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The Effects of Exercise Training on Physical Activity Level, Daily Living Activities, and Participation in Children with Hemophilia

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What is already known on this topic?

- *Hemophilia is an uncommon disorder that is difficult to diagnose and manage. While bleeding events in people with hemophilia is usually lifelong, they often occur in muscles and joints.*
- *One of the most important steps in the treatment of hemophilia is to detect and prevent bleeding events and joint damage.*
- *The World Health Organization, adopting the International Classification of Function (ICF) framework, suggested that the severity of hemophilia can best be described in terms of "body structures and functions," "activities and participation," "environmental," and "personal" factors.*

What this study adds on this topic?

- *Few studies have investigated the effects of exercise training in children with hemophilia (CwH) within the ICF framework.*
- *This study aimed to determine the efficiency of individually planned exercises in CwH within the ICF framework.*
- *Our objective was to develop an effective physiotherapy approach to improve participation, functional level, physical activity, and joint health in CwH.*

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ABSTRACT

Objective: Hemophilia is an uncommon disorder that is difficult to diagnose and manage. Effective movement and individual physiotherapy interventions can improve physical activity levels, quality of life, and participation in children with hemophilia. This study aimed to investigate the effects of individually planned exercise on joint health, functional level, pain, participation, and quality of life in children with hemophilia.

Materials and Methods: Twenty-nine children with hemophilia (aged 8-18 years) were randomized into either an exercise group with physiotherapists (n = 14) or a counseling home-exercise group (n = 15). Pain, range of motion, and strength were measured using a visual analog scale, goniometer, and digital dynamometer, respectively. Joint health, functional capacity, participation, quality of life, and physical activity were assessed using the Hemophilia Joint Health Status, 6-Minute Walk Test, Canadian Occupation Performance Measure, Pediatrics Quality of Life, and International Physical Activity Questionnaire, respectively. The exercises were planned individually according to the needs of both groups. Additionally, the exercise group performed the exercise with a physiotherapist. Interventions were performed 3 days/week for 8 weeks.

Results: The Hemophilia Joint Health Status, 6-Minute Walk Test, Canadian Occupation Performance Measure, International Physical Activity Questionnaire, muscle strength, and range of motion (elbow, knee, and ankle) were significantly improved in both groups ($P < .05$). Compared with the counseling home-exercise program group, the exercise group had better results in the 6-Minute Walk Test, muscle strength, and range of motion (knee and ankle flexion) ($P < .05$). No significant difference was found in pain and Pediatrics Quality of Life scores in both groups.

Conclusion: Using individually planned exercise in children with hemophilia is an effective physiotherapy approach to improve physical activity, participation, functional level, and joint health.

Keywords: Exercise, hemophilia, physical activity, quality of life, participation

INTRODUCTION

Recurrent hemarthroses in the early years and hemophilic arthropathy (HA) in the later years may lead to altered movement patterns and movement limitations.[1-3] Some structural changes are associated with HA in cartilage and bone, which can lead to diminished joint range of motion (ROM), atrophy of surrounding muscles, and stiffness.[4,5] Hemophilic arthropathy negatively affects patients' quality of life (QoL) and physical activity (PA) progressively.[6] The general principle in the treatment of hemophilia is to prevent the development of arthropathy. However, while the medical treatment of patients at the time of bleeding

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is successfully maintained, physiotherapeutic measures to prevent or manage existing joint problems before bleeding occurs have not been fully implemented.[7]

The World Health Organization's International Classification of Functioning (ICF) considers health to be "the demonstration of the relationship between body structure and function, activities, participation, and personal and environmental factors."[8] The ICF has some set standards that are fundamental to provide people with hemophilia (PwH) with ideal individualized treatment.[8,9] The main outcome measures are self-reported bleeding and clinical joint situation assessment, which are already being used, whereas outcome at the level of activity and participation still needs to be used more often in hemophilia studies and treatment.[8] For physiotherapists, the framework provided by the ICF will prevent or minimize complications, functional limitations, and social isolation due to HA by effectively planning both evaluation and treatment.[10] Structured exercise programs are one of the most important ways of reducing physical inactivity in children. Participating in structured PA programs early in life is key to preventing complications from chronic diseases in adulthood by ensuring an active lifestyle.[11]

For PwH to be able to continue their daily life activities with quality, painlessness, and without any restriction, and to ensure social participation, musculoskeletal system functions should be protected and improved with physiotherapy and rehabilitation from an early age.[12] Degenerative changes in the joints and the severity of arthropathy increase over time in patients with HA who do not undergo physiotherapy. Accordingly, joint pain, limitation, and changes in gait pattern affect the functionality, social participation, and QoL of PwH, and limit functional independence.[13]

Therefore, there is a need to develop individually planned physiotherapy programs, which are effective, accessible, applicable, and evidence-based non-invasive treatment practices for HA that may occur in the joints in the early stages of the disease. We believe that the effects of individually planned exercise should be examined as an innovative approach that can be added to routine medical treatment programs by experienced physiotherapists to meet the need for physiotherapy services for PwH and to improve the services in the long term. Joint movements, muscle strength, and functions can be improved by applying for this specially selected treatment program with a physiotherapist or a home-based program. In addition to these parameters, the evaluation of PwH in terms of bleeding frequency, joint health, extremity functions, and QoL is very valuable in terms of the ICF framework and can be used as an indicator of PA and social participation in these individuals.

Our results reveal a comprehensive and solution-oriented physiotherapy and rehabilitation approach that increases joint health, functional independence level, QoL, and participation without any risk of bleeding in the patient. This study aimed to investigate the effects of exercise with a physiotherapist and those of an individualized planned home-exercise program on PA, joint health, muscle strength, functional level, pain, QoL, and participation in children with hemophilia (CwH). We hypothesized that compared to the home-exercise program, the exercises carried out with and under the supervision of a physiotherapist are superior.

MATERIALS AND METHODS

Study Group

Twenty-nine male participants (aged 8-18 years) with hemophilia A or B, participated in the present study. Participants were informed through the messaging group of the the Hemophilia Society of Turkiye. Patients who had a history of bleeding in any joint in the last 2 weeks or did not follow exercise sessions minimally twice a week for 8 consecutive weeks were excluded from the present study. Participants were recruited from the Hemophilia Society of Turkiye at the Physiotherapy Unit between January and May 2021. The patients were divided randomly, and the RCT allocation ratio of 1:1. A serial number, generated using the Statistical Package for Social Sciences (SPSS) version 22.0 (IBM Corp., Armonk, NY, USA), was assigned to each participant and randomly allocated to 1 of 2 study groups. The study comprised 2 groups: an individualized exercise program group (EG) with a physiotherapist that included a total of 14 CwH and an individual counseling home-exercise program group (CG) with 15 age-paired CwH.

The study was approved with the numbered 13022260-300-63450 by the Ethics Committee of the İstanbul University-Cerrahpaşa Faculty of Medicine and conducted in accordance with the principles of the Declaration of Helsinki. Written informed consent was obtained, and information on the research was provided to the parents or guardians of the selected CwH. The CwH attending the hemophilia clinic was invited to participate in the research only after providing their full and informed consent.

Clinical Assessments

Assessments were conducted at baseline and after treatment. Information about all participants' ages, body mass index (BMI), hemophilia treatments, types and severity of hemophilia, and inhibitor development were recorded.

Body Structures and Functions Measures

To obtain a comprehensive description and evaluation of health at the ICF framework in terms of "body structures and functions," we assessed muscle strength, ROM and functional tests and pain.

Muscle strength was measured using a digital dynamometer (Lafayette Hand-Held Dynamometer). Elbow extensors and flexors were measured in patients with 90° elbow flexion and the forearm in the neutral by applying the proximal part of styloid process resistance in the sitting position. Knee extensors and flexors were measured in the sitting position with the hip and knee flexed at 90° by applying resistance over the malleolus. Dorsiflexors and plantar flexors were measured while the lower legs of the patient were stabilized in the supine position. Resistance was applied over the metatarsal heads, the plantar surface of the foot for dorsiflexors, and the dorsal surface of the foot for plantar flexors. Each measurement was repeated 3 times, and the average of the evaluations was used for statistical analysis.[14]

The elbow, knee, and ankle ROMS were measured using a goniometer, the axis of the goniometer was placed at the joint line, stationary arm lateral midline of the humerus, moving arm parallel to the midline of the radius, stationary arm lateral midline to the femur, and moving arm lateral midline of the fibula and stationary arm fibular head and moving arm parallel to the lateral midline of the fifth metatarsal, respectively.[15]

Joint health status was assessed using the Hemophilia Joint Health Status (HJHS) 2.1. The maximum HJHS score was 124, which indicates poorer joint health and higher scores.[16] The 6-Minute Walk Test (6MWT), they were instructed to walk at their own pace and not jump or run until they were told to stop. The therapist closely followed the number of laps using a chronometer to measure the exact distance walked. The 6MWT, including CwH, has long been used in children with various chronic conditions.[17]

A visual analog scale (VAS) was used to measure the presence of joint pain. The scores on the scale ranged from 0 (no pain at all) to 10 (worst pain imaginable).

Activities and Participation Measures

According to the ICF model, a comprehensive view of health involves the measurement of activities and participation. These domains also influence each other and are moderated by environmental and personal factors.

Table 1. Intervention Training Program

Group	Intervention	Characteristics of Intervention
Exercise group (EG)	• **Warming Exercises:** (Gentle, slowly, and prolonged stretch within the pain-free range were used) Joint ROM and soft tissue flexibility were prescribed based on limitations (5 minutes) Especially for knee extension and ankle dorsiflexion and elbow extension active ROM and muscle stretching exercises (biceps, triceps, quadriceps, hamstrings, and calves). To aim maintenance and improvement of ROM (5 minutes) • **Strengthening exercise:** Especially for identified target joints, or previously injured muscles. To aim maintaining and improving strength options for resistance exercise with theraband (medium or mild resistance) and functional strengthening activities (15 minutes) Performed isometric exercises of quadriceps, and calf raise, using resistive therabands in submaximal ranges of dorsiflexion, plantar flexion, knee extension and flexion, elbow extension and flexion, and squat. The upper and lower extremity exercises were performed bilaterally and also considering the musculoskeletal risk of bleeding in CwH • **Balance and proprioceptive exercises** (15 minutes) Weight-bearing exercise: cat-camel exercise. Progressed with stable and unstable surface or lifting arm or leg. Forward, sideways, and backward bending exercises on 1 foot. Standing exercises were progressed as follows: (i) 1-leg stance on a stable surface, (ii) playing the ball with hand, (iii) 2-leg stance on an unstable surface (balance ped, balance wood, or bosu), and (iv) playing the ball with hand on the unstable surface. All the above exercises progress from open eyes to closed eyes. • **Cool-down** (same as warm-up) (10 minutes) • **Frequency**	1 set of 8-10 reps 10 s of contraction with 5-second intervals between each reps. Moderate tension and duration of 20-30 s 1 set of 3 repetitions, increase gradually to 5 reps. Starting 10 reps, 1 time for first week. If no increased pain or swelling occurred, the intensity would be increased per week. 2 times for 2-5 weeks, 3 times for 5-8 weeks 10 sec of contraction with 5 s intervals between each rep, slowly done performed in the pain-free range. 1 minute between sets and exercises 10 reps, 10 s per repetition with 10-second interval between each rep in the pain-free range 10 reps, 10 s of contraction with 5-second intervals between each rep in the pain-free range. 2 days/week under physiotherapist's supervision at the hemophilia society of Turkey center 1 session/day, 3 days/week under parents' supervision at home
Counseling Group (CG)	• In ergonomics and joint protection principles were taught. • Informing Family (a) Why are the exercises necessary (b) To what extent the families should be protected (c) The harmful effects of inactivity (d) physical activity and sport: risks and benefits(d) There was information about the resting-activity cycle when there was bleeding. (e) Active/passive stretching exercises were performed within the limits of pain. (f) Patients performed exercises under a supervised exercise program at home. (g) The videos of all the exercises were recorded from their own phones.	The CG was encouraged to be invited for a check-up after 8 weeks and to do their exercises regularly until then. Exercise and bleeding conditions were followed up by phone call every 2 weeks.

CG, counseling group; CwH, children with hemophilia; EG, exercise group; reps, repetitions; ROM, range of motion.

The short version of the International Physical Activity Questionnaire (IPAQ) was used to measure PA in patients. The IPAQ is a self-reported 7-day recall questionnaire designed to assess current levels of PA.[18] Quality of life was evaluated using the Pediatrics Quality of Life Scale (PedsQL), which assesses physical, social, emotional, and school functioning. In the scale, there are both parent proxy reports and child self-reports to reflect their potentially unique perspectives. Scores can range from 0 to 100, with higher scores indicating better QoL.[19] The Canadian Occupation Performance Measure (COPM) evaluates an individual's performance perception of both activity and participation domains. First, patients chose the 5 most important problems regarding their major concerns about self-care, leisure, and productivity. The scores and ratings were from 1 to 10, and low scores reflect more difficulties or less satisfaction. Finally, the average score was calculated to determine the satisfaction and performance of the 5 identified problems. The COPM is useful in planning individualized management plans and the effectiveness of intervention strategies in PwH.[20]

Interventions

All measurements and exercise programs were performed by the same expert physiotherapist for each participant based on individual needs. The exercise program for the patients was performed within 1-2 hours after the routine coagulation factor prophylaxis treatment was administered. In the EG, the interventions for each session lasted for 60 minutes, 3 days/week for 8 weeks. In the CG counseling regarding PA was provided.

Table 1 illustrates the detailed contents of the interventions according to each group. Exercises for flexibility, strength, proprioception, and cardiovascular function were included in the program. All major muscle groups were exposed to practice all the exercises. Each patient was informed on how to identify adverse results, such as muscle-joint bleeding, pain, swelling, or fatigue. The intervention progressed in the following weeks by changing the number of repetitions, amount of resistance, and amount of time.

Statistical Analysis

Statistical analyses of the data obtained in this study were performed using SPSS version 22.0 (IBM Corp., Armonk, NY, USA). Descriptive statistics are presented as means and SDs or frequencies (percentages). The Shapiro–Wilk test was used to check whether the data were normally distributed. Data with a normal distribution were analyzed using the paired sample *t*-test and independent sample *t*-test within and between groups, respectively, for parameters before and after treatment. Data without normal distribution were analyzed using the Wilcoxon signed-rank test and Mann–Whitney *U*-test within and between groups, respectively. The effect size (ES) of the treatment administered within the group (Cohen's *d*) (https://www.socscistatistics.com/effectsize/) was calculated by dividing the mean difference before and after treatment by the pre-treatment SD for each parameter. An ES close to 0.20 was considered a minor effect, a medium effect close to 0.50, and a high ES was close to 0.80.

RESULTS

Twenty-nine participants completed the study. The flow diagram of the study is shown in Figure 1. One patient with severe hemophilia with inhibitors had bleeding; in addition, 4 participants left the study because of the COVID-19 pandemic and could not participate. The intervention groups did not differ

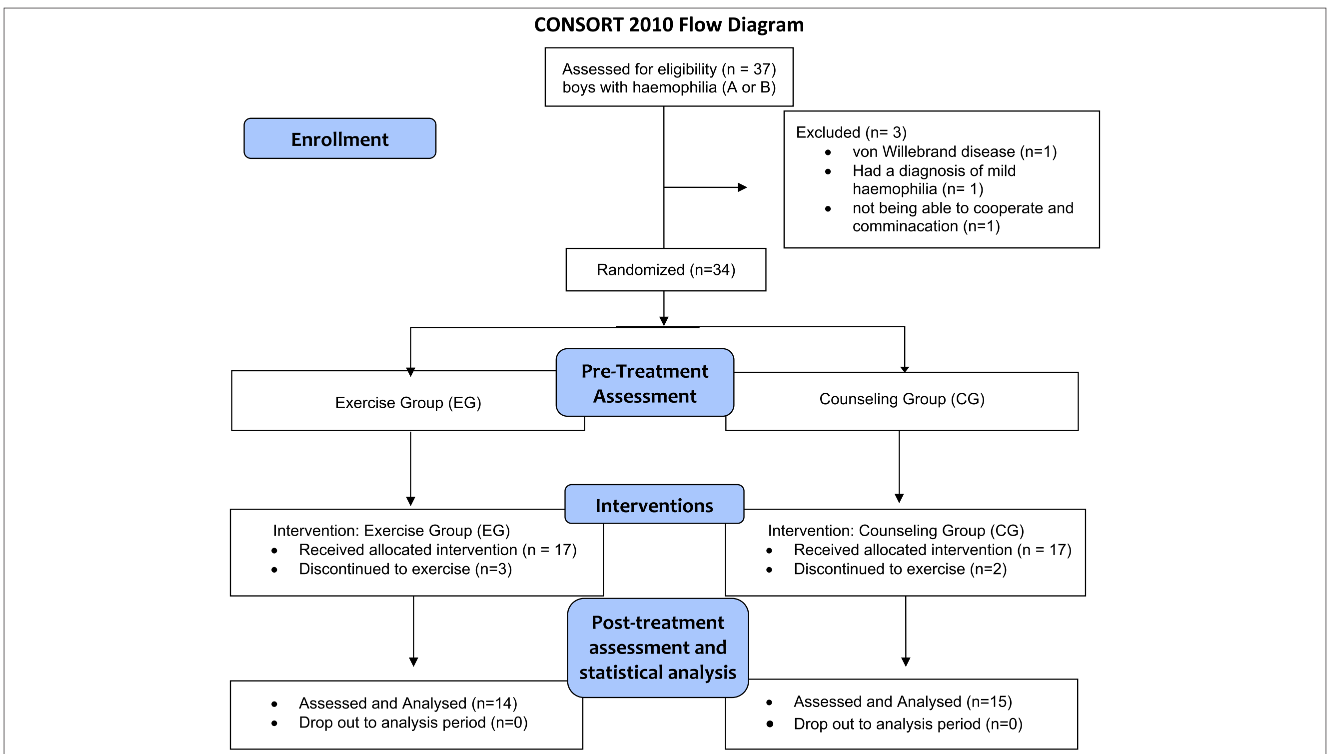

Figure 1. CONSORT 2010 flow diagram.

Table 2. Descriptive Characteristics of Patients (n = 29) With Hemophilia

	EG (n = 14)	CG (n = 15)	P*
Age (years), mean ± SD	14.86 ± 2.07	13.61 ± 3.12	.208
BMI kg/m^2, mean ± SD	20.78 ± 4.25	20.98 ± 4.78	.902
Type (hemophilia A/B), n (%)	13/1 (92.9/7.1)	12/3 (80/20)	.075
Severity (severe/moderate), n (%)	12/2 (85.7/14.3)	12/3 (80/20)	.432
Inhibitor status (present/absent), n (%)	2/12 (14.3/85.7)	1/14 (6.7/93.3)	.621
Treatment (prophylactic/on demand), n (%)	11/3 (78.6/21.4)	12/3 (80/20)	.732

BMI, body mass index; CG, counseling group; EG, exercise group.
*Independent samples *t*-tests.

significantly in terms of age, BMI, hemophilia type and severity, inhibitor status, or treatment method ($P > .05$). The baseline descriptive characteristics of the participants are shown in Table 2. Most of the participants had a severe clinical type of hemophilia A.

Comparing the measurements taken at the baseline and during the post-intervention period, it is seen in Table 3 that HJHS, 6MWT, STS, IPAQ ($P < .001$), and COPM ($P < .05$) were substantially improved in both groups. When the changes occurring in the groups were analyzed, it appeared that taking 6MWT and IPAQ ($P < .05$) into consideration, the EG was superior to the CG. As shown in Table 4, when comparing the baseline with the final treatment, muscle strength, knee ROM ($P < .001$), and ankle joint ROM ($P < .05$) were significantly improved in the EG. Muscle strength, ankle, and elbow joint ROMs except elbow left extension ROM improved significantly after treatment in the CG ($P < .05$). There were significant differences detected in the results related to muscle strength of the elbow, knee, and right plantar flexion as well as ROM of the left knee and both plantar flexion in favor of the EG ($P < .05$).

DISCUSSION

Our results indicate that both physiotherapy programs were effective in treating CwH. Despite this, the EG was statistically superior to the CG at the functional level as shown by the 6MWT and IPAQ, including changes in knee and plantar flexion ROMs, for several outcomes in muscle strength with especially remarkable changes at the elbows, knees, and plantar flexions.

According to the studies, it was reported that COPM is a practical measurement tool for musculoskeletal dysfunction in PwH.[8,20] Information about the needs of each patient was provided in order for the rehabilitation team to allow the planning of individualized intervention strategies.[20] David et al[9] suggested that alongside musculoskeletal healing, COPM can also improve bio-psychosocial issues patients might have. Canadian Occupation Performance Measure has been shown to be effective in setting goals in hemophilia comprehensive care (HCC); however, it is not practically helpful to compare the outcomes among different cohorts, as the items assessed as domains are not predetermined. As a contribution to the literature, in the framework of ICF, we compared the effects on COPM to evaluate participation, as well as different physiotherapy approaches. A remarkable increase was found in the COPM (performance and satisfaction) in both groups. However, no significant differences were observed between the groups. Nevertheless, the post-intervention COPM assessment found better performance and satisfaction scores in the EG than in the CG. This is a personalized assessment; therefore, the scores for the meaning of change may differ for each person individually.[9] Our results suggest that COPM is essential in a detailed assessment for physiotherapy HCC.

There were no remarkable differences between the groups in our PedsQL scale results for either parents or patients in this study. Similar to our study, Niu et al.[21] used QoL scales in the general population; they preferred this scale for those younger

Table 3. Comparison of Pre- and Posttreatment in Functional Level, Physical Measurements, and Quality-of-Life Parameters Within and Between Groups

	EG				CG				
	BT, mean ± SD	AT, mean ± SD	P*	ES***	BT, mean ± SD	AT, mean ± SD	P*	P** Difference Between Groups	ES***
HJHS (point)	11.29 ± 8.32	5.36 ± 4.71	**<.001**	0.877	13.11 ± 11.1	8.72 ± 10.1	**<.001**	.320	0.413
6MWT (meters)	343.93 ± 28.8	407.5 ± 44.56	**<.001**	1.694	349.11 ± 51.2	382.44 ± 68.4	**<.001**	**.009**	0.551
COPM-P	7.52 ± 1.92	8.41 ± 1.43	**.005**	0.525	6.20 ± 1.87	6.89 ± 1.44	**.040**	1.000	0.413
COPM-S	7.40 ± 2.39	8.64 ± 1.52	**.005**	0.636	6.12 ± 2.16	6.97 ± 1.73	**.017**	.214	0.434
IPAQ	1163.93 ± 329.79	2286.79 ± 558.11	**.001**	0.888	976.50 ± 377.03	1454.83 ± 343.83	**.001**	**<.001**	0.726
PedsQL-C (0-100)	0.70 ± 0.53	0.65 ± 0.62	.534	0.086	1.09 ± 0.68	1.12 ± 0.72	.791	.804	0.042
PedsQL-P (0-100)	1.15 ± 0.87	1.03 ± 0.63	.572	0.157	1.19 ± 0.46	1.02 ± 0.63	.169	.849	0.308

6MWT, 6-Minute Walk Test; AT, after treatment; BT, before treatment; CG, counseling group; COPM-P, Canadian Occupation Performance Measure-Performance; COPM-S, Canadian Occupation Performance Measure-Satisfaction; EG, exercise group; ES, effect size; HJHS, Hemophilia Joint Health Score; IPAQ, International Physical Activity Questionnaire; PedsQL-C, Pediatric's Quality of life Scale for Children; PedsQL-P, Pediatric's Quality of life Scale for Parents.
*Wilcoxon signed-rank test.
**Mann–Whitney *U*-test.
***Cohen's *d*.
**P* < .05: significant, **PP* < .01: highly significant.

Table 4. Comparison of Pre- and Posttreatment in Muscle Strength, Range of Motion, and Pain Within and Between Groups

	EG				CG				
Variables	**BT, mean ± SD**	**AT, mean ± SD**	***P*****	**ES*****	**BT, mean ± SD**	**AT, mean ± SD**	***P*****	***P***, difference Between Groups**	**ES*****
Muscle strength, lbs									
Elbow flex (R)	12.57 ± 1.85	17.75 ± 3.84	**<.001**	1.718	12.27 ± 3.76	15.13 ± 5.53	**<.001**	**.04**	0.604
Elbow flex (L)	11.96 ± 2.86	16.54 ± 4.20	**<.001**	1.274	12.56 ± 3.18	14.83 ± 5.28	**.002**	**.007**	0.520
Elbow ext (R)	11.32 ± 3.34	13.97 ± 3.46	**<.001**	0.779	10.78 ± 4.02	11.88 ± 4.45	**<.001**	**.019**	0.259
Elbow ext (L)	9.42 ± 4.19	12.02 ± 4.57	**<.001**	0.593	10.89 ± 4.20	12.25 ± 4.68	**.001**	**.018**	0.305
Knee flex (R)	12.10 ± 2.75	16.02 ± 2.27	**<.001**	1.554	12.62 ± 3.98	14.11 ± 4.23	**.01**	**<.001**	0.362
Knee flex (L)	12.20 ± 2.49	15.64 ± 2.54	**<.001**	1.367	12.10 ± 3.57	13.99 ± 3.95	**.002**	**.027**	0.502
Knee ext (R)	10.72 ± 1.51	16.02 ± 2.75	**<.001**	2.389	11.05 ± 4.56	14.60 ± 5.24	**<.001**	**.017**	0.722
Knee ext (L)	10.09 ± 1.93	14.88 ± 3.18	**<.001**	1.821	11.16 ± 3.69	14.21 ± 4.35	**<.001**	**.033**	0.756
Dorsi flex (R)	10.64 ± 1.33	15.90 ± 3.72	**<.001**	1.882	10.05 ± 2.65	13.17 ± 3.92	**<.001**	.055	0.932
Dorsi flex (L)	9.40 ± 1.40	15.84 ± 5.08	**<.001**	1.728	10.27 ± 2.55	13.46 ± 4.31	**.001**	.057	0.900
Plan. flex (R)	18.05 ± 2.32	25.15 ± 4.62	**<.001**	1.942	17.21 ± 3.66	21.77 ± 3.96	**<.001**	**.038**	1.195
Plan. flex (L)	17.35 ± 2.21	24.34 ± 5.09	**<.001**	1.781	16.70 ± 3.93	21.61 ± 4.61	**<.001**	.095	1.146
ROM (°)									
Elbow flex (R)	133.57 ± 23.7	141.07 ± 5.60	.236	0.435	138.89 ± 7.58	141.11 ± 5.57	**.016**	.701	0.333
Elbow flex (L)	131.43 ± 20.3	140.36 ± 6.64	.091	0.591	139.17 ± 7.90	141.67 ± 6.41	**.015**	.221	0.347
Elbow ext (R)	3.93 ± 8.36	0.71 ± 2.67	.095	0.518	3.33 ± 7.85	2.22 ± 6.23	**.042**	.793	0.156
Elbow ext (L)	7.14 ± 10.69	3.57 ± 8.41	.055	0.371	3.06 ± 8.59	0.83 ± 4.92	.104	.445	0.318
Knee flex (R)	138.21 ± 5.75	142.14 ± 4.68	**.021**	0.749	137.22 ± 25.6	138.89 ± 20.9	.163	.185	0.071
Knee flex (L)	135.0 ± 8.08	142.14 ± 4.68	**.006**	1.081	142.78 ± 5.99	143.33 ± 5.14	.163	**.008**	0.098
Knee ext (R)	3.57 ± 4.97	0.79 ± 1.62	**.023**	0.752	3.06 ± 8.42	2.22 ± 7.32	.083	.133	0.106
Knee ext (L)	5.36 ± 6.92	1.79 ± 3.16	**.012**	0.663	3.06 ± 5.46	1.94 ± 3.88	.104	.083	0.236
Dorsi flex (R)	21.07 ± 5.25	25.36 ± 4.58	**.017**	0.870	19.72 ± 4.68	25.56 ± 6.39	**<.001**	.234	1.042
Dorsi flex (L)	20.0 ± 6.79	25 ± 5.54	**.007**	0.887	23.33 ± 5.94	26.94 ± 6.21	**.003**	.444	0.594
Plan. flex (R)	28.57 ± 6.33	38.21 ± 3.72	**<.001**	1.856	33.89 ± 9.00	38.33 ± 7.67	**.007**	**.025**	0.531
Plan. flex (L)	26.43 ± 6.33	38.21 ± 3.72	**<.001**	2.269	35.83 ± 7.52	39.72 ± 5.27	**.002**	**.001**	0.599
VAS (0-10)									
Elbow (R)	0.36 ± 0.92	0.21 ± 0.57	.62	0.196	0.78 ± 1.55	0.44 ± 1.14	.501	.755	0.249
Elbow (L)	1.79 ± 2.69	0.29 ± 1.06	.29	0.733	0.72 ± 1.44	0.17 ± 0.51	.086	.185	0.509
Knee (R)	0	0	1	-	0.39 ± 0.91	0.06 ± 0.23	.083	.114	0.497
Knee (L)	1.14 ± 2.34	0.36 ± 1.33	.102	0.409	0.39 ± 1.03	0.33 ± 0.84	.749	.241	0.063
Ankle (R)	0.5 ± 1.87	0	.336	-	0.56 ± 1.38	0	.106	.488	-
Ankle (L)	1.00 ± 2.66	0.07 ± 0.26	.177	0.492	0.5 ± 1.24	0.28 ± 1.17	.570	.759	0.182

AT, after treatment; BT, before treatment; CG, counseling group; EG, exercise group; ES, effect size; ext, extension; flex, flexion; L, left; plan. flex, plantar flexion; R, right; ROM, range of motion; VAS, visual analog scale.
*Wilcoxon signed-rank test.
**Mann–Whitney *U*-test.
***Cohen's *d*.
*$P < .05$: significant, *$P < .01$: highly significant.

than 18 years, and no statistically significant differences were discovered between the groups.

International Physical Activity Questionnaire is a widely used scale for measuring PA in the literature on hemophilia.[21-24] When the results were compared with the IPAQ survey to assess the intervention of PA among the groups, we found a significant increase in both groups, but IPAQ was superior in favor of the EG compared to the CG. The PA level pre-treatment was moderate in both groups. Post-intervention, the PA level in the EG increased to a vigorous level, while there was no change in the PA level of the CG. This is an expected result because the EG continued to exercise regularly with a physiotherapist 3 days a week. Another possible reason is that the interactive therapy sessions in the EG provided more significant improvements in PA. Furthermore, this result may be because the coronavirus (COVID-19) pandemic, necessitated students in our country to continue their classes online at home. However, it has been shown that there was a decrease in PA levels not only in CwH but also in healthy children during the pandemic due to online classes and quarantine.[25]

In our study, HJHS of PwH in both groups was significantly decreased after treatment, but there were no significant differences between the groups. However, this subtle difference may appear to be more important in a larger sample size. Similar to our study, Parhampour et al[26] examined the effects of resistance and aerobic and combined exercises, and found a dramatic decrease in the final HJHS scores of the intervention groups. We found greater improvements in the distance walked in the 6MWT, which were significantly increased after both interventions; however, when the groups were compared, a significant difference in 6MWT was observed in favor of the EG. This outcome may be attributed to the influence of exercise training on the enhancement of muscle strength, performance, and joint function, yielding a more comfortable and efficient gait. In support of this notion, Mulvany et al.[27] found that substantial gains in distance walked on the 6MWT ($P < .1$) affected supervised and individualized exercise programs. Furthermore, the data obtained by comparing the biomechanical gait parameters of young PwHs and their age-matched peers indicated that there was more impairment of the joint function of the lower limbs than can be attributed to the damage observed in the evaluations of current clinics.[28] Another study[29] found a strong correlation between walking patterns and 6MWT, knee extensor muscle strength, and timed up-down steps test. Hence, they suggested that information regarding clinical conditions based on physical function results in PwH can be provided.

Muscle strength increased significantly after both interventions, but the effect of the EG (except for right dorsiflexion and left ankle) was superior. This could be attributed to the beneficial effects of individually planned exercises on physical function and muscle physiology. Mulvany et al.[27] reported that muscle strength improved after an individualized, supervised exercise program, similar to our results in the EG. Goto et al.[30] showed that self-monitoring and home exercise had the same positive effect on the strength of knee flexion in PwH with arthrosis. Likewise, Calatayud et al.[31] found that progressive elastic resistance training, a significant increase in muscle strength in most joints compared to controls, appeared in the intervention group.

The study's results demonstrated that, following rehabilitation, ROM improved in both groups, but in some of the joints these improvements were not significant. According to the obtained results, left knee extension and bilateral plantar flexion increased significantly in the EG compared to the CT. Home stretch exercises were instructed for PwH to be performed in another study,[30] and significant improvements in dorsiflexion and knee ROM were found. Mazloum et al[32] observed improvements in knee ROMs at the end of a session of performing flexibility exercises as a cool-down. Compatible with the literature, the findings obtained in our study reveal that starting an early treatment exercise program in PwH who individually followed the planned exercise program may significantly improve joint ROM.

The pain scores of PwH in both groups were found to have decreased after treatment but were not significant. This may be due to low pain during the pre-treatment period. A recent review by McLaughlin et al[33] showed that the effect of interventions on pain was minimal. They reported that the effects were not obvious irrespective of whether there was low pain before treatment or the intervention was not impactful.

The main limitation of our study is that the follow-up seemed to be short; however, this can be attributed to the COVID-19 pandemic. On the other hand, our findings indicate the results obtained from 29 CwH at a hemophilia center through an 8-week intervention; therefore, our findings cannot be generalized to all PwH in Turkey. Therefore, we believe that further studies will yield better results, with extensive follow-up research and multicenter studies. Additionally, we propose that future studies should evaluate both the pediatric hemophilia activity list and the COPM.

CONCLUSION

The use of individually planned exercise in PwH of the ICF is an effective physiotherapy approach to contribute to joint health, increase functional and PA levels, and motivate participation. If PwH cannot follow a regular exercise program owing to some shortcomings, such as if PwH lives far from HCC centers or has limited access to experienced healthcare people there in their town, QoL, musculoskeletal system functions, and participation component can be preserved by at least regular individually adapted home-based exercise. It can be said that this is a pioneering randomized trial study aimed to explore the connection between the effects of 2 different physiotherapy programs on PA, QoL, participation, and performance of children/adolescents with hemophilia within the framework of the ICF. In addition to improving QoL and joint health status, increasing participation situations must be included in exercise or rehabilitation programs. Together with the novelty, individually prescribed and supervised exercise programs by experienced physiotherapists improved the physical function of people with bleeding disorders without increasing pain and bleeding.

Ethics Committee Approval: Ethical committee approval was received from the Ethics Committee of Istanbul University-Cerrahpasa University (Approval No: 13022260-300-63450).

Informed Consent: Written informed consent was obtained, and information on the research was provided to the parents or guardians of the selected CwH.

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