-tests, two-tailed, $P=0.02$ and $P=0.002$, respectively). F-values were also significantly different between M3 and M6 (paired t-test, two-tailed, $P=0.02$) (Table 3) (Figure 2).

BAMF at M0 was significantly lower than at M3 (paired t-test, two-tailed, $P=0.014$), but there was no significant difference between M0 and M6 ($P=0.11$, $\beta=0.6$). Mobility scores were not different between M3 and M6 (Table 5).

Tilting-angles were significantly linear correlated to mobility scores ($N=24$, $r=0.5$, $P<0.05$), meaning that improvement of tilting-angle reflects improvement of motor function.

F-values were significantly linear correlated to tilting-angles ($N=24$, $r=0.61$, $P<0.05$), but not to mobility-scores ($P=0.22$). The statistical results are shown in Table 3.

Each patient had individual problems of motor function at start of whole body vibration and individual benefits from the training, which were not completely reflected by the assessment of BAMF. These individual benefits of the training are displayed in Table 4. We report changes in body length and weight during the training period in Table 5. We calculated changes in body length and body weight for the study group (paired t-tests, two-tailed). Height and weight increased significantly over six months (mean of increase for height $3+2.4$ cm and for weight $4.2+4.9$ kg) with $P=0.009$ and $P=0.049$, respectively. But height SDS and weight SDS did not significantly increase. Therefore, the present increase of weight and height is likely associated with normal growth.

One patient developed a localized pain at the end of an intramedullary rod, which was already dislocated before starting whole body vibration. In this case, there was no need for surgical intervention. Otherwise, skeletal pain was not reported during therapy. Two patients received fractures (one forearm, one femur) in situations not related to whole body vibration during the training period. The incidence of fractures seems to be

Table 3 Results of whole body vibration in eight children with osteogenesis imperfecta at start (M0), after three months (M3) and after six months (M6)

	M0			M3				M6			
	M ± SD	Median	Range	*M* ± SD	Median	Range	*P*-value	*M* ± SD	Median	Range	*P*-value
Mobility score	5.0 ± 1.8	5.0	3–7	5.5 ± 1.6	6.0	3–7	0.014	5.5 ± 1.7	6.0	3–7	0.11
Tilting-angle	16.9 ± 11.0	10.0	10–40	42.5 ± 22.5	35.0	20–80	0.014	55.0 ± 27.5	45.0	25–90	0.0048
Ground reaction forces related to body weight (*F*), N/kg	56.00 ± 47.56	30.0	14.48–134.21	114.63 ± 52.20	108.5	22.85–193.22	0.02	155.38 ± 73.82	146.0	41.46–245.25	0.002

comparable or even slightly decreased to the number of fractures these patients received during the last two years before whole body vibration. There were no other severe side-effects during the study. Some patients reported about some itching directly after the vibration as a result of the increased vascularization.

Another patient suffered from a dislocation of a telescopic rod after training on a standing device for a few weeks. This patient was not included in the present study. Moreover, this patient had had a dislocation already two years before and another one months after she had already stopped the whole body vibration. Dislocation of telescopic rods is a frequent event in individuals affected with osteogenesis imperfecta.[23,24] Furthermore, the analysis of the individual anatomic characteristics of these patients could not draw any connections between whole body vibration and the dislocation of osteosynthetic material. Nevertheless, a negative effect of whole body vibration on stability of implanted material cannot be excluded due to the present preliminary data.

Discussion

All participants were described to have profited from the conducted exercising programme despite their initial status of motor function. The benefits of the patients can only be compared individually because of the different status at start of therapy. Moreover, whole body vibration was accepted with a high compliance and without severe negative side-effects. Some of the patients were characterized by an improved mobility (increased BAMF). The BAMF is a validated test to characterize mobility in motor impaired patients. It is a test which can be used in different settings and is independent of age and pubertal stages. It is not possible to reflect small changes in motor function with this test, but for orientation of motor function it is reliable and useful measurement.

Regarding muscle force all patients showed a significant increase of ground reaction force after six months of training with the Cologne Standing and Walking Trainer System Galileo. The highest benefits were accomplished during the first three months of training. Further data showed a

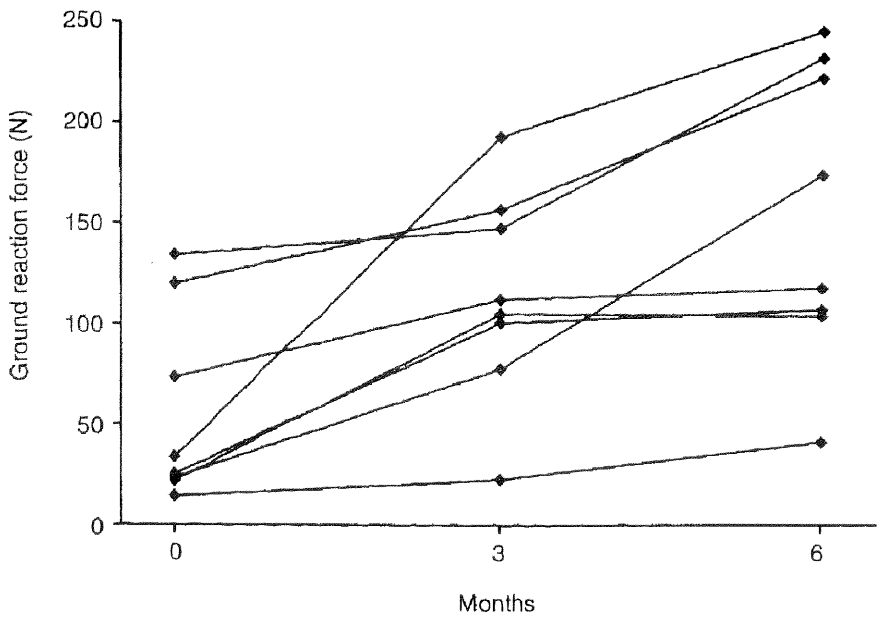

Figure 2 Changes of calculated ground reaction force during six months of whole body vibration.

stabilization of the improvement and no further improvement of BAMF in most patients. This implies that six months seem to be a good training period. In this time the patients are motivated to perform the training with a high compliance and they can achieve benefits in muscle force and mobility. Due to the lack of other studies we cannot decided if six months is the optimal training period but this interval seems to be appropriate.

Concluding, whole body vibration with the Cologne Standing and Walking Trainer System Galileo seems to be a promising approach to increase muscle force and more important mobility in immobilized children with osteogenesis imperfecta. This training should not be limited to patients with osteogenesis imperfecta, but can be also applied to most immobilized children. Recent data by Ward *et al.*[20] showed a beneficial effect of whole body vibration in motor-impaired children with cerebral palsy.

Immobilization of the musculoskeletal system is typically followed by a loss of muscle mass (sarcopenia) and a subsequent decrease of bone mass (osteopenia). Therefore, immobilization is always associated to sarcopenia and osteopenia despite its primary origin. The loss of muscle and bone mass decreases the functional capabilities and might be the reason for further immobilization. This consideration is the basis of the empirically based concept of primary and secondary bone diseases.[25] Primary bone diseases are characterized by a structural or metabolic defect of the skeletal development, in contrast to secondary bone diseases based on immobilization.[26] Therefore, functional activation of the musculoskeletal system is a promising approach to improve mobility in motor-impaired children and adolescents.

The present participants of the study were characterized by a high heterogeneity of motor impairment. Therefore, the present results are not comparative between different individuals. During the training the participants grew older but it is not likely that this contributes much to the improvement of mobility. The natural development in motor function in patients with osteogenesis imperfecta is very slow and the mobility has not changed relevant in the year before the study started. This heterogeneity and the lack of a control group are limitations in this trail. Nevertheless, the present data can be regarded as preliminary results to enhance the importance of this promising therapeutic strategy to regain mobility in severely motor-impaired children and adolescents.

Table 4 Individual benefits of whole body vibration

Patient number	Individual improvements
1	Sitting, now OP for limb deformities required
2	Walking with posterior walker
3	Standing with assistance
4	Knee and ankle orthesis not longer needed
5	Verticalization up to 90 degrees on Cologne Standing and Walking Trainer System Galileo
6	Less help needed in wheelchair (obesity)
7	Independent getting in and out of his wheelchair, walking distance 30 → 250 steps with posterior walker
8	Walking distance 3 m → 18 m with walker

Table 5 Height and weight development at start (M0) of whole body vibration and after six months (M6) of therapy and BAMF at M0, M3 and M6

Patient number	Length M0 (cm)	SDS M0	Length M6 (cm)	SDS M6	Weight M0 (kg)	SDS M0	Weight M6 (kg)	SDS M6	BAMF M0	BAMF M3	BAMF M6
1	68.0	−8.90	70.0	−9.56	8.5	−8.95	10.0	−8.36	3	4	4
2	86.0	−8.41	88.0	−8.90	15.0	−3.42	17.0	−3.43	5	6	7
3	80.0	−10.96	85.0	−9.98	13.0	−4.74	15.0	−4.19	3	4	4
4	108.0	−5.47	109.0	−5.27	29.0	−0.33	32.0	0.50	7	7	7
5	88.0	−8.82	88.0	−9.05	14.0	−4.52	18.0	−3.88	5	5	5
6	105.0	−8.71	112.0	−7.81	40.0	−1.82	56.0	0.00	3	3	3
7	77.0	−10.37	79.0	−10.45	11.7	−5.45	12.0	−5.07	7	7	7
8	108.0	−5.47	113.0	−5.20	20.0	−2.81	25.0	−2.10	7	7	7

BAMF, Brief Assessment of Motor Function.

The study was approved by the ethical committee of the university Cologne, Germany.

Clinical messages

- Whole body vibration is a promising approach to improve mobility in children with osteogenesis imperfecta.
- The Cologne Standing and Walking Trainer System Galileo is a safe system to improve muscle force in these children.
- Despite the heterogeneity of the sample population, all the patients had individual benefits from whole body vibration.

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