Organized Sports Activities Are Safe for Children With Sickle Cell Disease: A Pilot Intervention Study

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Summary: Historically, children with sickle cell disease (SCD) are advised to refrain from sports activities, based on the assumption that physical exercise can trigger vaso-occlusive episodes. This pilot intervention study examined the safety (ie, no vaso-occlusive episodes) of a 10-week organized sports program for children with SCD. Eight children with SCD (5 boys/3 girls), aged 7 to 12 years old, received 10 training sessions (each 90 min) once a week. Training sessions were performed by a professional soccer club under the supervision of a medical team from the Wilhelmina Children's Hospital. During the study period, one child experienced a vaso-occlusive crisis, which could not be directly related to the organized sports program. None of the other children experienced vaso-occlusive episodes. The results of this study indicate that children with SCD can participate safely in moderate-intensity organized sports activities when personalized medical background and practical training information is shared with the trainer beforehand. All children continued their sports participation after the study period.

Key Words: sickle cell disease, exercise, sports, physical literacy, children

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Sickle cell disease (SCD) is the most frequent genetic disease worldwide. The disease is characterized by vaso-occlusive episodes (crises) and chronic anemia, which induces a large variety of complications that ultimately lead to organ damage.[1] There have been concerns that intensive exercises can trigger vaso-occlusive episodes,[2,3] which results in the avoidance of organized sports activities in children with SCD.[4] However, recent studies have demonstrated that well-calibrated, moderate-intensity organized sports activities in adults with SCD are safe and improve functional capacities and quality of life.[5–7] So far, no studies have investigated the safety of organized sports activities in children with SCD.

Children with SCD are less physically active and have lower physical competence than their healthy peers.[8,9] Before children with SCD start participating in organized sports activities, assessment of their physical competence is advised to avoid any risk of vaso-occlusive episodes.[3] Psychological factors play an important role in beginning and continuing organized sports participation.[10] Physical literacy provides a theoretical framework to understand the association between organized sports activities and people's physical and psychological well-being. More specifically, physical literacy is described as the physical competence, motivation, confidence, knowledge, and understanding to value and take responsibility for engagement in physical activities (ie, organized sports activities) for life.[11] Higher physical activity levels are associated with higher physical literacy levels in healthy children.[12]

Participation in organized sports activities has a positive effect on children's physical and psychological well-being.[13–16] Organized sports activities could therefore if found safe, have large physical and psychological health benefits for children with SCD. This pilot study examines the safety (ie, no vaso-occlusive episodes) of a 10-week organized sports program for children with SCD. In addition, we investigated physical literacy domains and perceived health in these children.

MATERIALS AND METHODS

Eight children with SCD (5 boys/3 girls), aged 7 to 12 years old, participated in this pilot intervention study. Inclusion criteria were: (a) diagnosed with SCD (types HbSS, HbSC, or HbS/beta(+), HbS/beta(0) thalassemia); (b) aged 7 to 12 years old; (c) no serious complications in the past 12 months (eg, acute chest syndrome, stroke, ≥ 3 vaso-occlusive crisis requiring opiates, >2 hospital admissions); (d) beside physical education at school, no regular ($\geq 1\times$/week) sports participation in past 12 months; (e) child's place of residence <30 km from the Wilhelmina Children's Hospital Utrecht. Children were included between April and September 2021. This study was performed in accordance with the declaration of Helsinki and approved by the Medical Research Ethics Committee of the University Medical Center Utrecht (protocol 20-565/C). All families gave written informed consent for their child's participation. Clinical and disease-specific characteristics of the children are presented in Table 1.

The treating pediatric hematologists invited children with SCD to participate in this study. Children were assessed at baseline (T0) and after 10 training sessions (T1). Based on the baseline results, and additional information from the pediatric hematologist, a personal medical training advice was constructed. This training advice was communicated with the trainer before the start of the first training and included information about children's physical and psychological well-being. The trainer also received practical training information concerning the importance of adequate

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TABLE 1. Clinical and Disease-specific Characteristics of the Children

	Sex	Genotype	Age	Hemoglobin (g/dL)	MCV (fL)	HbF (%)	Reticulocytes ($\times 10^9$/L)	WBC ($\times 10^9$/L)	Platelets ($\times 10^9$/L)
Child 1	Girl	Homozygous, HbSS	8	9.5	106	16.1	191	12.0	486
Child 2	Girl	Homozygous, HbSS	10	8.5	83	NA	294	10.5	268
Child 3	Boy	HbS/HbC	9	10.0	87	NA	152	4.0	171
Child 4	Boy	HbS/HbC	12	9.7	80	NA	203	11.1	388
Child 5	Boy	Homozygous HbSS, heterozygous alpha thalassemia—a (3.7)/aa	7	9.3	103	21.4	133	10.4	344
Child 6	Boy	HbS/beta(+) thalassemia, heterozygous alpha thalassemia—a (4.2)/aa	9	9.2	91	19.4	244	7.9	297
Child 7	Girl	Homozygous, HbSS, heterozygous alpha thalassemia—a (3.7)/aa	10	9.0	85	NA	214	10.5	382
Child 8	Boy	Homozygous, HbSS, heterozygous alpha thalassemia—a (3.7)/aa	11	9.5	61	5.1	167	6.2	211

	LDH (U/L)	Bilirubin (μmol/L)	Hydroxycarbamide	VOC requiring medical consultation (previous 12 mo)	Hospital admissions (previous 12 mo)	Other clinical details
Child 1	433	31	Yes	1	0	
Child 2	590	31	Yes	2	2	
Child 3	467	36	No	1	0	Asthma
Child 4	308	23	No	1	0	Chronic abdominal discomfort/constipation
Child 5	383	28	Yes	1	0	
Child 6	455	27	Yes	0	0	
Child 7	530	36	Yes	0	0	Hydroxyurea recently started
Child 8	271	17	Yes	3	1	Limited compliance for hydroxyureua

LDH indicates lactate dehydrogenase; MCV, mean corpuscular volume; NA, not available; VOC, vaso-occlusive crisis; WBC, white blood cell.

hydration and temperature regulation in children with SCD. Training sessions were performed in collaboration with a professional soccer club in The Netherlands (FC Utrecht) and consisted predominantly of soccer and soccer-related activities. Each training session started with a playful warming-up (eg, playing tag). Next, soccer-related activities, like dribbling, shooting, and passing, were practiced individually, in pairs, or with the whole group. Each training ended with a soccer match among the children. The intensity of the activities could be categorized as moderate-to-vigorous and varied between aerobic and anaerobic. No restrictions were made with regard to the intensity of the training, but multiple water breaks were set. In addition, if children felt tired, they could take a short break from a large stuffed tiger. Special attention was paid to playful exercises, working together, and error-free learning during the training sessions. Children received 10 training sessions (each 90 min) once a week. A certified trainer performed the training sessions with medical supervision of the study team. After the study period, children could continue participating in the training program.

MEASUREMENTS

Clinical Course

Registration of SCD-related clinical events, in specific the frequency of vaso-occlusive episodes, was performed by the treating pediatric hematologist during the training period. More specifically, if children could not be present during a training session, parents were asked to explain their absence beforehand. If they did not, the pediatric hematologist contacted the parents directly after the training session to ask them why their child was not present. In addition, the pediatric hematologist attended half of the training sessions to observe training intensity and the children's well-being during the sessions (eg, asked parents if children experienced any vaso-occlusive episodes).

Sport Participation

Children's participation in organized sports activities was recorded before, during, and after the training period.

Physical Literacy

The theoretical framework of the Canadian Assessment of Physical Literacy second edition (CAPL-2) was used to investigate children's physical literacy at baseline and after the 10-week training period, which discriminates the domains: (a) physical competence (ie, motor performance and cardiorespiratory fitness [CRF]); (b) daily activity (ie, moderate-to-vigorous physical activity); (c) motivation and confidence; and (d) knowledge and understanding.[17]

Physical Competence

Motor Performance. The Canadian Agility and Movement Skill Assessment (CAMSA)[17,18] was used to assess children's motor competence. Children were instructed to complete a circuit of movement exercises as fast and good as possible performance of the skills. A total score (1 to 28) was calculated based on time (in seconds) (1 to 14) and quality of the performance (0 to 14). Scores are compared with age-matched and sex-matched Canadian controls and converted into categories: (a) beginning (< 17th percentile), (b) progressing (17th to 65th percentile), (c) achieving (65th to 85th percentile), and (d) excelling (> 85th percentile). In this study, we distinguished between children who scored age-appropriate (ie, progressing, achieving, and excelling) and children who scored not age-appropriate (ie, beginning).[17]

CRF. Cardiopulmonary exercise testing (CPET) was used to assess: (a) CRF, expressed as predicted peak oxygen uptake (mL/min/kg) (predicted VO_{2peak}), (b) work rate (predicted Watt), and (c) ventilatory anaerobic threshold (VAT) (predicted L/min). Children performed a maximal CPET on a cycle ergometer using the Godfrey protocol.[19] The CPET was considered valid if children scored an respiratory exchange ratio (RER) > 1.0 at peak exercise (RERpeak). VO_{2peak} was defined by the mean value of the last 30 seconds during the maximal exercise test. Predicted VO_{2peak} values (%) and predicted Watt (%) were obtained from age-matched and sex-matched Dutch controls.[20] In addition, the pattern of breathing was analyzed using the Rapid Shallow Breathing Index. During progressive exercise at low and moderate levels of exercise, ventilation increases primarily through increases in tidal volume (VT), whereas, at high levels of exercise, changes in breathing frequency (BF) are dominant.[21] Children's Rapid Shallow Breathing Index (ie, VT/BF at peak work rate) was calculated and compared with the exercise pattern in age-matched and sex-matched Dutch control subjects (%).[20]

Daily Activity

Objectively measured moderate-to-vigorous physical activity (MVPA) was assessed with the Actigraph GT9X Link accelerometer (ActiGraph Corporation). This waist-worn accelerometer measures accelerations across 3-axis and was worn for 7 consecutive days. MVPA was assessed between 7:00 AM and 9:00 PM. Epoch length was set on 1s and a cutpoint of 2296 counts per 60 seconds was used to indicate MVPA.[22] A valid day was defined as having 8 or more hours of wear time, and a valid measurement was defined as having a minimum of 2 weekdays and 1 day on the weekend. MVPA (%) of all valid days was summed up and divided by the number of days. Furthermore, parents filled in a questionnaire used by the National Institute for Public Health and the Environment (RIVM) to investigate children's weekly activities in minutes. Activities are divided in: (a) commuting, (b) activities at school, (c) leisure time, and (d) sports. Self-perceived MVPA was assessed by asking children how many days during the past week were physically active for at least 60 minutes a day, whereby their heart rate and breathing increased.

Motivation and Confidence and Knowledge and Understanding

The CAPL-2 questionnaire was used to assess motivation and confidence (scoring range: 6.6 to 30) and knowledge and understanding (scoring range 0 to 10).[17,23] Scores were compared with age-matched and sex-matched Canadian controls and converted into categories: (a) beginning (< 17th percentile), (b) progressing (17th to 65th percentile), (c) achieving (65th to 85th percentile), and (d) excelling (> 85th percentile). In this study, we distinguished between children who scored age-appropriate (ie, progressing, achieving, and excelling) and children who scored not age-appropriate (ie, beginning).[17]

Perceived Health. Perceived health was measured by asking the following question: "How do you perceive your health in the past 3 months?" The question is scored on a 10-point scale from 1 (lowest) to 10 (highest).

DATA ANALYSES

We reported the number of vaso-occlusive episodes that occurred during the intervention period and the number of children that participated in organized sports activities before, during, and after the intervention. Results on the physical literacy domains and perceived health are reported on an individual and group (ie, means and SDs) level. In addition, motor performance, motivation and confidence and knowledge and performance scores are compared with normative data provided by the CAPL-2 manual for each child individually.

RESULTS

A total of 8 children (5 boys/3 girls), aged 9.4 (1.7) years, participated in this study. Nine children with SCD were approached for participation, one child declined because she disliked soccer(activities). No adverse side effects occurred during the assessment of the tests. Advised by the treating pediatric hematologists, one training session was canceled due to hot weather conditions. All children participated in ≥ 6 training sessions. Results are reported in Table 2.

Clinical Events and Number of Vaso-occlusive Episodes

During the study period, a VOC was reported in 1 participant (#2), requiring hospital admission and treatment with opiates. This vaso-occlusive episode started 6 days after the training session and could not be directly related to organized sports activities. None of the other children experienced vaso-occlusive episodes during the study period.

Sport Participation

At baseline, none of the children participated in organized sports activities. After the study period, all participants continued participating in the training program (n = 6) or an alternative organized sports activity (n = 2). Three children enrolled in a second organized sports activity.

Physical Literacy

Physical Competence

At baseline (T0), 7 children performed a valid maximal CPET (RER > 1.0). All children (n = 7) scored low for predicted VO_{2peak}, mean 64.9 (9.3), and predicted work rate, mean 59.1 (9.1), (all <80% predicted). VAT scores ranged between 30% and 55%, mean of 42.4 (10.3). During the CPET, most children (n = 5) showed a rapid shallow breathing pattern ($\geq 95\%$). The CPET was stopped because of muscle fatigue (n = 4) or exercise dyspnea (n = 3). Motor performance, mean 18.6 (3.2), was age-appropriate in almost all children (n = 7).

After the study period (T1), all children (n = 8) performed a valid maximal CPET (RER > 1.0). All children scored low for predicted VO_{2peak}, mean 61.6 (12.8) (all <80% predicted). Predicted work rate, mean 64.5 (14.0), was low in 7 children, while child #5 scored age-appropriate (92%). VAT scores ranged between 22% and 50%, mean 40.3 (10.1). During the CPET, most children (n = 6) showed a rapid shallow breathing pattern ($\geq 95\%$). The CPET was stopped because of muscle fatique (n = 6) or exercise dyspnea (n = 2). Motor performance, mean 20.1 (2.2), was age-appropriate in all children (n = 8).

Daily Activity

At baseline (T0), valid accelerometer data was available in 7 children, because of accelerometer malfunctioning in one child. Time (%) spent in MVPA ranged between 4.2% and 13.2%, mean 7.9 (3.3). According to parents, children's physical activity ranged between 305 and 1395 minutes per week, a mean 620 (395). Children indicated that they were 2 to 7 days physically active for at least 60 minutes a day, mean 4.0 (1.9).

After the study period (T1), valid accelerometer data was available in 4 children because of insufficient wear time (n = 3) and lost in the mail (n = 1). Time (%) spent in MVPA ranged between 4.5 and 9.7%, mean 6.5 (2.4). According to parents, children's physical activity ranged between 500 and 1395 minutes per week, mean 834 (342). Children indicated that they were 3 to 7 days physically active for at least 60 minutes a day, mean 6.1 (1.6), whereby one child did not fill in this question.

Motivation and Confidence and Knowledge and Understanding

At baseline (T0), motivation and confidence, mean 23.6 (3.5), ranged between 20.2 and 29.5, and was age-appropriate in all children (n = 8). Knowledge and performance, mean 5.3 (1.8), ranged between 2 and 7, and was age-appropriate in most children (n = 5).

After the study period (T1), motivation and confidence, mean 24.2 (4.2), ranged between 18.0 and 29.0, and was age-appropriate in all children (n = 8). Knowledge and performance, mean 6.8 (0.5), ranged between 6 and 7, and was age-appropriate in all children (n = 8).

Perceived Health

At baseline (T0), perceived health scores ranged between 5 and 10 points, mean 7.5 (1.9), whereby most children (n = 7) scored ≥ 6 points. After the study period (T1), scores ranged between 5 and 10 points, mean 8.4 (1.8), whereby most children (n = 7) scored ≥ 6 points.

DISCUSSION

SCD is a severe and chronic disease characterized by painful vaso-occlusive crises, chronic anemia, and a significant risk for secondary organ damage. Historically, it was believed that participation in sports activities harbors a potential health risk for patients with SCD, yet studies investigating exercise and sports participation in this disease population are scarce.[4–7] This is the first study that investigated the safety of an organized sports program in children with SCD.

Children with SCD participated safely in our pilot intervention study that consisted of moderate-intensity organized sports activities whereby personalized medical background and practical training information was shared with the trainer beforehand. Here, personalized medical background information included the children's physical and psychological well-being, and practical training information concerns the importance of adequate hydration and temperature regulation in SCD. In line with 3 larger studies in adults with SCD, our study demonstrates that a moderate-intensity organized sports program appears to be safe for children with SCD.[5–7]

The results of this pilot study opens the door for children with SCD to participate in organized sports activities. While it was believed that physical exercise triggers vaso-occlusive episodes and, therefore, long time was not

TABLE 2. Scores on Physical Literacy Domains and Perceived Health

		Motor performance (1-28)		Cardiorespiratory fitness (mL/min/kg) (VO_{2peak} predicted %)		Work rate (Watt predicted %)		VAT (L/min) (VAT predicted %)	
	Sex	T0	T1	T0	T1	T0	T1	T0	T1
Child 1	Girl	15	19	70	78	55	69	48	48
Child 2	Girl	22	20	—	59	—	54	—	43
Child 3	Boy	19	21	67	69	65	72	33	37
Child 4	Boy	24	22	60	39	58	61	30	22
Child 5	Boy	18	21	75	72	71	92	55	42
Child 6	Boy	15	16	55	56	57	59	39	50
Child 7	Girl	17	19	75	69	65	64	55	50
Child 8	Boy	19	23	52	51	43	45	37	30
Mean (SD)		18.6 (3.2)	20.1 (2.2)	64.9 (9.3)	61.6 (12.8)	59.1 (9.1)	64.5 (14.0)	42.4 (10.3)	40.3 (10.1)
		Rapid shallow breathing Index (%)		Objectively measured MVPA (%)		Parental proxy report physical activity (min/wk)		Self-perceived MVPA (d/wk)	
Child 1	Girl	221	291	9.9	7.0	1395	1395	4	7
Child 2	Girl	—	193	13.2	—	955	1265	7	5
Child 3	Boy	98	98	10.6	9.7	470	890	3	—
Child 4	Boy	134	227	4.2	4.7	380	890	3	7
Child 5	Boy	165	222	6.2	—	310	610	2	7
Child 6	Boy	188	226	5.0	—	305	585	3	7
Child 7	Girl	266	156	6.7	4.5	795	534	7	7
Child 8	Boy	104	92	—	—	350	500	3	3
Mean (SD)		168.0 (61.9)	188.1 (68.8)	8.0 (3.3)	6.5 (2.4)	620 (395)	834 (342)	4.0 (1.9)	6.1 (1.6)
		Motivation and confidence (6.6-30)		Knowledge and understanding (1-10)		Perceived health (1-10)			
Child 1	Girl	20.4	28.5	5	6	5	8		
Child 2	Girl	20.2	20.0	7	7	7	5		
Child 3	Boy	26.6	27.8	5	7	7	9		
Child 4	Boy	21.9	23.0	7	7	6	8		
Child 5	Boy	23.9	21.5	4	7	10	10		
Child 6	Boy	20.6	18.0	2	7	6	7		
Child 7	Girl	29.5	29.0	5	7	10	10		
Child 8	Boy	26.0	25.4	7	6	9	10		
Mean (SD)		23.6 (3.5)	24.2 (4.2)	5.3 (1.8)	6.8 (0.5)	7.5 (1.9)	8.4 (1.8)		

MVPA indicates moderate-to-vigorous physical activity; VAT, ventilatory anaerobic threshold.

recommended by physicians, we demonstrated that moderate-intensity organized sports activities can be safe. In addition, we observed that children continued their sports participation after the study period, which contributes to a healthier lifestyle. Three children (3/8) also started participating in an additional organized sport activity.

Organized sports participation has a positive effect on children's physical and psychological well-being.[13–16] We used the physical literacy framework to investigate children's physical and psychological well-being to create a personalized medical training advice. There were large differences between children, which emphasizes the importance of a personalized medical training advice before children with SCD start their organized sports activities. Notably, all children scored age-appropriate for motivation and confidence and low for CRF (VO_{2peak} and work rate; <80% predicted). This result points out that, in this pilot study, children with SCD are already motivated to participate in physical activities, but the assessment of their CRF is necessary to provide a personalized training advice for trainers. A larger group of children with SCD is needed to investigate the effect of organized sports activities on their physical and psychological well-being, whereby attention is paid to the intensity of the training. Based on the results of this pilot study, researchers can calculate (expected) effect sizes which are needed for sample size calculation for larger intervention studies with children with SCD in the future.

Children's physical literacy domains were assessed before and after the study period to provide an insight in their individual physical and psychological well-being. We did not aim to investigate the effect on a group level, because of the small sample size and the number of weekly training sessions. More specifically, other studies that investigated the effect of a once-a-week (school-based) organized sports program in children with a chronic disease found no effect on children's CRF, physical activity, strength, perceived competence, and health-related quality of life.[24,25] However, children with a chronic disease who participated at least 2 times a week in organized sports activities scored better for CRF, muscle strength, physical activity, health-related quality of life, perceived athletic competence, exercise self-efficacy and social acceptance than children with a chronic disease who did not.[26,27] We, therefore, argue that, to improve domains of physical literacy in children with a chronic disease (ie, SCD), organized sports programs should at least consist of 2 training session a week.

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In terms of strengths, this is the first study that investigated the safety of moderate-intensity organized sport activities for children with SCD. Furthermore, we used the physical literacy framework to get insight in children's physical and psychological well-being. A weakness of our study is the small sample size, although analyses on a group level was not the aim of this study. Unfortunately, in The Netherlands, race-specific reference values for the CPET are unavailable, allowing us to only use age-matched and sex-matched Dutch controls to calculate predicted CPET (%) outcomes. We aim to include age-matched, race-specific controls (eg, healthy family members) in our follow-up studies. In addition, we did not investigate parental perceptions, while parental perceptions play a significant role in the physical activity of children with disabilities.[28] Future intervention studies should therefore consider parental perceptions to enhance children's organized sports participation. Finally, children with SCD in this pilot study were motivated to participate in soccer activities, making it difficult to generalize our results to children with SCD who are less motivated to participate in organized sports activities. Future intervention studies should therefore specifically focus on children who are less motivated to participate in organized sports activities by, for example, use motivational strategies based on the self-determination theory.[29]

To conclude, children with SCD can participate safely in moderate-intensity organized sports activities when personalized medical background and practical training information is shared with the trainer. Children continued their sports participation after the study period. Further research in larger, controlled, studies are needed to investigate the effects of sports participation on physical and psychological well-being in children with SCD.

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