

Physical Therapy Modalities in Children with Thalassemia and Sickle Cell Disease: Narrative Review

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Abstract

Background: Physical therapy is playing an important role in enhancing and promoting health related quality of life in children with thalassemia and sickle cell disease by decreasing the associated disease symptoms as pain, anxiety, depression and fatigue and enhancing the cardiopulmonary system, bone mass index, ferritin and serum levels by using different physical therapy modalities as exercise training, Yoga, Massage therapy, transcutaneous electrical nerve stimulation (TENS), spirometer and vibration therapy.

Aim of Study: To identify the effectiveness of using physical therapy modalities in children with thalassemia and sickle cell disease.

Subjects and Methods: This review included Children with thalassemia and sickle cell disease aged between 6 to 18 years, receive different physical therapy modalities.

Design: A search of electronic databases that included, PubMed, Physical therapy Evidence Database, Google scholar, Science Direct and Cochrane was searched since ever till December 2019 using the following keywords: 'Physical therapy modalities', 'thalassemia', 'exercise training', 'sickle cell disease', 'breathing exercise', 'health related quality of life', 'transcutaneous electrical nerve stimulation' and 'children'.

Results: Twelve articles that were retrieved met the inclusion criteria.

Conclusion: From clinical point of view using physical therapy modalities can promote quality of life in children suffering from thalassemia and from sickle cell disease but furthermore studies are needed to help the researchers and the patients.

Key Words: *Thalassemia – Sickle cell disease – Physical therapy modalities – Children – Health related quality of life – Exercise training – Breathing exercise – Transcutaneous electrical nerve stimulation.*

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Introduction

THALASSEMIA, classified as the main types α - and β -thalassemia, is a single gene disorder resulting from globin chain synthesis impairment through the mutation or deletion of globin genes. The incidence of thalassemia is high worldwide, with high associated mortality. Therefore, treatment is important to improve patient outcomes [1].

Its impact on physical appearance, bone deformities and short stature contributes to a poor self-image. The common complications among those patients are heart failure, cardiac arrhythmia, liver disease, endocrine complications, and infections [2].

Sickle cell anemia (SCA) is a common inherited blood disorder associated with abnormal hemoglobin production and characterized by chronic hemolysis, a proinflammatory state and endothelial dysfunction [3].

Physical therapy may help to improve the functional ability, quality of life and rehabilitate patients with Thalassemia and SCD, it performs a vital role in the multidisciplinary management of (SCD) symptoms, especially range of motion (ROM), balance, and airway clearance issues [4,5].

Subjects and Methods

A search of electronic databases that included, PubMed, Physical therapy Evidence Database, Google scholar, Science Direct and Cochrane was searched since ever till December 2019 using the following keywords: 'Physical therapy modalities', 'thalassemia', 'exercise training', 'sickle cell disease', 'breathing exercise', 'health related quality of life', 'transcutaneous electrical nerve stimulation' and 'children', this review approved by the Ethical

Committee of the Department of Physical Therapy for Pediatrics, Faculty of Physical Therapy, Cairo University. As the study did not require human participation, therefore; ethical approval regarding participants was not required.

Inclusion criteria:

This review concerned studies that published in English with all research designs except expert opinions, full length articles or full written reports of RCTs and NRCTs since Ever to December 2019 were included and concerned in children with thalassemia and sickle cell disease aged between 5 to 18 years, receive different physical therapy modalities, the Primary outcome was promoting health related quality of life by decrease pain, depression & Anxiety, enhance fatigue level and the Secondary outcomes were improvement of cardio-pulmonary system, Body structure and function (decrease Iron overload, enhance bone mineral density).

Main text:

Role of physical therapy modalities:

1- Vibration therapy:

In whole body vibration therapy, vibration stimuli are transmitted to the body via a vibrating platform or chair. The vibration signals activate the sensory receptors in the muscles (e.g. muscle spindles), which causes reflexive activation of motor units when whole body vibration applied to the human skeleton, it is thought to have beneficial effects on bone health through enhancing bone density indirectly through its effects on muscle activation [6].

2- Incentive spirometry:

It is also referred to as sustained maximal inspiration, which is carried out by using a device that provides feedback when the patient inhales at a predetermined flow or volume and sustains the inflation for at least 5 seconds. The patient is instructed to hold the spirometer in an upright position, exhale normally, and then place the lips tightly around the mouthpiece. The next step is a slow inhalation to raise the ball (flow-oriented) or the piston/plate (volume-oriented) in the chamber to the set target. At maximum inhalation, the mouthpiece is removed, followed by a breath-hold and normal exhalation [7].

Incentive spirometry can be used in management of ACS (acute chest syndrome) as primary supportive care besides other respiratory therapy (positive expiratory pressure [PEP], and bronchodilators), antibiotics, and red-cell transfusions [8],

and can be used also in prevention of atelectasis, Alternatively, the use of mechanical chest physiotherapy maneuvers, such as PEP devices, may be considered in younger children who may not be able to coordinate incentive spirometry or is limited by chest wall pain [9].

3- Yoga:

Yoga asanas have been known to have beneficial effects by controlling stress and depression through relaxation and breath control techniques.

Yoga leads to Strengthen and increase tone of weak muscles and correction of faulty postures can be pain relieving, help with conscious control over autonomic functions of the body, help with developing correct breathing patterns, bowel habits, and regular sleeping patterns and teaches the art of relaxation, relieving muscular and nervous tension that leads to increase pain control and pain tolerance, increased energy and decreased anxiety and depression via decrement the activation of the brain secondary to decrease the input of stimuli from the internal and external environment.

Deep breathing, which includes prolonged expiration, tends to relax skeletal muscles and reduce pain, also gentle stretching has similar effects as yoga [10].

4- Transcutaneous electrical nerve stimulation:

It is a technique that passes electrical currents across the intact surface of the skin to activate underlying nerves, the term is generally used to describe currents delivered using a 'standard TENS device' to relieve pain by activation cutaneous afferents rather than motor efferent from the skeletal and autonomic systems [11].

5- Exercise:

Performing regular exercise may cause a biochemical response in children brain that plays a role in improving their moods and mental health, thus it can be beneficial in fighting depression compared to antidepressant medications as strength training. Also it reduces the risk of broken bones and osteoporosis and reverse the effects of bone loss [12,13].

6- Massage therapy:

Massage therapy can be defined as the systematic manipulation of soft tissues of the body for diagnostic purposes, pain reduction and other therapeutic purposes. 'Classic' ('Swedish') massage includes effleurage (stroking and gliding), petrissage (kneading), and tapotement (percussion) [14,15].

7- Fluidotherapy:

In January 1981, the Physical Therapy Department at Texas Children's Hospital (TCH) received its first referral patient with sickle cell anemia for Fluidotherapy. Their objective was to relieve pain and allow ROM free from pain and ambulation. they found that Fluidotherapy was extremely helpful in reducing pain and ROM problems because the treatment was successful by immediately relieving the patient's pain and ROM problems [16].

Description of the studies included:

1- Eid & Aly (2019):

In this study the intervention was whole body vibration therapy (25-30Hz, 2mm amplitude, 10 repetitions (30-60s) with 1 min rest, 15-20min/day, 3 days/week/24 weeks) besides the same physical therapy program as in the control group, Bone mineral density and functional capacity were assessed before and after 24 weeks, children in the study group demonstrated a significant increase in the functional capacity and the BMD of the lumbar spine, femoral neck and total body compared with that of the control group [17].

2- Moody et al. (2016):

This study investigates the effect of yoga for decreasing pain and anxiety in children hospitalized with sickle cell vaso-occlusive crisis (VOC), seventy-three children and adolescents were stratified based on disease severity and randomized to the yoga or control group, the yoga instructor devised this yoga protocol used in the study based on her yoga training and experience with hospitalized children with SCD VOC, the protocol consists of four key elements of yoga: Mindfulness, asanas, breathing exercise, and guided relaxation, the primary outcome was change in pain score after the first session and was measured by the WBFPRS for children, the secondary outcome was change in anxiety, was measured by the STAI-S, a reliable and validated anxiety scale for children and young adults, compared with the control group, children randomized to yoga had a significantly greater reduction in mean pain score after 1 yoga session, there were no significant differences in anxiety, LOS, or opioid use between the two groups [18].

3- AbuSaad & Sarhan (2016):

This study investigates the effect of exercise training program and telenursing effects on depression and fatigue level in sixty children suffering from B-Thalassemia Major which randomly selected after fulfilling the criteria of selection for three months, the exercise training program consists of

endurance warming up, stretching and relaxation exercise which were self administrated performed two times weekly for 30-35min and given as home program, the studied children followed-up for sixteen calls by the researcher nurse, the tools used to collect and assess the data were depression inventory scale, fatigue scale and a semi-structured interview questionnaire, the exercise training program combined by follow-up calls was effective in decreasing and fatigue among thalassemic children after one and three months of intervention [13].

4- Molazem et al. [19]:

In this study the intervention was moderate exercise such as walking for 15 minutes every day, blood samples were collected before and after two months, the serum iron level and ferritin was lowered in the intervention group but the difference wasn't statistically significant.

5- Alotaibi & Waked [5]:

In this study the intervention was standard incentive spirometry device. The exercise was performed twice per day for 15 minutes and 5 times/week for 8 weeks, pulmonary functions were measured before and after 8 weeks, the results showed significant difference in pre and post of FVC, FEV1, MVV in the IS group while non-significant difference in the pre and post of the control group.

6- Bagheriyan et al. [20]:

This study investigates the analgesic effect of breathing exercises with the aim of distraction during venipuncture in forty children (6-12 years) with thalassemia randomly categorized into study and control groups, the pediatric pain behavioral symptoms and numeric pain rating scale were used to assess pain caused by venipuncture, in the breathing exercise group children were taught how to do regular breathing exercise (Hey-hu method) and were asked to do one minute before and during catheter insertion until the fixation of angiocath, distraction by breathing exercises demonstrated to be effective in reducing pain and requires minimum effort and time.

7- Fung et al. [21]:

In this study the intervention was vibration therapy using vibrating platform (30Hz, 0.3g) for 20min/day for 6 months, Areal bone mineral density (aBMD) by DXA and volumetric BMD by peripheral quantitative computed tomography (pQCT) was assessed at baseline, 6 and 12 months. The

results suggest that vibration therapy may be an effective non pharmacologic intervention in Thalassemia but Future research is needed to confirm these results in a larger sample for longer duration.

8- Adeniyi & Saminu [22]:

In this study the intervention was local incentive spirometer used for six weeks, thrice daily, the PEFr was assessed at the baseline and after the third and six weeks, the results showed significant improvement in the study group than the control one.

9- Lemanek et al. [23]:

This study investigates the effect of massage therapy on decreasing depression, anxiety, pain and health service utilization and enhancing functional status in children with SCD, thirty-four children and adolescents, and their parents were randomly assigned to a massage therapy or an attention control group, parents were trained to give a standard massage by a therapist once a week for 4 weeks with instructions to provide nightly massages, family in the control group were visited weekly by a research assistant, center for epidemiological studies of depression scale-depression scale (CES-D), State-Trait Anxiety Inventory (STAI), Functional Status-II(R) (FS-IIR), Children's Depression Inventory(CDI), State-Trait Anxiety Inventory for Children (STAIC), Pediatric Pain Scale, Health Service Utilization Rates were used to measure the outcomes. parents in the massage group reported higher levels of depression and anxiety following the intervention but youth in the same group showed higher levels of functional status and lower levels of depression, anxiety and pain, health service utilization rates were unchanged from pre-to post-intervention.

10- Lewis et al. [24]:

In this study the intervention was positive expiratory pressure device used for 2 to 3 times per day by the therapist while patient awake till he was discharged from the hospital, the control group used incentive spirometry, the progression of acute chest syndrome defined by new infiltrate on chest radiograph plus respiratory symptoms, patient satisfaction and length of hospital stay were also assessed at baseline and at the discharge from the hospital. No children in either group progressed to acute chest syndrome, patient satisfaction was high and not significant.

11- Bellet et al. [25]:

In this study the intervention was incentive spirometer, chest radio graph and bone scanning were performed at baseline and at least three days after admission to the hospital, the results showed significant difference in the study group than the control one.

12- Wang et al. [26]:

In this study the intervention was TENS (transcutaneous electrical nerve stimulation) used to decrease pain, the severity of pain was reported by the patient on a scale from 0 to 10, with 10 being the severest pain the patient had experienced. Pain ratings were recorded on cards following the onset of the trial at 1 & 4 hours. This study did not include in the meta analysis because there wasn't sufficient statistical information and I have tried to connect with the author by e-mail but there was no reply.

Data extraction sheet:

Data from all the twelve included studies were summarized in the following table.

Table (1): That includes: Participants' characteristics (number in each group, target population, diagnosis, numbers in each diagnostic subgroup and ages), intervention, control used and research design.

NO / study	Subject	Control/Intervention	Outcome measure	Patient Assessment/ Follow-up	Results/comments
1- Lemanek et al., 2009	N=34 youth with sickle cell disease and their primary caregivers.	Attention (control): n=16 Massage therapy: n=18 The massage protocol was that used by Field (2001), which consisted of two phases: (1) child is in supine position and continuous stroking movements are applied to face, stomach, legs, and arms, and (2) child is in prone position and the back is massaged.	Pediatric Pain Scale: This depicts a series of six faces representing ascending levels of hurt from 0 ("I don't hurt at all") to 5 ("I hurt as much as you can imagine"). Children's Depression Inventory (CDI): Is a 27-item standardized self-rated symptom scale of depression used with school-age children and adolescents. Scores range from 0 to 54 based on item ratings of 0, 1,	- The massage therapist visited families weekly for 3 more weeks (total of four home visits) to collect anxiety measures and pain ratings, the therapist also monitored caregivers' technique and provide corrective feedback in giving a massage. - At baseline, after one month and then after three months.	Results of the ANCOVAs for the CDI (34,2), F= 4.02, p=.05, the STAIC state anxiety scale (24,2), F=6.47, p=.01, and pain ratings (21, 2), F=4.11, p=.05 were significant with youth in the massage therapy group rating their level of depression, anxiety, and pain lower than those youths in the control group.

Table (1): Cont.

NO / study	Subject	Control/Intervention	Outcome measure	Patient Assessment/ Follow-up	Results/comments
		Caregivers were required to give a 20-minute massage using this protocol for those days between therapist visits; thus, youth received massages for a total of 30 days.	2, with higher scores indicating increasing severity of depression. A cut-off score of 12 or 13 is recommended to minimize the number of false positives. Standardized a for the CDI for this sample was .77.		
			State-Trait Anxiety Inventory for Children (STAIC): The STAIC is a 20-item self-report measure of state anxiety based on how children feel at a "particular moment in time." Each item is rated on a 3-point scale, with total scores ranging from 20 to 60, and where higher scores indicate greater anxiety. Standardized a coefficient for this sample was .78.		
2- Wang et al., 1988	N= 22 Sickle cell disease (20 Hb SS, 1 Hb SC, 1 Hb S-Bo thalassemia) 12-27 years with median age of 17.5 years There were 12 females.	Intervention: TENS (transcutaneous Electrical Nerve Stimulation) in this study the pulse rate was set at approximately 100 HZ (pulses per second) and the pulse width at 30 MS. TENS electrodes were applied to the area of severest pain and patients' pain ratings and medication usage were evaluated over a 4-hour period. Control: Placebo (the settings were left at Zero. The study involves 60 trials in 4 crisis severity categories.	Severity of pain was reported by the patient on a scale from 0 to 10, with 10 being the severest pain the patient had experienced. Pain ratings were recorded on cards. There are 4 severity grades: Grade I: mild pain, pain scale ratings 1- 4. complete or substantial relief from last dose of oral nonnarcotic analgesic Grade II: moderate pain, pain scale ratings 5-7. Complete or substantial relief from last dose of oral narcotic analgesic Grade III: sever pain. pain scale ratings 8-10. Complete or substantial relief from last dose of parenteral narcotic analgesic Grade IV: same pain scale ratings as grade III, but little or no relief from the last dose of parenteral narcotic.	Following the onset of the trial, pain ratings were recorded at 1 and 4 hours. The patient's analgesic usage was recorded before, during and after each trail.	There were no significant differences in the changes in pain ratings in the two groups. Overall, 37% improved their pain rating by 1 h and 49% by 4h. The two groups were similar in analgesic usage. Twelve patients (20%) required narcotic analgesics before the 1-hour rating with no significant difference between placebo (25%) and TENS (14%) ($x^2 = 1.07, p=0.30$). Thirty-eight patients (63%) required pain medication before the 4-hour rating, again with no significant difference between placebo (66%) and TENS (61%) ($x^2 = 0.16, p=0.69$).
3- Abusaad & Sarhan, 2016	N=60 Beta thalassemia major, suffering from fatigue and depression. 10-17 years.	A quasi- experimental study: The exercise program consisted of endurance warming up, stretching, and relaxation exercises. These exercises were self-administered performed two times weekly for	Depression Inventory Scale: is a 27 - multiple - choice self - report composed of items relating to symptoms of depression (such as social isolation, feeling of sadness, fatigue, low energy, loss	Baseline assessment and after one & three months of intervention.	The total mean score of depression was decreased after one month of exercise performance 19.2 ± 4.6 , T_3 13.502 than before 24.7 ± 3.8 , T_1 15.32 and the mean score of depression continuously decreased

Table (1): Cont.

NO / study	Subject	Control/Intervention	Outcome measure	Patient Assessment/ Follow-up	Results/comments
		30-35 min and given as a home program aimed at promoting good health and alleviate depression and fatigue.	of appetite and lack of safety) the child is instructed to choose the one statement that best describes them over the last two weeks. Scoring system: Each item-scored 0, 1 and 2 with score of 2 representing the most severe choice. The total score (54) marks, distributed for measuring the severity of depression as follows: None of depression with score 14 marks. Mild depression with score range from 15 to 22 marks. Moderate depression with score range from 23 to 29 marks. Severe depression with score range from 30 to 54 marks.		after three months of exercise performance 15.3 ± 6.04 , T2 17.84 with a statistical differences between pre and after one month, pre and after three month and between after Month and after three month, $p=.000$.
4- Moody et al., 2016	N=73 5-21 years Sickle cell disease, vaso occlusive crisis (VOC) and had an initial pain score >7	Intervention: Yoga N=35 The Yoga intervention was divided into 4 segments applied sequentially over 30 minutes. The segments were designed to introduce patients to 4 aspects of yoga: 1-mindfulness, 2-asanas, and 3-breathing techniques, 4-guided relaxation. Control: attention(relaxation) N=35 The control condition was matched to the yoga intervention for time, attention, and ambiance. Patients randomized to the control group were provided with a daily (M-F) 30-minute session wherein the yoga instructor played the Morning in the Mountains nature sounds CD at a volume of the patients choosing. During each session, the yoga therapist offered to stay with the patient for the duration of the CD but no movement exercises, breathing exercises, or guided relaxation were offered.	The primary outcome was change in pain score was measured by the wong baker FACES pain rating scale WBFPRS for children. It is a visual scale with 6 anchors (pictures of faces) at even integer intervals and ranges from 0 (no pain) to 10 (worst possible pain), and is the most preferred scale by children with SCD. The secondary outcome, change in anxiety, was measured by the state trait anxiety inventory state STAI-S, a reliable and validated anxiety scale for children and young adults. The S-subscale measures anxiety at one point in time (now). The T-subscale refers to relatively stable individual differences in anxiety, and was administered only at baseline. Scores greater than 40 are considered consistent with clinically significant anxiety.	Baseline pain scores and the STAI-S and TRAIT (T) were collected just prior to the first yoga or control session. Pain scores were collected again within 30 minutes following each subsequent yoga or control session. The STAI-S was collected again after the first session, however due to the length and time to complete this scale it wasn't collected again during the admission.	Children in yoga group had a significantly greater reduction in mean pain score after the first yoga session compared with the control in univariate and multivariate analysis, (-0.6 ± 0.96 v. 0.0 ± 1.37 ; $p=0.029$). scores following subsequent yoga sessions; post-session 1 analyses were limited by sample size attrition due to hospital discharge. The mean state anxiety scores for yoga was $-7.7(\pm 9.6)$ and for control was $-6.2(\pm 7.3)$. Both the yoga and control groups experienced similar decreases in anxiety that were slightly greater than 0.5 SD; however, these differences were not statistically significant.

Table (1): Cont.

NO / study	Subject	Control/Intervention	Outcome measure	Patient Assessment/ Follow-up	Results/comments
5- Bagheriyan et al., 2012	N=40 (6-12 years) major Thalassemia and requiring venipuncture	Intervention: n=20, regular breathing, exercise. Breathing method of Hey-Hu (child takes a deep breath, exhale while whispering Hey, then inhale deeply again and exhale whispering hu) Children were asked to do the breathing exercise at one minute before and during catheter insertion until the fixation of angiocath. Control: n=20, without any intervention.	The pediatric pain behavioral symptoms (FLACC) and Numeric Pain Rating Scale (NRS) pain graded from 0 (no pain) to 10 (worst pain) were used to assess pain caused by venipuncture.	At baseline and after injection.	The mean of pain score based on the numerical scale was 3.13 ± 5.60 in the control group and 1.42 ± 1.85 in breathing exercises Results showed a significant difference between the mean of pain scores ($p < 0.001$).
6- Alotaibi & Waked., 2015	N=40. 7- 15 years Homozygous sickle cell anemia, Reasons for hospital admission were severe pain unrelieved by analgesics, fever, respiratory distress, a sharp decrease in the hemoglobin concentration	-Control (n=20): medical treatment only. -Intervention(n=20): incentive spirometry: standard incentive spirometry device. The exercise was performed twice per day for 15 minutes and 5 times/week for 8 weeks. The exercise was split into 5 minutes if the subject was unable to train for 15 minutes without interruption. After each set of 10 deep breaths practice coughing to be sure his lungs are clear. + Medical treatment	a-Measurement of forced vital capacity "FVC". b-Measurement of forced expiratory volume at 1 second" FEV1" c-Measurement of maximum voluntary ventilation "MVV. Each patient was instructed to breathe as rapidly and fully as possible for 12-15 seconds. The total volume was obtained through multiplying this volume by the appropriate number (5 if tested for 12 seconds, 4 if tested for 15 seconds).	-Pulmonary function were measured before and after 8 weeks.	Measurement of Forced vital capacity "FVC": The results of study showed significant difference of FVC pre 1.931 ± 0.534 & post 2.464 ± 0.396 treatment in IS group as p -value < 0.05 while it showed non-significant differences in Control group pre 2.05 ± 0.483 & post 2.064 ± 0.477 treatment as p -value > 0.05 . Measurement of forced expiratory volume at 1 second "FEV1": The results of study showed significant difference of FEV1 pre 1.67 ± 0.332 & post 2.095 ± 0.366 treatment in IS group as p -Value < 0.05 while it showed non-significant differences in Control group pre 1.69 ± 0.294 & post treatment 1.71 ± 0.348 as p value > 0.05 . Measurement of maximum voluntary ventilation "MVV": The results of study showed significant difference of MVV pre 55.95 ± 14.45 & post 73.80 ± 21.21 treatment in IS group as p -value < 0.05 while it showed non-significant differences in Control group pre 58.80 ± 13.18 & post 59.70 ± 17.07 treatment as p -value > 0.05 .

Table (1): Cont.

NO / study	Subject	Control/Intervention	Outcome measure	Patient Assessment/ Follow-up	Results/comments
7- Adeniyi & Saminu, 2011	N=49 Age: 13-19 years Sickle cell Anemia(SCA) With disorders of pulmonary functions.	Control: N=25 Intervention: N=24 local incentive spirometer, (six weeks, thrice daily).	The peak expiratory flow rate (PEFR) was measured using the (PEFR meter). The measurements were taken 3 times and the highest recorded.	The PEFR was assessed in the clinic at the beginning of the study (baseline) and at the end of the third and sixth weeks in both spirometry and control groups while it was done only once for the non-SCA group.	The PEFR of the SCA spirometry group improved significantly ($p=0.001$) between the third and sixth week (211.04 ± 55.67 to 292.08 ± 40.86 liters/min) unlike that of the SCA control group ($p=0.605$). At six weeks, PEFR of the SCA spirometry group improved significantly ($t=0.624$, $p=0.003$) over that of the SCA control group, however, the improved PEFR of the SCA spirometry group didn't match that of their non-SCA counterparts.
8- Bellet et al., 1995	N= 29 (14 females, 15 male) Age: 8 to 21 years Sickle cell disease who had 38 episodes of acute chest or back pain above the diaphragm and were hospitalized, 23 had homozygous SCA, 3 had sickle cell hemoglobin C disease, 2 had SC-B thalassemia, 1 had SC hemoglobin D disease.	Control: N= 19 Intervention: (incentive spirometry) N=19 Each patient in the spirometry group took 10 maximal inspirations using incentive spirometer every 2 hours between 8 a.m. and 10 p.m. and while awake during the night until the chest pain subsided. Each episode of pain considered to be an independent event.	Chest radiograph and bone scanning	Baseline assessment (radiograph to determine the incidence of pulmonary complications, bone scanning was performed no sooner than two days after hospital admission to determine the incidence of thoracic bone infarction) then a second chest radiograph was obtained at least three days after admission to the hospital.	The incidence of thoracic bone infarction was 39.5 percent (15 to 38 hospitalization). pulmonary complications (atelectasis or infiltrates) developed during only 1 to 19 hospitalizations of patient assigned to the spirometry group as compared with 8 to 19 hospitalizations of patients in the non-spirometry group ($p=0.019$). Among patients with thoracic bone infarction, no pulmonary complications developed in those assigned to the spirometry group during a total of 7 hospitalization whereas they developed during 5 to 8 hospitalization in the non-spirometry group ($p=0.025$)
9- Lewis et al., 2005	N= 20 Sickle cell anemia with pain in the thorax (chest wall or back)	Control: n= 9 (incentive spirometer group). Intervention: n= 11 (positive expiratory-pressure device group): each PEP breathing maneuver consist of the patient inhaling normally and then exhaling through a mouthpiece and a restrictor size of 1 to 4 which prolongs exhalation over a period of approximately 2 to 3 times normal. this was repeated for a total of 10 breaths.	a-patient satisfaction: children rated their satisfaction with the respiratory therapy device on a likert scale (0=completely unsatisfied, 5=completely satisfied) b-length of hospital stay C-progression of acute chest syndrome defined by new infiltrate on chest radiograph plus respiratory symptoms.	Baseline assessment and till discharge from the hospital.	Patient satisfaction was high and not significant: mean and SD were 4.5 ± 0.5 for PEP and 4.4 ± 0.5 for IS, $p=0.81$. -No children in either group progressed to acute chest syndrome. -Length of stay: Mean and SEM were 5.0 days ± 2.5 for PEP and 4.3 days ± 2.6 for IS, $p=0.56$.

Table (1): Cont.

NO / study	Subject	Control/Intervention	Outcome measure	Patient Assessment/ Follow-up	Results/comments
10- Fung et al., 2012	N=18 9 adults, 10 males (22.1±10.7 years) Thalassemia with low bone mass.	All treatment were administrated by therapist every hour while awake and continued until the patient's discharge from the hospital or progression to ACS Intervention: N=18 (9 adults, 9 adolescents), Subjects were asked to stand on a vibrating platform (30 Hz, 0.3g) for 20 min/day for 6 months. Within subject design. Control: N=18. (within subject design).	Bone densitometry was used to assess BMC and BMD at the PA spine, left hip and whole body on all subjects at baseline, 6 and 12 months. Prebaseline clinical BMD data was also available for all subjects one year prior to entry into the study. The following variables were collected from each DXA scan: bone mineral density (aBMD), bone mineral content (BMC), and bone area. Bone mineral apparent density (BMAD) was calculated as BMC/Area. Anthropometric and pubertal assessment: Pubertal status (in adolescents only) was determined at baseline using a validated self-assessment pictorial questionnaire. Dietary intake and physical activity: Subjects were instructed not to change their use of nutritional supplements during the 12-month study. Calcium and vitamin D intake were assessed using a combined tool that was individually validated for calcium and vitamin D intake. Physical activity was assessed using the validated Block Work and Home Activities Survey.	Areal bone mineral density (aBMD) by DXA and volumetric BMD by peripheral quantitative computed tomography (pQCT) was assessed at baseline, 6 and 12 months	Adolescents subjects: At Baseline: Osteocalcin, ng/ml= 14.1±6.3 CTx. Ng/ml= 1.48± 1.34 Osteocalcin/CTx = 12.2±4.4 At 6 months: Osteocalcin, ng/ml=14.9±3.4 CTx. Ng/ml= 1.14± 0.87 Osteocalcin/CTx =16.9±8.0 At 9 months: Osteocalcin, ng/ml=15.6±4.7 CTx. Ng/ml= 1.13±0.54 Osteocalcin/CTx =17.9±11.8 At 12 months: Osteocalcin, ng/ml=16.8 ±4.5 CTx. Ng/ml=1.45 ±0.68 Osteocalcin/CTx =12.9±4.7 These preliminary findings suggest that vibration therapy may be an effective nonpharmacologic intervention in Thal. Future research is needed to confirm these findings in a larger sample for longer duration.
11- Eid & Aly, 2019	39 children (23 boys and 16 girls) with β-thalassemia major, with ages ranging from 6 to 10 years	The control group (n = 20) received the medical treatment and the physical therapy program.	-Bone mineral density was assessed by Dual-energy X-ray absorptiometry (DEXA). - Functional capacity was measured using the Six-Minute Walk Test (6MWT).	Bone mineral density and functional capacity were assessed before and after 24 weeks.	- BMD of the total body ((g/cm ²) in the control group posttest was 0.74±0.08, in the study group was 0.82 (0.09).

Table (1): Cont.

NO / study	Subject	Control/Intervention	Outcome measure	Patient Assessment/ Follow-up	Results/comments
		The study group (n = 19) received the same program as the control group in addition to WBV training (25-30 Hz, 2 mm amplitude, 10 repetitions (30-60 s) with 1 min rest, 15-20 min/day, 3 days/week/ 24 weeks	- Anthropometric Measurements Weight(kg)and height(m) were recorded by the use of a calibrated floor scale (ZT-120 model).		- 6MWT (m) in the control group posttest was 302.05 (35.01), in the study group was 334.63 (41.21). -Both groups showed a significant increase in BMD and functional capacity after treatment compared with that before treatment ($p < 0.05$). However, children in the study group demonstrated a significant increase in the functional capacity and the BMD of the lumbar spine, femoral neck and total body compared with that of the control group ($p > .01$).
12- Molazem et al., 2016	N=38 15-35 years Beta thalassemia	Intervention: N=18 The patients were asked to do moderate exercises such as walking at home for 15 minutes every day and increase or decrease the duration according to their tolerance. Control: N=20, received the routine trainings and cares.	The outcomes were collected using: - The participants' demographic characteristics. - Basic iron content was measured in a specialized laboratory.	Blood samples were collected from the participants before and two months after the intervention.	The intervention group's mean of ferritin two months after the intervention was significantly lower compared to before the intervention ($p=0.04$). However, no significant change was observed in the control group in this regard ($p=0.29$). Besides, the mean level of serum iron was reduced in the intervention group, but the difference was not statistically significant ($p=0.81$). Finally, changes in serum iron, UIBC, and TIBC levels were not statistically significant ($p=0.96$, $p=0.12$, and $p=0.20$, respectively).

Discussion

This review aimed to collect the evidence on the effectiveness of using different physical therapy modalities on children with thalassemia and sickle cell disease based on clinically relevant primary outcomes including enhance health-related quality of life as decreasing anxiety, pain and depression, enhance fatigue level as well as some secondary outcomes including improvement of cardio-pulmonary system and body structure and function (decrease iron overload, enhance bone mineral density).

The review included studies were searched in the electronic databases since Ever until December 2019. Five databases; Pub Med, Science direct,

Cochrane Library, Pedro and Google Scholar were searched using the following keywords; Thalassemia, Sickle cell disease, physical therapy modalities, children, exercise training, transcutaneous electrical nerve stimulation.

Only published trials were included in the current review. Unavailable relevant articles which may support or disagree with the results were excluded. The main reasons for the exclusion of other studies were that they were published in language other than English, review articles, published abstracts with no full text articles available and they did not meet the inclusion criteria.

The articles included in this review are characterized by providing immediate and follow-up

results and this help in determining the immediately and long run effect of the different physical therapy modalities on children with thalassemia and sickle cell disease.

Thalassemia and sickle cell disease are both considered a major health problem for the children affected and their families.

The consequences of Thalassemia on physical health can lead to physical deformity, growth retardation, and delayed puberty, its impact on physical appearance, bone deformities and short stature contributes to a poor self-image. The common complications among those patients are heart failure, cardiac arrhythmia, liver disease, endocrine complications, and infections. Although cure of Thalassemia become possible, attention is given to evaluate the associated psychiatric disorders such as depression (exerts a negative influence on child life, with a prevalence of 2%-3%) [13] anxiety, fatigue and the associated pain that frequently accompany these chronic diseases also attention is given to chest rehabilitation to reduce the acute chest syndromes associated with them.

SCD is characterized by chronic hemolytic anemia, poor growth status, altered body composition, delayed skeletal and sexual maturation, and nutritional deficiencies have long been recognized in children with SCD, particularly with type SS (SCD-SS). But Recurring or chronic pain is the hallmark clinical feature of sickle cell disease (SCD). Children and adolescents with SCD typically report pain occurring in the extremities, hip, or trunk on 7-30% of diary days, with an average duration of 2.5 days and an average pain rating of 5 on a 10-point scale [24].

Pulmonary complications are also one of the commonest set of complications in SCD and considered a major cause of acute morbidity and mortality in SCD, Pulmonary function abnormalities in SCD are frequent and are characterized by airway obstruction, restrictive lung disease, abnormal diffusion capacity, and hypoxemia [5].

Physical therapy may help to improve the functional ability, quality of life and rehabilitate patients with Thalassemia and SCD, it performs a vital role in the multidisciplinary management of (SCD) symptoms, especially range of motion (ROM), balance, and airway clearance issues [5].

Conclusions:

The current level of evidence to support the effectiveness of physical therapy modalities on improving the health related quality of life in

children with thalassemia and sickle cell disease is strong. But it need further research to clinically support and explore more effects.

There are few conclusions that can be drawn from the existing evidence as follows:

- 1- There appears to be a strong evidence of improving the health related quality of life in children by decreasing pain, depression and anxiety.
- 2- There is some evidence of effect of using spirometer, vibration, moderate exercise in enhance the pulmonary functions, bone mineral density and ferritin and serum levels.

Ethical committee: Faculty of Physical Therapy, Cairo University approved the protocol of this study.

There is no conflict of interest and it is self-funding study.

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العلاج الطبيعي لأطفال أنيميا البحر المتوسط والخلايا المنجلية: دراسة توضيحية

هدفت هذه الدراسة التوضيحية إلى دراسة تأثير طرق ووسائل العلاج الطبيعي المختلفة لدى الأطفال المصابين بأنيميا البحر المتوسط ومرض الخلايا المنجلية.

للإجابة على هذا السؤال، بحثنا في الباحث العلمي في Google و PubMed و Science Direct و Pedro و Ovid و Cochrane باستخدام الكلمات الرئيسية (Physical Therapy Modalities) و (Thalassemia) و (Sickle Cell Disease) و (Exercise Training) (Transcutaneous Electrical Nerve Stimulation) (Breathing Exercise) (Children) (related quality of Life Health).

قمنا بتوسيع نطاق بحثنا ليشمل جميع تصميمات البحث باستثناء آراء الخبراء والدراسات التي تقيس النتائج التي لا تتعلق بنطاق هذه الدراسة.

تم تلخيص البيانات من جميع الدراسات المشمولة بالتنسيق التالي الذي يتضمن خصائص المشاركين (العدد في كل مجموعة، والتشخيص، والأرقام في كل مجموعة فرعية للتشخيص والأعمار)، والمجموعة العلاجية، والمجموعة المقارنة، وتصميم البحث، ومستوى دليل على الدراسة ونتائج الفائدة.

تبعاً للبحث تم إيجاد ١٢ بحث وإدراجهم في هذه الرسالة وفقاً لهذه الأبحاث وجدنا تأثير إيجابي لإستخدام وسائل العلاج الطبيعي المختلفة على الأطفال المصابين بأنيميا البحر المتوسط والخلايا المنجلية من حيث تقليل الأعراض المصاحبة للمرض من تعب واكتئاب والشعور بالقلق وتحسين نمو العظام ومستوى مخزون الحديد في الدم وتحسين وظائف الرئة.