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ORIGINAL ARTICLE *Clinical hameophilia*

Haemophilia & Exercise Project (HEP): The impact of 1-year sports therapy programme on physical performance in adult haemophilia patients

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Summary. Episodes of bleeding in people with haemophilia (PWH) are associated with reduced activity and limitations in physical performance. Within the scope of the 'Haemophilia & Exercise Project' (HEP) PWH were trained in a sports therapy programme. Aim of this study was to investigate subjective and objective physical performance in HEP-participants after 1 year training. Physical performance of 48 adult PWH was compared before and after sports therapy subjectively (HEP-Test-Q) and objectively regarding mobility (range of motion), strength and coordination (one-leg-stand) and endurance (12-min walk test). Sports therapy included an independent home training that had previously been trained in several collective sports camps. Forty-three controls without haemophilia and without training were compared to PWH. Of 48 PWH, 13 performed a regular training (active PWH); 12 HEP-participants were constantly passive (passive PWH). Twenty-three PWH and 24 controls dropped out because of incomplete data. The activity level increased by 100% in active PWH and remained constant in passive PWH, and in controls ($P \leq 0.05$). Only mobility of the right knee was significantly improved in active PWH ($+5.8 \pm 5.3°$) compared to passive PWH ($-1.3 \pm 8.6°$). The 12-min walk test proved a longer walking distance for active PWH ($+217 \pm 199$ m) compared to controls (-32 ± 217 m). Active PWH reported a better subjective physical performance in the HEP-Test-Q domains 'strength & coordination', 'endurance' and in the total score ($+9.4 \pm 13.8$) compared to passive PWH (-5.3 ± 13.5) and controls ($+3.7 \pm 7.5$). The 'mobility'-scale and one-leg-stand remained unchanged. Sports therapy increases the activity level and physical performance of PWH, whereby objective effects do not always correspond with subjective assessments.

Keywords: exercise, haemophilia, HEP-Test-Q, motor skills, physical performance, self-assessment

Introduction

Epidemiological studies confirm the importance of physical activity for prevention as well as rehabilitation of different diseases. However, 40 years ago, sportive activities for people with haemophilia (PWH) were unthinkable. They were advised to remain inactive to lower any risks of a trauma [1].

Consequently, inactivity led to muscle atrophy surrounding the joints. Without sufficient muscle conduction the affected joint is more vulnerable, which causes a higher risk of injury and bleeding. This is the beginning of an inexorable circuit, which mostly ends in joint damage and haemophilic arthropathy [2,3]. Previous studies concerning inactivity of PWH and its consequences on joint status have shown significant deficits in motor skills compared with healthy controls [4–11]. In addition to objective examinations, patients described an impaired subjective physical performance in all above-named domains [12].

The sufficient availability of Factor VIII and Factor IX in specific regions as well as the possibility of home treatment since the beginning of the 1970s led to a new consensus regarding sportive activities [13]. Many authors recommend appropriate training programme for PWH, whereby recommendations and consequential effects are based on a few scientific examinations [14–18].

Since 1999, the personnel of the German sports therapy project 'Haemophilia & Exercise Project' (HEP) gathered experience in the field of haemophilia

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and sports therapy (http://www.haemophilia-exercise.de). The HEP-project targets adult patients with moderate and severe haemophilia A or B. Knowledge in the area of physical activity for participants was introduced with the help of a specified and individualized sports therapy programme. The whole programme included a controlled and independently conducted home training accompanied by regular sports camps for all. Own studies showed the positive influence of motor skills due to this physical training [17]. Current results also proved that the self-assessment did not always correlate highly with objective data [11].

The present study addresses two research questions: first, can a specific sports therapy programme over 1 year influence the subjective physical performance in PWH? Second, how does the self-assessment of physical performance correlate with the objective data? We hypothesized an increased subjective physical performance in PWH after 1 year of sports therapy and differences between subjective and objective parameters.

Materials and methods

Study design and subjects

Between 2006 and 2009, 48 German patients with severe and moderate haemophilia A or B participated in HEP. In addition, 43 controls without haemophilia or other bleeding disorders were recruited in Thuringia and Saxony (Germany) via announcements posted in public institutions. Socio-demographical and clinical data of both samples were described in another article [11].

All HEP-participants were encouraged to do an independent sports therapy programme and were observed over 1 year. Instructions and advanced education concerning physical training were incorporated into semi-annual collective sports camps at the beginning of the study, after 6 and 12 months. Each camp was 3.5 days long and took place at the Regional School of Sports of Thuringia, Germany. Home training was performed in the periods between the sports camps. To monitor the effects of the training, physical examinations were conducted at the beginning of the study and were repeated after 12 months. Controls were monitored and tested simultaneously before and after 1 year. They were instructed to retain their activity level in the course of the study.

The project met the standards of the Human Research Ethics Committee, and written informed consent was provided by all participants prior to study entry.

Programmed sports therapy

The key aspects of the sports therapy were exercises and methods to increase focal points in terms of body awareness, muscle tone regulation, joint mobilization and muscle activation (see Table 1). In addition to these focal points, holistic therapeutic techniques such as Tai Chi and Progressive Muscle Relaxation were also imparted and trained. More details about the sports therapy programme can be found under Herbsleb *et al.* 2008 [19].

Exercises were individually adapted to the patients' health status and should be performed at least two times per week. Participants were instructed and guided by a team composed of medical doctors of sports medicine, sports scholars and specialized sports therapists, who could be contacted at any time during home training phase via e-mail and phone.

Measurements

Within the scope of the sports camps, initial and regular physical and subjective examinations monitored the effects of the training. Following assessments were carried out and were already described in a previous publication [11].

- *Clinical data (*age, body mass index (BMI), Orthopaedic Joint Score (OJS) [20], type of haemophilia, severity, bleeding events, treatment modalities, inhibitor, viral infections).
- *Activity level (*five-point Likert scale from 0 ('not active') to 4 ('active more than three times/week').
- *Objective physical performance* (range of motion in knees, ankles and elbows measured by a goniometer [19], one-leg-stand (holding position time with a maximum of 30 s) [21], 12-min walk test on cinder track [heart rate before and at the end of the test, walking distance, Borg scale, visual analogue scale (VAS)] [22]).
- *Subjective physical performance* (HEP-Test-Q questionnaire [23]).

Furthermore, HEP-participants were supposed to document the extent and manner of their sports therapy programme over the study period as well as their

Table 1. Contents of the sports therapy programme according to the four primary focal points.

Body awareness	Muscle tone regulation	Joint mobilization	Muscle activation
Regulation of respiration	Post isometric relaxation (PiR)	Active range of motion	Short foot by Janda
Relief position by Bruegger	Myofascial release techniques	Traction	Isometric resistance exercise
Selective muscle activation	Stretching		Dynamic low resistance exercises using Thera-Band®
Variation in centre of gravity			Knee bend

bleeding incidence and factor consumption in a monthly provided protocol.

Statistical analyses

All statistical analyses were conducted using the SPSS programme version 18.0 (SPSS Inc., Chicago, IL, USA). Data are shown as mean (M) ± standard deviation (SD) and range (min to max) and were tested for normal distribution using Kolmogorov–Smirnov test and homogeneity. Because of group's disparities, longitudinal data were described and compared as differences between the two measurements. For the comparison of clinical and physical data of the different groups, univariate ANOVA or Kruskal–Wallis test was utilized according to distribution and was verified with the *post hoc* test by Tukey. Chi-squared test was used to compare patients' specific data. $P \leq 0.05$ was defined as significant.

Results

Socio-demographical and clinical data

Of 48 haemophiliac patients, only 13 performed the regular sports therapy programme at home with a complete data protocol (active PWH). Twelve patients did not take part in the introduced home sports therapy programme (passive PWH). Twenty-three patients were excluded from the analysis because of irregular training frequencies (four), inevitable operations during intervention period (four) or lack of further examinations as patients terminated the study early due to private reasons (seven) or patients entered later into the study (eight). Nineteen of 43 healthy control subjects could be re-examined after approximately 1 year.

Active PWH were older than passive PWH and controls. Controls showed a much better OJS compared with PWH and reported no viral infections (see Table 2).

The only difference found between haemophilic subgroups was related to the presence of chronic hepatitis C (HCV) (see Table 3).

For the comparison of patients and controls before and after 1 year of sports therapy programme, no data of the dropped out group were available.

Activity level

Active PWH performed an average of two training elements per day. Their activity level increased by 100% and remained constant in passive PWH and controls (see Table 4). No bleeding occurred due to the training programme.

Objective physical performance

Concerning the range of motion, the right knee was significantly improved in active PWH after 1 year of sports therapy programme compared with passive PWH. The mobility in the other joints as well as the one-leg-stands was the same. Four PWH missed the one-leg-stand and 12-min walk test due to illness, whereby six controls could not attend the walking test

Table 2. Clinical data and activity level; subgroups of people with haemophilia (PWH) and controls before observation period.

	Active PWH (n = 13)	Passive PWH (n = 12)	Dropped out PWH (n = 23)	Controls (n = 19)	P-value
Age (years)	45 ± 5 (36–55)	36 ± 15 (19–65)	48 ± 9* (29–61)	39 ± 11 (23–59)	0.006†
BMI (kg m^{-2})	26.2 ± 5.2 (20.8–37.7)	22.6 ± 3.6 (18.3–28.7)	26.3 ± 4.6 (19.2–38.6)	25.9 ± 2.9 (17.6–29.6)	n.s.
OJS total score (0–100)	32 ± 10 (18–48)	26 ± 10 (10–47)	29 ± 9 (8–43)	4 ± 3*** (0–10)	≤ 0.001
Activity level (times/week)	1.2 ± 1.2 (0.0–3.0)	0.8 ± 1.2 (0.0–4.0)	1.6 ± 1.3 (0.0–4.0)	0.8 ± 1.1 (0.0–3.0)	n.s.

Data are shown as mean ± standard deviation and range (min to max); n.s., not significant.
†Univariate ANOVA, the others with Kruskal–Wallis test.
*$P \leq 0.05$ (dropped out PWH vs. passive PWH and controls).
***$P \leq 0.001$ (controls vs. active PWH, passive PWH and dropped out PWH).

Table 3. Patients' specific data; subgroups of people with haemophilia (PWH).

		Active PWH (n = 13)	Passive PWH (n = 12)	Dropped out PWH (n = 23)	P-value
Type of haemophilia	A (thereof severely/moderately affected)	12 (92.3) (10/2)	12 (100.0) (11/1)	22 (95.7) (22/0)	n.s.
	B (thereof severely/moderately affected)	1 (7.7) (1/0)	0 (0.0) (0/0)	1 (4.3) (1/0)	
Target joint(s)	Yes	5 (38.5)	3 (25.0)	4 (17.3)	n.s.
Treatment	Prophylaxis	6 (46.2)	6 (50.0)	14 (60.9)	n.s.
	On-demand	7 (53.8)	6 (50.0)	9 (39.1)	
Inhibitors	Yes	0 (0.0)	2 (16.7)	2 (8.7)	n.s.
HCV	Yes	10 (76.9)	5 (41.7)	18 (78.3)*	0.029
HIV	Yes	3 (23.1)	0 (0.0)	8 (34.8)	n.s.

Data are shown as frequency distribution in percentage; n.s., not significant; Kruskal–Wallis test.
*$P \leq 0.05$ (dropped out PWH vs. passive PWH).

Table 4. Changes in activity level, range of motion, one-leg-stand and 12-min walk test after 1-year sports therapy programme; active and passive people with haemophilia (PWH) and controls; positive values imply an increase of the activity level, motion, one-leg-stand holding position or the endurance capacities.

	Active PWH (n = 13)	Passive PWH (n = 12)	Controls (n = 19)	P-value
Activity level	+1.1 ± 1.2* (−1.0 to 3.0)	−0.3 ± 1.4 (−4.0 to 1.0)	−0.1 ± 1.0 (−2.0 to 1.0)	0.021
Range of motion (degree)				
Knee left	+2.2 ± 10.5 (−14.0 to 17.0)	+2.5 ± 8.8 (−8.0 to 25.0)	+2.5 ± 5.3 (−9.0 to 11.0)	n.s.†
Knee right	+5.8 ± 5.3‡ (−2.0 to 19.0)	−1.3 ± 8.6 (−16.0 to 12.0)	+3.3 ± 5.8 (−9.0 to 14.0)	0.029†
Ankle left	+0.4 ± 8.8 (−27.0 to 8.0)	+1.8 ± 4.9 (−6.0 to 9.0)	+0.4 ± 5.7 (−11.0 to 10.0)	n.s.
Ankle right	+2.4 ± 5.8 (−6.0 to 15.0)	+0.1 ± 6.0 (−12.0 to 7.0)	+0.4 ± 5.1 (−9.0 to 12.0)	n.s.†
Elbow left	−0.1 ± 6.7 (−12.0 to 10.0)	−1.8 ± 5.9 (−11.0 to 9.0)	−1.3 ± 3.7 (−8.0 to 4.0)	n.s.†
Elbow right	−4.0 ± 12.7 (−36.0 to 10.0)	+0.3 ± 5.6 (−10.0 to 7.0)	−0.5 ± 5.0 (−12.0 to 10.0)	n.s.
One-leg-stand (s)	(n = 11)	(n = 10)	(n = 19)	
Left	+0.2 ± 2.4 (−5.3 to 3.7)	−0.8 ± 5.5 (−9.7 to 10.7)	+0.6 ± 2.7 (−5.0 to 9.7)	n.s.
Right	−2.0 ± 4.3 (−12.3 to 3.3)	−0.1 ± 7.3 (−16.7 to 12.7)	−0.2 ± 5.3 (−15.0 to 13.3)	n.s.
12-min walk test	(n = 11)	(n = 10)	(n = 13)	
Pre-heart rate [1/min]	+2.4 ± 11.5 (−13.0 to 24.0)	−2.4 ± 12.0 (−23.0 to 15.0)	+0.2 ± 8.6 (−11.0 to 17.0)	n.s.
Post-heart rate [1/min]	+18.3 ± 23.9 (−14.0 to 62.0)	+11.6 ± 26.3 (−40.0 to 64.0)	+4.8 ± 14.7 (−26.0 to 38.0)	n.s.†
Walking distance [meter]	+217 ± 199 (−52 to 579)	+151 ± 135 (−22 to 407)	−32 ± 217** (−743 to 95)	0.013
Borg scale [6–20]	+1.8 ± 5.1 (−4.0 to 13.0)	+1.8 ± 3.6 (−2.0 to 11.0)	+2.5 ± 3.1 (0.0 to 12.0)	n.s.
VAS [0–10]	−1.1 ± 1.9 (−5.0 to 0.0)	+1.8 ± 3.0 (−8.0 to 1.0)	−0.5 ± 1.4 (−5.0 to 0.0)	n.s.

Data are shown as mean ± standard deviation and range (min to max); n.s., not significant.
†Univariate ANOVA, the others with Kruskal–Wallis test.
*$P \leq 0.05$ (active PWH vs. passive PWH and controls).
‡$P \leq 0.05$ (active PWH vs. passive PWH).
**$P \leq 0.01$ (controls vs. active PWH).

because of logistic reasons. The 12-min walk test proved a longer walking distance for the active PWH compared with controls. Two patients of the active haemophilic group, who had to stop the 12-min walk test during the first measurement because of low back pain or troubles in the knee, were able to realize the test after 1 year without a break. No significant differences were detected in terms of heart rate and Borg scale. By tendency, VAS showed less pain in active PWH (see Table 4).

Subjective physical performance

One control patient did not fill out the HEP-Test-Q during the first examination. After 1 year of sports therapy, active PWH reported a significantly better subjective physical performance in the HEP-Test-Q domains 'strength & coordination', 'endurance', 'body perception' as well as the total score (+9.4 ± 13.8) compared to passive PWH (−5.3 ± 13.5) and controls (+3.7 ± 7.5). The 'mobility'-scale showed no significant changes (see Fig. 1).

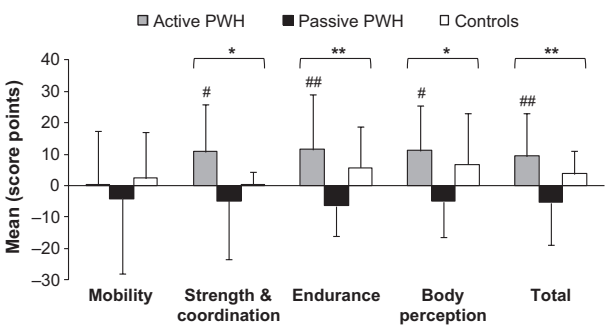

Fig. 1. Changes in subjective physical performance (HEP-Test-Q) after 1-year sports therapy programme; active (n = 13) and passive (n = 12) people with haemophilia (PWH) and controls (n = 18); data are shown as mean and standard deviation; domains 'mobility' and 'strength & coordination' with Kruskal–Wallis test, the others with univariate ANOVA; *$P \leq 0.05$, **$P \leq 0.01$; #$P \leq 0.05$ (active PWH vs. passive PWH); ##$P \leq 0.01$ (active PWH vs. passive PWH); positive values imply an increase of the physical performance.

Discussion

This is the first observational study, which investigates the subjective as well as the objective physical performance before and after 1 year of sports therapy programme in PWH using the questionnaire HEP-Test-Q. Subjective data were compared with objectively measured data.

Active PWH showed a significant improvement in their subjective physical performance compared to passive PWH after 1 year of sports therapy with the exception of the subscale 'mobility'. On the other hand, the goniometer detected an increase in the range of motion in active PWH, but only for the right knee. One-leg-stand was unchanged in both groups. The extension of the walking distance in active PWH was reflected in the self-assessment. Furthermore, data demonstrated an increase in general activity level, which was not related to a higher bleeding frequency or increased factor consumption.

Supervised sports therapy appears to be safe and practical for severe adult haemophilia patients. The effects after 1 year were small, but substantiate the recommendation to include haemophilia subjects to a

sports therapy programme. Patients' report of their own experience of well-being and functioning compared to objective data showed partial differences; therefore subjective evaluation provides additional information and should be combined with objective measurements.

Investigated groups showed differences in clinical data. Compared to passive PWH and controls, active PWH and dropped out PWH were not only older and had a worse OJS but were also more active. This implies that people with physical limitations were probably more willing to do more for their health. Dropped out PWH had more often HCV than the other two haemophilia groups; this is associated with the undesirable side effects of antiviral treatments and could explain why these patients did not participate regularly. To eliminate such effects, comparable groups would be desirable. At last, the high number of dropouts led to the smaller sample size.

Although nowadays sport activities are considered beneficial, their importance as an integral element in haemophilia treatment has not yet been widely recognized. Recommendation of sport activities in haemophilia has not always been taken into consideration. Recently, PWH have been asked to actively participate in sports and do regular physical activity. As of today, only a few studies exist which have been dealing with the investigation of sports related changes in PWH [17,24,25], but with limitations in terms of the number of subjects, the manner of research and statistical methods as well as the training description. In the majority of cases, the results are based on clinical experience and not on scientific studies.

A recent study in haemophilic boys in the UK demonstrated that boys doing sports reported a significantly better subjective physical performance, assessed with a child-adapted version of the HEP-Test-Q, than boys not doing sports; and that a sedentary lifestyle had a negative impact on their subjective physical performance [26].

Thus, there are initial indicators that target-oriented training, focusing on the needs of PWH, is practicable and reasonable without substantial complications. Coordination skills as well as stamina in PWH are trainable; even 'gentle' training leads to an improvement of maximal isometric strength [17]. Von Mackensen *et al.* showed especially a significantly better self-assessment of the endurance after a 1-year specific aqua-training programme for PWH [27].

An adequate sports therapy based on the clinical picture, e.g. like it has been established for cardiovascular diseases, is not an integral part of the adjuvant treatment of haemophilia. Especially the vagueness about specific training contents, methods and forms as well as their effects on PWH illustrate the difficulty related to the development and realization of a targeted sports therapy.

Although physical exercise in groups, two to three times per week, is also difficult to manage for PWH, long distances to the respective treatment centres hinder this classical type of training. This problem led to the development of the model 'Programmed Sports Therapy', which is a unique combination of group training and guided independent home training. Group training takes place in aggregate sport camps. Independent home training is reinforced by sports therapists and regulated by use of individualized training guidelines. This concept and therapeutic contents employed in recent years within the framework of the HEP-project have proven to be effective, sensitive and adaptable to individual needs [28].

Conclusion

One year of 'Programmed Sports Therapy' is able to change parameters of subjective and in a smaller dimension of objective physical performance. On one hand, this supports the necessity of an adequate sports-therapeutic training in PWH – supervised by experienced persons – to improve the physical fitness. On the other hand, this study sharpens the awareness of differences between subjective and objective physical performance. The HEP-Test-Q seems to be a reliable questionnaire to assess the subjective physical performance and to control sports-therapeutic treatments. Subjective training effects can be measured with the HEP-Test-Q and should be combined with objective assessments to reveal all different

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