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Original Article

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A specialized rehabilitation approach improves mobility in children with osteogenesis imperfecta

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Abstract

Objective: Osteogenesis imperfecta (OI) is a rare disease leading to recurrent fractures, hyperlaxicity of ligaments, short stature and muscular weakness. Physiotherapy is one important treatment approach. The objective of our analysis was to evaluate the effect of a new physiotherapy approach including side alternating whole body vibration on motor function in children with OI. **Methods:** In a retrospective analysis data of 53 children were analyzed. The 12 months approach included 6 months of side alternating whole body vibration training, concomitant physiotherapy, resistance training, treadmill training and 6 months follow up. Primary outcome parameter was the Gross Motor Function Measure after 12 months (M12). **Results:** 53 children (male: 32; age (mean±SEM): 9.1±0.61, range 2.54-24.81 years) participated in the treatment approach. A significant increase of motor function (GMFM-66 score 55.47±2.45 to 58.67±2.83; p=0.001) and walking distance (47.04 m±6.52 to 63.36±8.25 m (p<0.01) between M0 and M12 was seen. Total body without head bone mineral density increased significantly at M12 (p=0.0189). **Conclusions:** In the cohort of OI children which participated in the specialized treatment approach improvements of motor function were observed. Therefore this program should be considered as additional therapeutic approach for children with severe OI.

Keywords: Whole Body Vibration, Osteogenesis Imperfecta, Gross Motor Function Measurement, Physiotherapy, Mobility

Introduction

Osteogenesis imperfecta (OI) is a rare hereditary disease (OI; MIM 166200, 166210, 259420, and 166220) characterized by an increased fracture rate, scoliosis, hypermobility of joints, muscular hypotonia and short stature[1]. In most patients (~85%) it is caused by dominant mutations in the collagen genes *COL1A1/A2* or *IFITM-5*. In ~15% it is inherited in a recessive manner caused by mutations in genes affecting bone modelling and resorption[2]. Severe affected individuals are often depending on a wheelchair[3]. Due to this reduced activity level and recurrent periods of immobilization after fractures most children with OI present with a delayed motor development[4]. It is known that immobilization of the musculoskeletal system cause muscle mass loss which is followed by reduced bone mass and a higher risk of low energy fractures and further immobilisation[5,6]. Therefore in addition to drug treatment e.g. antiresorptive treatment with bisphosphonates[7] and surgical procedures[8] continuous physiotherapy seems to be mandatory to improve gross motor function and bone strength in these children[9]. Reports about the efficacy of different training concepts in OI children are rare[10]. Van Brussels et al evaluated the

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The retrospective analyses were performed independently of the manufacturer by HHK, OS, ES and CS. HHK, OS, ES, CS, OG and NS cared for the patients clinically. The manufacturer of the used device was not included in data collection, data analyses and preparing of the manuscript. The manufacturer had no access to the collected data as they were collected in the regular patient's charts within the routine appointments of the rehabilitation program. The analyzed and presented data were not part of a study as it is a retrospective evaluation of a specialized treatment approach which is part of the german healthcare system and covered by the basic healthcare insurances.

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Abbreviations

BMC	Bone Mineral Content
BMD	Bone Mineral Density
BWSTT	Body Weight Supported Treadmill Training
DXA	Dual-energy X-ray Absorptiometry
GMFM	Gross Motor Function Measure
HZ	Hertz
NDT	Neurodevelopmental training
OI	Osteogenesis imperfecta
RT	Resistance Training
TBLH	Total Body Less Head
WBV	Whole Body Vibration

efficacy of physical training in children with OI after 3 months of training[11]. Furthermore recommendations for an active life style in OI were published in 2011[12]. In the last decade side alternating whole body vibration (WBV) arouse interest as a therapeutic modality to improve neuromuscular performance in disabled children[13-16]. There are rare reports of the effect of WBV in animal models and children with OI showing a beneficial impact on mobility[17,18]. Special concepts including classical physiotherapy (neurodevelopmental treatment, resistance training) and WBV for activation of the musculoskeletal system in children with OI have been missing.

The functional, intensive 12 months physiotherapy approach "*On your feet*" combines resistance training (RT), body weight supported treadmill training (BWSTT), neurodevelopmental treatment and side-alternating WBV using a Galileo® WBV system for 6 months within the 12 months period. The aim is to improve gross motor function in children with OI as the basis for an independent life style in the long term. To the best of our knowledge reports about the effects of a specialized approach for children with OI on mobility are missing yet. The primary objective of our retrospective analysis was to evaluate the effect on mobility after 12 months in 53 children with OI who participated in the program "*On your feet*".

Subjects and methods

Subjects

"On your feet"

53 children (male: 32; age (mean±SEM): 9.1±0.61, range 2.54–24.81 years) participated in the treatment approach. For baseline data see Table 1 in the results part. The treatment approach "*On your feet*" is a routine program in Germany. Costs are covered by the insurances of the basic health care system in Germany. It was started in 2006 as a 12 months program in a specialized paediatric rehabilitation centre in affiliation to the Children's University Hospital. The physiotherapy program is performed in one centre. Participation is offered to OI children from the whole country. The treatment approach includes different therapeutic strategies. An overview of the schedule and the strategies used is given in Figure 1. After a medical and physiotherapeutic assessment children were included in the program. Inclusion criteria for the program are: age of the child ≥2 years; ability to follow exercises mentally; ability to continue exercises at home. Exlusion criteria are: fractures or elective surgeries within the last 3 months; known gallstones or urolthiasis; current pregnancy; herniated vertebral disks. Criteria are adapted to criteria provided by the manufacturer (Novotec Medical GmbH, Germany). Based on the fact that the rehabilitation centre is affiliated to the Children's University Hospital patients were informed and recruited to participate in the treatment approach at the regular appointments in the outpatient centre for skeletal dysplasia and Osteogenesis imperfecta. Additionally, information about the rehabilitation centre is given at the patient meetings of the German OI self support groups and to health care providers; doctors and physiotherapists.

Participants n	53
Male n (%)	32 (60.4)
Age Mean [years] (SEM)	9.07 (0.609)
Height Mean [cm] (SEM)	103.2 (2.897)
Weight Mean [kg] (SEM)	22.33 (2.112)
BMI Mean [kg/m2] (SEM)	18.96 (0.725)
Ability to walk n (%) (GMFM item 69)	19 (35.8)
OI Type 1 n (%)	8 (15)
Able to walk (GMFM item 69) n (%)	4 (50.0)
OI Type 4 n (%)	26 (49)
Able to walk (GMFM item 69) n (%)	11 (42.3)
OI Type 3 n (%)	17 (32)
Able to walk (GMFM item 69) n (%)	4 (23.5)
OI Type 5 n (%)	2 (3)
Able to walk (GMFM item 69) n (%)	0 (0)
Concomitant/ former treatment with bisphosphonates n (%)	46 (87)

Table 1. Baseline characteristics are presented from 53 patients at M0. Patients were characterized according to the "expanded Sillence classification"[1].

Informed consent for data collection and analyses was obtained from legal guardians prior to participation. Ethical approval was obtained from the local ethics committee of the University (Nr: 06-020).

The first in-patient stay contained of 13 consecutive training days with one day break. Therapies were applied as listed in Figure 1. During this stay the baseline assessment (M0) was taken. After the first in-patient stay the children exercised with the Galileo® system (Galileo® or Galileo TT® Novotec Medical GmbH, Pforzheim, Germany) at home twice daily (each time 3x3 minutes) for three months. After these three months the second in-patient stay (six consecutive days) took place also including the components shown in Figure 1. Therapy and treatment aims were adjusted to the progress of the child. Again, three months home-based Galileo® training followed. Six months after M0, the children were assessed in an out-pa-

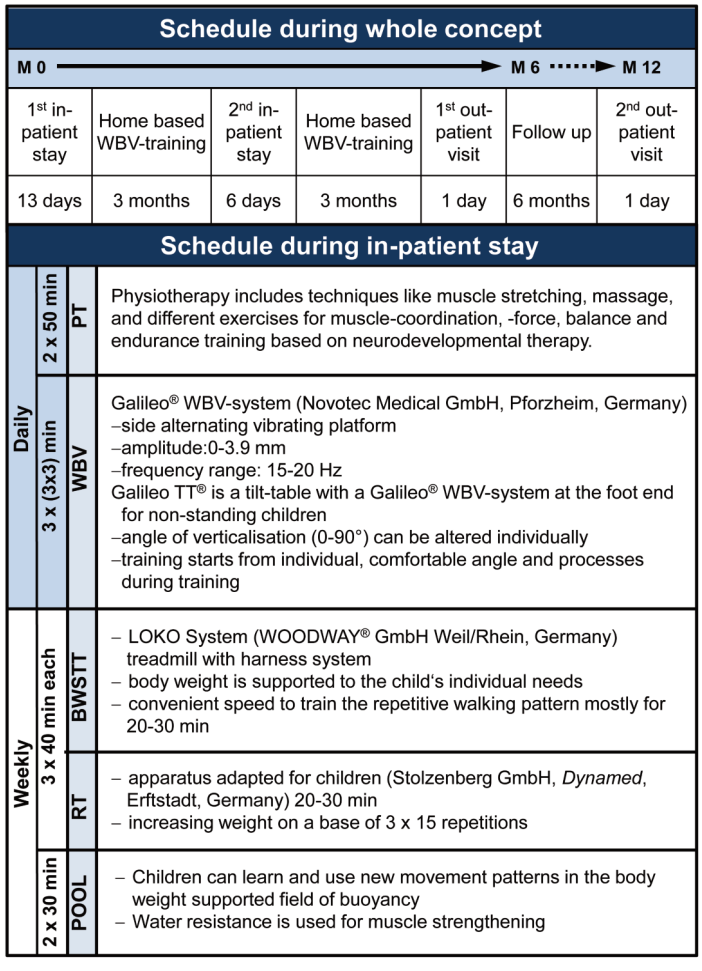

Figure 1. Schedule of the rehabilitation program "*On your feet*". In the upper part the schedule for the whole program is demonstrated. In the lower part the different therapeutic tools of the in-patient stay periods are presented[27].

tient examination (M6) and the Galileo® system was returned to the clinic. At home patients continued their regular previous physiotherapy. Pool therapy, resistance training and treadmill training were only added during the inpatient stays. Compliance was monitored by a parental training diary. Patients were judged as compliant if ≥80% of exercises were performed. To detect side effects parents were instructed to report side effects directly by phone and in the parental diary. Additionally, patients and parents were asked for side effects at the visits in the rehabilitation centre.

After 6 further months (M12) another outpatient visit was performed to analyze motor function after 6 months follow up without WBV training. Regular physiotherapy was continued over this period but WBV was discontinued in the follow up period.

Specific physiotherapeutic interventions:

The whole body vibration training is based on reflex-induced muscle contractions. The side-alternating vibration platform is used in a standing position without external support if the child is able to stand without support. In case the child is not able to stand freely there is a special platform in combination with a tilt table available in which the tilt angle is individually adjustable according to the weight bearing ability of the child (0 to 90 degrees).

Advantages of the side-alternating WBV are the reflectory activation of the muscles and the low forces applied to the body by the system. Vibration settings were chosen depending on the results of the former pilot trial[19,20] and individually adapted according to the child's progress and therapeutic aims.

The vibration frequency (Hertz=Hz) was 15-20 Hz to increase muscle function and endurance. The amplitude is dependent on the position of the feet on the platform between 0 and ±3.9 mm (peak to peak displacement maximum 7.8 mm; peak acceleration related to frequency was between 3.53 g (15 Hz) and 6.28 g (20 Hz))[13]. Skidding was controlled by barefoot standing and manual fixation of the feet if necessary. Patients were standing on two legs in dynamic exercise positions (squatting during the exercise).

Besides WBV patients received resistance training for selective muscle activation during the inpatient stays (training

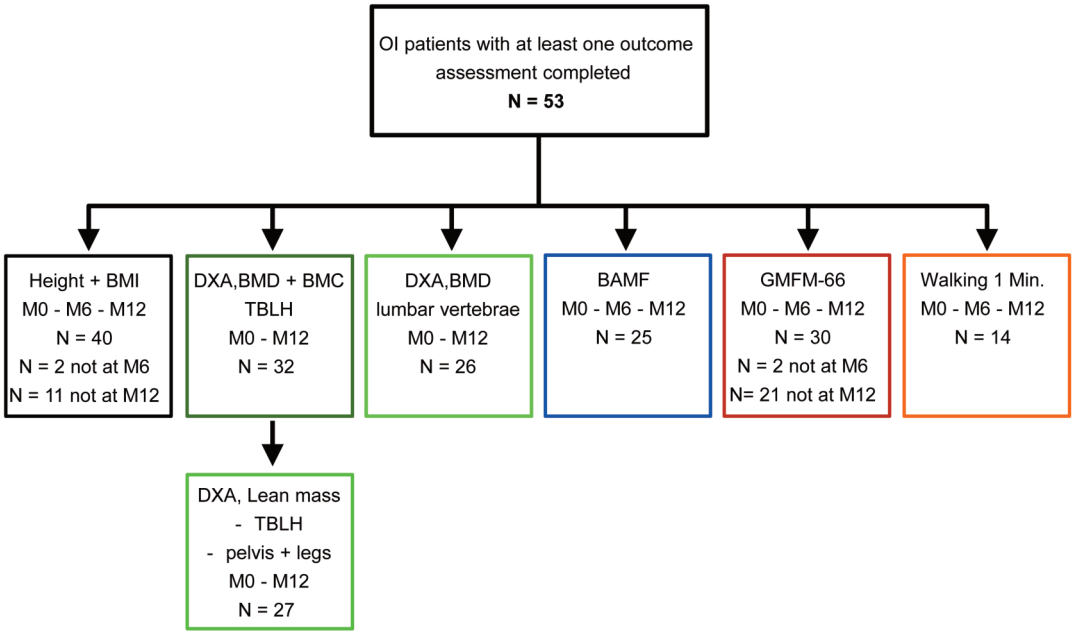

Figure 2. Sample sizes stratified for the different outcome parameters.

apparatus adapted to children's body size by Stolzenberg GmbH-Dynamed, Erftstadt, Germany). A selection of five different training apparatus is available (abductor/outer thigh, leg press, cable machines, triceps dips and extension leg curl). A selection of four different apparatus was used to target isolated muscle activity of the lower extremities according to individual goal settings. For upper extremity training in order to use walking aids triceps dips were also included. Furthermore patients got body weight supported treadmill training (BWSTT; LOKO Station 55 Woodway GmbH, Weil/Rhein, Germany). Pool therapy uses the water resistance and buoyancy for induction of muscle strength. Neurodevelopment treatment was implemented as concomitant therapy.

Outcome parameters

Outcome measures were taken at baseline (M0, first in-patient stay), after 6 months of training (M6) and after 12 months (6 months follow up period without WBV training= M12). The primary endpoint of mobility changes after 12 months was assessed using the "Gross Motor Function Measure" (GMFM 66; points range 0-100)[21]. The GMFM is a semi quantitative, standardized and validated assessment for motor function primarily developed for children with cerebral palsy[21]. Meanwhile the GMFM-88 has been validated for traumatic brain injury[22], Down syndrome[23] and OI[24].

Additionally, mobility was described by the "Brief Assessment of Motor Function" (BAMF; 10-point ordinal scale, score 0-10)[25]. It is a rapid description of gross motor performance and was specifically designed for children with disabilities and tested for reliability in the OI population[25]. The one minute walking distance was assessed by a standardized walking parcour on a flat ground. Areal bone mineral density (aBMD), bone mineral content (BMC) and lean mass as surrogate for muscle mass were assessed using dual-energy X-ray absorptiometry (DXA) at the lumbar spine (L2–L4) and for the total body less head (TBLH) using a GE Lunar iDXA densitometer (GE Ultraschall GmbH, Germany) and Encore software version 13.6. Areal BMD results were transformed to age-specific z-scores using reference data provided by the company[26,27]. To reduce the radiation dosage DXA scans were only performed at M0 and M12.

Height/ length were measured either using a stadiometer or lying on a bench for immobilized children. All patients were measured with the same method throughout the program. Body weight was taken using a sitting scale.

Data analysis

The analysed data have been collected in the children's rehabilitation centre within the scope of the treatment approach. Data were analyzed retrospectively by chart review including all 53 OI children participating "*On your feet*" between 2006 and 2013.Therefore sample sizes may vary due to incomplete data sets.

The primary endpoint was defined as the change of GMFM-66 points between M0 and M12. Each patient's change in GMFM points was analyzed between M0-M6, M6-M12 and M0-M12. The mean and standard error of the mean was calculated and a Wilcoxon test was performed to test for a mean change from M0. The main analysis was performed in all included patients with a 12 month's participation period after M0 and GMFM-66 assessment results at M0, M6 and M12.

Wilcoxon test (mean and standard error of the mean (SEM))

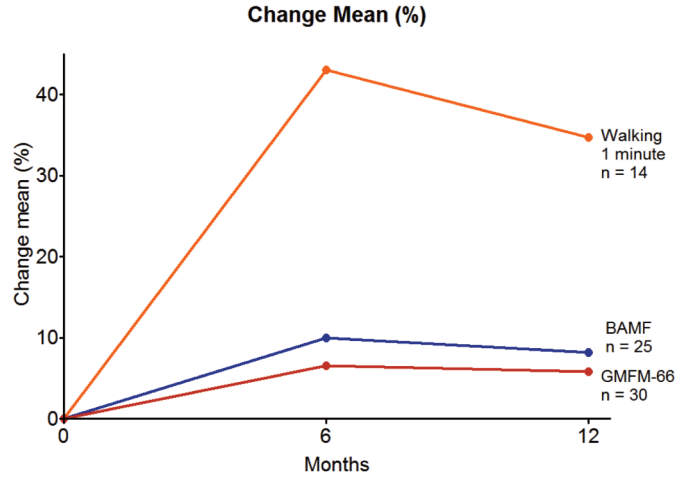

Figure 3. Percentual changes of motor function over the whole program of 12 months. Changes of one-minute walking distance are presented in orange line. Changes of brief assessment of motor function (BAMF) are presented in blue line and Gross-motor-function-measurement (GMFM-66) changes are presented as red line[21,25].

	M 0	M 6	M 12	Delta 0-6 p	Delta 6-12 p	Delta 0-12 p	n
GMFM 66 (Score) SEM	55.47 2.455	59.09 2.82	58.67 2.832	3.62 <0.0001	-0.42 0.6014	3.20 0.0010	30
Walking 1 Min (m) SEM	47.04 6.517	67.29 7.203	63.36 8.249	20.25 0.0017	-3.93 0.7334	16.32 0.0105	14
BAMF (Score) SEM	6.84 0.4785	7.52 0.4128	7.40 0.3786	0.68 0.0010	-0.12 0.5781	0.56 0.0803	25
BMD lumbar vertebrae (g/cm²) SEM	0.4344 / 0.0322	------ ------	0.4839 0.03589	------ ------	------ ------	0.05 0.0018	26
BMD lumbar vertebrae z-value (g/cm²) SEM	-3.442 0.2803	------ ------	-3.312 0.3144	------ ------	------ ------	0.13 0.4311	26
BMD total body without head (g/cm²) SEM	0.5382 0.01598	------ ------	0.5529 0.01861	------ ------	------ ------	0.01 0.0189	32
BMD total body without head z-value (g/cm²) SEM	-3.076 0.2459	------ ------	-3.108 0.2517	------ ------	------ ------	-0.032 0.6627	25
BMC total body without head (g) SEM	299.8 49.14	------ ------	362.9 52.89	------ ------	------ ------	63.10 P<0.0001	32
Lean Mass total body without head/Height (kg/cm) SEM	0.1059 0.00537	------ ------	0.111 0.005729	------ ------	------ ------	0.01 0.0006	27
Lean mass pelvis+legs/Height (kg/cm) SEM	0.04611 0.003147	------ ------	0.05004 0.003288	------ ------	------ ------	0.00 P<0.0001	27
Height (cm) SEM	101.6 3.438	103.9 3.422	105.7 3.495	2.30 <0.0001	1.80 <0.0001	4.10 <0.0001	40
Height SD (cm) SEM	-5.624 0.4634	-5.689 0.4472	-5.754 0.4594	-0.07 0.4450	-0.06 0.7293	-0.13 0.3056	40
BMI SD (kg/m²) SEM	0.6718 0.2263	0.7085 0.2169	0.6535 0.218	0.04 0.8933	-0.06 0.2750	-0.02 0.4299	40

Table 2. Absolute data of DXA results and motor function are presented for M0, M6 and M12 and differences between the time points (M0-M6; M6-M12; M0-M12). P levels <0.05 were considered statistically significant. Data of the individual patient were included if results of one assessment were available.

was also employed to analyze differences in GMFM points, one minute walking distance, BAMF, body height, body weight between M0-M6, M6-M12 and M0-M12 in all patients with at least one outcome assessment completed. In BMD, BMC and lean mass Wilcoxon test (mean and standard error of the mean) was employed to analyze differences between M0-M12.

Changes of GMFM, 1-minute walking distance, BAMF, lean mass, BMD (TBLH), BMD lumbar vertebrae (L2-L4) and BMC are presented descriptively over time. P-values <0.05 were considered significant As the presented data report the results of a retrospective observational evaluation they were presented and analyzed adapted to the STROBE statement[28].

Data was analysed using PC Statistics version 4.0 (Hoffmann-Software, Giessen, Germany) and Graph pad prism 3.0.

Results

53 children were included at M0 and completed the 6 months period of intensive training with WBV within the rehabilitation approach "*On your feet*" between 2006 and 2013 with at least one outcome assessment completed at two visits (Figure 2). Of these 53 children 11 children visited at M0 and M6 but did not participate in the follow up visit M12. Two children skipped the visit at M6 and just send back the parental diaries and Galileo system to our centre at M6, but came for the follow up visit at M12. Therefore for these children height and weight parameters are not available for M0, M6 and M12. In summary loss of follow up between M6 and M12 was described for 11 patients. Altogether after evaluation of patients diaries (n=53) 93.2% of the WBV exercises were absolved between M0 and M6 which was judged as an adequate compliance rate. In 30 children GMFM-66 testing was performed during the complete program with follow up period until month 12 at M0, M6 and M12 (Figure 2).

Baseline data (M0)

A synopsis of clinical data on all 53 children at start of the program is given in Table 1. 19 out of 53 children were able to walk 10 meters independently at start of the program (Score of 3 points in item 69 testing).

Mobility

The gross motor function measure score increased between M0 and M6 significantly from 55.47±2.45 (Mean±SEM) to 59.09±2.82 points (n=30; p<0.0001) (Figure 3 and Table 2). There was no significant decrease in the follow up period between M6 and M12 (n=30; p=0.60) (Figure 3 and Table 2).

The 1-minute walking distance increased between M0 and M6 from 47.04±6.52 to 67.29±7.20 meters (n=14; p<0.0017). Between M6 and M12 there was a slight decrease of 3.9 meters (n=14; p=0.73 (Figure 3 and Table 2).

From M0-M12 a significant increase of motor function (GMFM-66 score 55.47±2.45 to 58.67±2.83; p=0.001) and 1-minute walking distance (47.04 m ±6.52 to 63.36±8.25 m (p<0.01) was seen.

BAMF levels increased significantly from score 6.84±0.47 to 7.52±0.41 (n=25; p=0.001) between M0 and M6 (Figure 3 and Table 2). Between M0 and M12 no significant difference in BAMF was detected (p=0.08).

Descriptive evaluation of OI type based subgroups revealed the following gains of ambulation levels: 4 out of 8 OI I patients were able to walk ten steps without help at start of the program (GMFM item 69 score 3 M0 and M12). 2 out of 4 (50%) OI type I non-walkers learned to walk ten steps without help within the program (Change of GMFM item 69 score from 0 to 3 between M0 and M12). 4 out of 17 (21%) OI III patients already walked ten steps at start of the program. 1 out of the 13 non-walking OI type III patients learned to walk ten steps without help after the program. 11 out of 26 OI IV patients were able to walk ten steps at start of the program. 6 out of 15 (40%) OI type IV patients were able to walk ten steps without help after the program (Change of GMFM item 69 score from 0 to 3 between M0 and M12).

Areal bone mineral density

Results are presented in Table 2. Absolute values of the areal bone mineral density of the lumbar spine (aBMD L2-L4) increased significantly between M0 and M12 from 0.4357±0.17 to 0.48±0.19 g/cm^2 (n=26; p=0.0054).

BMD of the TBLH increased significantly between M0 and M12 from 0.4357±0.17 g/cm^2 to 0.48±0.19 (n=32; p=0.0189).

Z-scores (age adjusted reference data) of aBMD did not change significantly during the program (M0 vs. M12 L2-L4 (-3.442±0.2803 vs. -3.312±0.314; p=0.43); M0 vs. M12 TBLH (-3.076±0.246 vs. -3.108±0.252; p=0.67)).

Absolute levels of BMC showed a significant difference (n=32; p<0.0147) of 63.1 g from M 0-M12.

Lean mass measured by DXA as surrogate for muscle mass of TBLH and pelvis and legs was adjusted to height. An increase was seen between M0-M12 in TBLH (0.1059 kg/cm ±0.00537 to 0.111 kg/cm ±0.005729; n=27; p=0.0006) and pelvis/legs (0.04611 kg/cm ±0.003147 to 0.05004 kg/cm ±0.003288; n=27; p=<0.0001), respectively.

Anthropometry

Participating children gained height/ length and weight while training (Table 2). SD scores of height and body mass index did not change significantly during the program (n=40) (Table 2).

Adverse events

As adverse events patients and parents reported itching and redness at the extremities. Pain in association with training episodes was not reported. During the exercises no patient suffered a fracture. Fracture rates were not assessed in detail – no counting was performed.

As mentioned above 11 patients did not perform visit M 12. 6 patients reported a fracture prohibiting their evaluation at M12. During the observational period patients continued their

regular orthopaedic consultations. No dislocation of osteosynthetic rods (Fassier-Duval, Bailey) was observed by clinical examination. Routinely performed radiographs at the regular orthopaedic consultations did not reveal any dislocations of intramedullary rods. No additional x-rays were performed within the rehabilitation approach. Progression of scoliosis was not evaluated within the rehabilitation period.

Vessel rupture or intracranial hemorrhage was not reported in the participants.

Discussion

The evaluation of our rehabilitation approach gives evidence that an intensive functional therapeutic approach including side-alternating whole body vibration leads to an improvement of mobility, lean mass and areal bone mineral density in children with OI. Independent of the underlying OI type 9 patients were able to walk 10 steps without help after the training period.

Patients presented with different levels of mobility at start of the program. 35.8% of the included patients were able to walk 10 meters without help at start of the program. As we know from our outpatient centre this composition nearly represents the motor function of the total OI cohort continuously receiving medical treatment in Germany[3]. Even the analysis is not based on a stratified study collective the cohort had a balance of ambulators and non-ambulators at start of the Program". In general most patients profited of the constant training period and no severe side effects have been seen. Especially no pain in extremities with former osteosynthetic treatment was reported and no dislocation of intramedullary rods during the WBV treatment occurred. Patients reported itching and redness at the extremities as mild side effect after training resolving completely within a short time after the treatment cycle. Therefore this intervention seems to be a safe training option even in children with multiple intramedullary materials in their long bones in severe OI. Adherence to repetitive continuous physiotherapy is difficult to obtain. The diary based adherence to training in our collective was 93.2% which was higher than expected (≥80%). Therefore implementing a physiotherapeutic approach in the procedures of daily life seems to contribute to a high acceptance and adherence.

Based on a pilot trial in our centre with 8 patients the training approach was included in the basic health care system in Germany[20]. In comparison to former trials showing a benefit of WBV for muscle strength the demonstrated data underline these effects in our cohort of 53 children[20,29,30]. Additionally, in 2004 a benefit of mechanical loading on osteogenesis in 20 children with different disabling conditions was demonstrated[15].

Immobilization of the musculoskeletal system is typically followed by a loss of muscle mass and a progredient loss of bone mass[31]. A primary bone disease as OI leads due to fractures and immobilization to a secondary osteopenia in a vicious circle[32]. The results of our analyses demonstrate that activation of the muscles in a special training approach leads to an increase of lean mass especially in the pelvis and legs, motor function (1-minute walking distance, GMFM-66 scores) and therefore inhibits further loss of BMC due to immobilization. There are no definitions for a minimum clinically important difference in GMFM-66 score changes available for children with OI. In 2008 Oeffinger and colleagues defined a minimum clinically important difference (large effect size) of 1.3 points as large effect size in children with cerebral palsy[33]. An increase of a mean of 3.20 points was shown in our cohort and was therefore evaluated as clinically important.

Children with disabling conditions based on musculoskeletal impairment present with a delayed motor development in general[4]. The treatment approach with a training duration of 6 months is an example for the functional muscle bone unit[32,34]. At first new movement patterns are trained during the in-patient stay repetitively. To increase endurance and motor function a 6 months home based training interval seems to be adequate. As presented in Figure 3 and Table 2 after 6 months of treatment a significant increase of motor function was seen. After another 6 months of follow up a slight decrease of the one-minute walking distance and GMFM-66 scores was seen but without statistical significance (-0.42 points). Parameters of BMC, aBMD and lean mass after 12 months showed the long lasting effect of the continuous muscle stimulation leading to an increase of bone mineral content. Z-scores did not change or deteriorate within 12 months which means an adequate age related increase compared to healthy children over the rehabilitation period.

It has to be considered that most of the patients (46 out of 53) receive bisphosphonates as i.v. treatment for many years (Table 1). As it is known from former publications the treatment duration might have had an impact on the BMC accrual because the gain of BMC is higher in the first years of bisphosphonate treatment compared to the following years[35].

Height SD data did not change or deteriorate within 12 months which means an adequate age related increase compared to healthy children over the rehabilitation period.

Our results are limited by the fact that the analysis was done without a control group in a retrospective setting. It is clear that retrospective analyses are biased; however retrospective analyses can provide useful information about adverse events. Our results are encouraging and should be assessed in a prospective controlled setting. In a clinical prospective setting the effect of WBV *per se* could be analyzed to address the fact that our results are based on an intensive approach with several interventions (WBV, treadmill training, etc.) leading to an improvement of mobility. Due to lack of blinding a bias which is based on the increased motivation of the patients using the new WBV device daily could not be excluded. Additionally, the group of included patients was very heterogeneous regarding the severity of the disease (Table 1). No conclusions about the individual effects of the different therapeutic strategies or the duration of training sessions used could be drawn. To analyze differences in the individual patients a higher sample size is needed. The presented results give evidence that the whole cohort improved in motor function in the mean.

Conclusion

An intensive functional therapeutic approach including side-alternating whole body vibration in a 12 months home based training approach leads to an increase of mobility in children, which is followed by an increase of bone mineral content and areal bone mineral density. Further prospective studies with larger cohorts are needed to assess the efficacy and the effects depending on severity of the disease and to evaluate efficacy in different genotypes with different pathophysiologies leading to the complex of symptoms in OI. There are no approved physiotherapy treatment approaches available in children with the rare disease OI yet. The presented data are encouraging that the physiotherapeutic approach "*On your feet*" including whole body vibration is safe and furthermore should be considered as additional therapeutic approach for children with severe OI to improve mobility and to gain an independent life style in the long-term.

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