International Journal of Health Sciences and Research
www.ijhsr.org ISSN: 2249-9571

Original Research Article

Recommended Physical Therapy Program for Improving Quality of Life for Patients with Sickle Cell Anemia

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Received: 11/12/2016 *Revised: 21/12/2016* *Accepted: 26/12/2016*

ABSTRACT

Objective: The aim of this study was to evaluate the efficacy of recommended physical therapy program for improving quality of life (QOL) for patients with sickle cell anemia.
Methods: Fifty-four subjects were randomly divided into physical therapy group (PT) and control group (CG). Patients in (PT) group received physical therapy program consisted of inspiratory training by incentive spirometry, transcutaneous electrical nerve stimulation, aerobic exercises in addition to medical treatment while (CG) received medical treatment only. Pulmonary functions, pain intensity and (QOL) scores were evaluated before and after eight weeks for all patients.
Results: The results of the study showed more reduction of pain intensity in (PT) group more than (CG), (p value <0.05). In addition the results of the study showed that the pulmonary functions and (QOL) scores were higher in (PT) more than (CG), (p value <0.05).
Conclusion: The recommended physical therapy program was effective in decreasing pain, improving pulmonary functions and improving (QOL) of the sickle cell patients so we recommend it as treatment program for improving health status of the sickle cell patients.
Key Words: Sickle cell anemia, Quality of life, Physical Therapy.

INTRODUCTION

Sickle cell anemia (SCA) is one of the inherited blood diseases that commonly affect individuals of African, Mediterranean, and Asian descent. (SCA) is a common disease that manifests as hemolysis and vaso-occlusion. [1] There are over 200,000 children affected with sickle cell diseases (SCD) are born every year, primary in sub-Saharan Africa. [2]

Sickle cell anemia is a phenotypic heterogeneity disease resulting from both genetic and environmental factors. [3] (SCA) could associate with some acute and chronic health problems, such as severe infections, attacks of severe pain (sickle-cell crisis), and several life-threatening complications, such as sepsis, stroke, Acute chest syndrome (ACS), pulmonary embolism, and hepatic disease. Besides, this condition leads to a shortened lifespan, a reduced quality of life (QOL), and significant anxiety and psychological depression as well. [1,4]

Sickle cell anemia is a chronic disease requiring prolonged comprehensive, life-long management. Over the time, enormous progress has been made in the care of patients with (SCA). Physical therapy plays a key role in rehabilitating patients with SCA. It performs a vital role in the multidisciplinary management of (SCD) symptoms, especially range of motion (ROM), balance, and airway clearance issues. [5-7] However, there are very few studies in the literature document the role of physiotherapy as a resource to prevent and treat various disorders of (SCA).

One of the most clinical hallmarks of (SCA) is the pain. Physical therapy plays a significant role in decreasing pain that

results in a shortened hospitalization and reduction of the amounts of potentially harmful and addictive analgesics. Many modalities such as transcutaneous electrical nerve stimulation (TENS), massage, relaxation, warmth may be helpful during acute pain episodes, but little evidence concerning the effectiveness of these strategies is available. [8-11]

The ultimate goal of health care worker is to maintain or improve the (QOL). Measuring health-related quality of life as an outcome in therapeutic trials has become increasingly common, as noted in ongoing and upcoming studies of (SCD). [12,13] Very little studies document the role of physical therapy for treating sickle cell patients and up to our knowledge, no previous study emphasized its effects on (QOL) of sickle cell patients. The main goal of this study was to introduce a physical therapy program in order to improve (QOL) of sickle cell patients through relieving pain crises which is the principle cause of frequent hospitalization and improving pulmonary functions hence prevent occurrence of (ACS).

PATIENTS AND METHODS

Patients

Fifty four patients with homogenous (SCA), were recruited from Al-Yamama Hospital, Riyadh, KSA. An experimental prospective randomized controlled trial was done between January 2015 and June 2016. Complete history, physical examination, selected laboratory tests such as complete blood count, reticulocyte count, and urine analysis were done for every patient as a routine investigation. The details of the rehabilitation program and assessments were presented to patients, after which those who were interested, were booked for recruitment into the program based on whether they met the eligibility criteria.

Subjects who fulfill the following criteria were enrolled in the study; patients with vaso-occlusion phenotype, patients age above 18 years and below 60 years, patients who did not participate in a physical therapy program within 12 months before the study, patients who exhibited clinical and hemodynamic stability, additional criteria also include Patient should sign a consent form before entry the study and agreed to be available until re-assessment at the end of treatment.

Reasons for exclusion were a history of stroke, prior rib infarctions, vertebral disease, function-limiting avascular necrosis, debilitating leg ulcers, pregnancy, Hb<5 g/dl. Patients with severe cardiac arrhythmia or evidence of ischemia, and significant valvular heart disease, right ventricular dysfunction, or primary cardiomyopathy were excluded from the study. Additionally, patients who did not agree to participate or sign a consent form were excluded from the study.

The sample size is estimated using G power (version 3.0.10). To avoid a type II error, we aimed to recruit 52 participants, giving 80% power, at $\alpha = 0.05$ and effect size =0.8. The sample was increased to (60) for possible dropout. Patients were randomly divided into two groups. Physical therapy group (PT) received physical therapy program in addition to medical treatment while the control group (CG) received only medical treatment. Simple randomization method was used by using computer-generated random numbers. Online randomizationsoftware was used, http://www.graphpad.com/quickcalcs/index.cfm , The research was conducted out according to the principles of the Declaration of Helsinki; the study protocol was approved by Research Ethical Committee, Basic & Health Science Research Center, Scientific Research Deanship, Majmmah University, Kingdome of Saudi Arabia.

Measurement procedures

Data was collected through individual interviews and physical assessments. Measurements were done for all patients in (PT) and (CG). Two blinded assistant investigators did an assessment. Pain intensity, pulmonary functions, and

QOL scores were measured at the beginning of the study (pre) and 8 weeks (post).

Primary outcomes measures

Measurement of pain intensity

Pain intensity was measured by a visual analog scale (VAS) Fig (1). It consists of a horizontal line labeled from zero to ten, with zero indicating "no pain" and ten indicating "worst pain possible." The patient circled the number that indicates the overall intensity of the pain. The patient was asked to mark the area of pain on a scaled body drawing. [14,15] Measurement were done before and after 8 weeks.

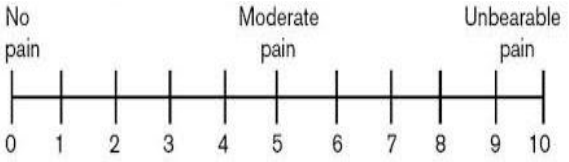

Fig. (1)visual analog scale

Measurement of pulmonary functions

Spirometry means measuring of breath. It is used to measure lung functions, specifically the measurement of the amount of volume and flow of air that can be inspired and exhaled. The spirometry test was performed using a device called Ergospirometry device Fig (2). Spirometer devise displays two graphs called spirograms, a volume-time curve, and a flow-volume loop. Pulmonary function is abnormal in 90% of adults with (Hemoglobin SS) Hb-SS. [16] In current study, forced vital capacity "FVC," forced expiratory volume after 1 second "FEV1," Diffusion capacity (DLCO)were measured. The height and weight were measured for each patient then the computer unit was fed up by the patient demographic parameters (name, age, weight, height, and sex). Each patient was instructed to lose any tight clothes and to sit in an upright position in front of the Ergospirometry system equipment. The patient closed nose with the nose clips and hold the mouthpiece by mouth. [17]

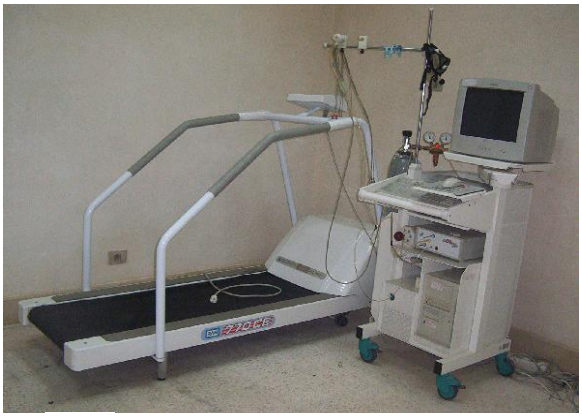

Fig. (2) Zan-680 Ergospiro "Ergospirometry System",

A) Measurement of Forced Vital Capacity "FVC"

The "FVC" is the amount of air which could be forcibly exhaled from the lungs after taking the deepest breath possible. FVC is the most basic maneuver in spirometry tests. Each patient was instructed to inspire slowly and deeply, and then expire with power as quick and as much as possible. The patient performed three trials at least, and the best performance was used for analysis. The unit of measurement is liter. [18]

B) Measurement of forced expiratory volume at 1 second "FEV1":

Forced expiratory volume (FEV) measures how much air a person can exhale during a forced breath. FEV1 is the amount of air exhaled measured during the first second of the forced breath. Predicted normal values for FEV1 depend on age, sex, height, weight, and ethnicity as well as the research study that they are based on. [18]

C) Diffusion capacity (DLCO)

Diffusing capacity (DLCO) is the carbon monoxide uptake from a single inspiration in a standard time (usually 10 sec). Since air consists of very minute or trace quantities of CO, 10 seconds is considered to be the standard time for inhalation, then rapidly blow it out (exhale). The exhaled gas is tested to determine how much of the tracer gas was absorbed during the breath. This will pick up diffusion impairments, for instance in pulmonary fibrosis. This must be corrected for anemia (because rapid CO diffusion is dependent on

hemoglobin in RBC's; allow hemoglobin concentration, anemia, will reduce DLCO). [19-21]

Secondary outcomes measures

Measurements of Quality of life

Measuring health related quality of life as an outcome in therapeutic trials has become increasingly common, as noted in ongoing and upcoming studies of (SCD). [22] The World Health Organization-Brief (WHOQOL-BREF) is the original version of WHOQOL-100 that may be more convenient for use in research studies or clinical trials for assessing (QOL) of patients. This questionnaire asks how patient feels about his (QOL), health, or other areas of his life. [23]

The WHOQOL-BREF creates a profile with four domains scores. It comprises 26 items, which measure the following broad domains: physical health, psychological, social and environment domains. The four domain scores are estimated in a positive direction in which the higher scores indicating a higher quality of life. Three items of the BREF should be reversed before scoring. The four domains are then scored, labeled, and transformed to a 0 to 100 scale used to interpret and compare to other validated instrument tools. [24-27]

Treatment procedures

The program was done for (PT) group for 8 weeks three times per week. The participants were asked to fill a diary indicating that the daily regimens were carried out.

Inspiratory training using incentive spirometry

Standard incentive spirometry device Fig (3) was used to provide sustained deep breathing exercise. It is a flow type device, consists of three champers with three balls that provide visual feedback to the patient. The patient was required to sit on the edge of the bed then hold the incentive spirometer in an upright position. The patient was asked to put the mouthpiece in his/her mouth and seals his/her lips tightly around it. The patient was ordered to breathe in slowly and as deeply as possible, raising the balls toward the top of the column then hold his/her breath as long as possible (for at least five seconds), then allow the balls to fall to the bottom of the column. The exercise was performed for 10 minutes three times/week for 8 weeks. [28]

Fig (3)Incentive Spirometry device",

Transcutaneous electrical nerve stimulation

Transcutaneous electrical nerve stimulation Fig (4) was used to relief pain for sickle patients. It was applied for the patients in (PT) group during hospitalization period. The electrodes were placed over the most painful areas. The frequency was set on 100 Hz at a sensory level for 30 minutes, three times weekly for 8 weeks.

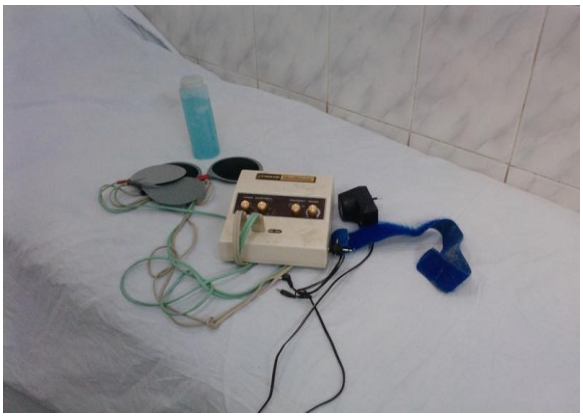

Fig (4) TENS apparatus

Aerobic exercises

Patients in (PT) group were instructed to start exercise slowly and progressively, to maintain adequate hydration during and after exercise. All

patients wore HR monitors. Exercises were done for 20 minutes. Patients were usually encouraged to exercise on a symptom-limited basis. Aerobic exercises involved pedaling a cycle ergometer, walking and aerobic games involving large muscle group. The duration and intensity of the aerobic training were gradually increased during the study period. Patients started with at least 10 min of aerobic exercises at 50% of age-predicted maximum heart rate (HRMax), (calculated as 220 minus age minus rest heart rate) and progressed to at least 20 min of continuous exercise at ≥ 70% HRmax by the end of the program. [29]

STATISTICAL ANALYSIS

SPSS version 20.0 (SPSS Inc., Chicago, Illinois, USA) was used to analyze the data. Continuous variables were summarized as mean±standard deviation (SD) and categorical variables as frequency and percentage (%). Independent Student's t-test was used to compare the quantitative parametric variables (Age, Height, Weight, BMI, HB, FVC, FEV1, DLCO) between (PT) and (CG), while Mann-Whitney test was used to compare the non-parametric variables (sex, QOL scores). For comparison of quantitative variables within group, a paired t-test was used while Wilcoxon was used to compare non-parametric variables within group. A P-value of <0.05 was considered significant.

RESULTS

Baseline demographic &clinical characteristics for patients in both groups

Sixty patients were screened for eligibility, and fifty-seven subjects fulfilled the inclusion criteria. They were initially randomized into two groups' 29 patients in (PT) group and 28 patients in (CG). Two patients withdrew from (PT) group and one patient from (CG) due to poor adherence. Poor adherence to program occurred when patient did not attend more than three consecutive sessions or more than 20% of all sessions. The data were available for 54 patients; (PT) group (n=27), and (CG) group (n=27) to the final analysis. Fig (5) presents the flow chart for patients throughout the study. Both groups were comparable to the baseline regarding the demographic and clinical characteristics. Table (1) showed the characteristics of the participants.

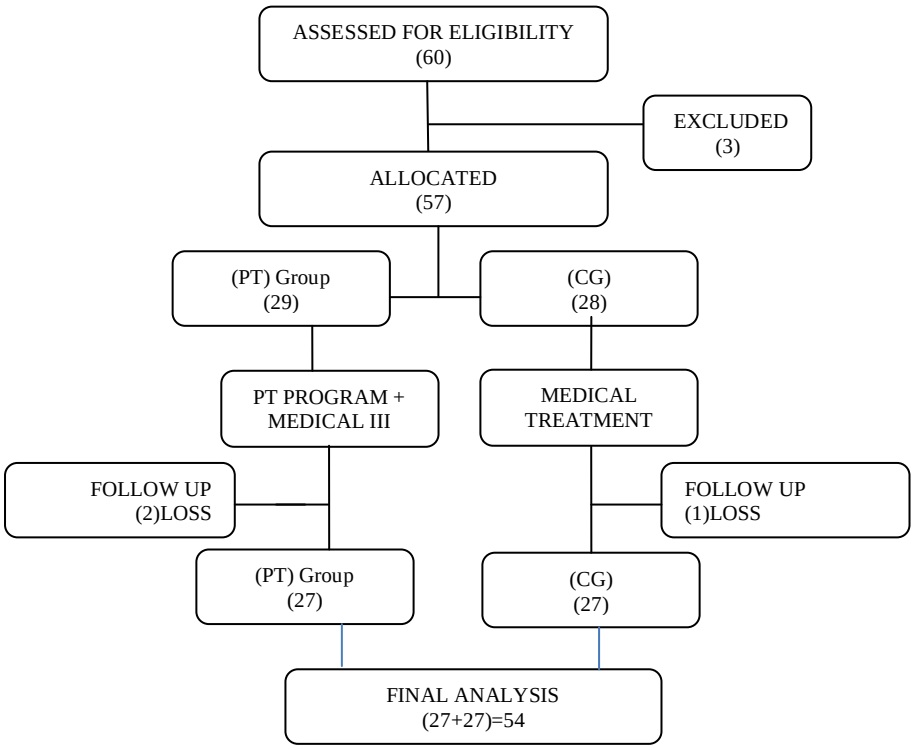

Figure (5) Flow of patients through the study

Table 1: Baseline demographic and clinical characteristics of patients

Variables	*PT group (n=27)*	*Control group (n=27)*	*P-value*	*95% Confidence Interval of the Difference*	
				Lower	**upper**
Age (years) Mean ±SD	37.00±8.03	39.44±7.62	0.256*	-6.71844-	1.82955
Sex (M/F) %	(13/14) (48.1% / 51.9%)	(10/17) (37% / 63%)	0.413*	-.38457-	.16235
Height (m) Mean ±SD	1.66±8.33	1.67±6.49	0.638*	-5.03980-	3.11388
Weight (Kg) Mean ±SD	63.96±9.78	68.77±9.00	0.066*	-9.95127-	.32164
BMI (kg/cm2) Mean ±SD	21.89±2.24	22.70±2.13	0.177*	-2.00822-	.37859
HB (g/dl) Mean ±SD	8.77±0.60	8.80±0.53	0.326*	-3.28106-	9.69810
FVC (0wk) Mean ±SD	75.40±5.38	76.33±5.25	0.525*	-3.83217-	1.98032
FEV1 (0wk) Mean ±SD	58.59±5.48	60.29±5.09	0.243*	-4.59574-	1.18833
DLCO (0wk)Mean ±SD	55.82±0.89	55.65±1.27	0.575*	-.43190-	.76968
VAS (0wk) median(range)	9(2)	9(2)	0.147*	-.69811-	.10552
Physical domain median(range)	42(27)	44(18)	0.275*	-4.49762-	1.97910
Psychological domain median(range)	49(19)	44(12)	0.862*	2.18843	7.73750
Social domain median(range)	37(19)	38(19)	0.869*	-2.85228-	2.92635
Environment domain median(range)	40(20)	38(21)	0.597*	-2.52410-	3.63521

*P-value compared between groups SD = standard deviation M= male, F= female, BMI = body mass index, VAS= visual analogue scale.

Comparative analysis of pain intensity measurements in both groups

Pain intensity measurements were summarized in Table (2), The results of the study showed that there was a significant decrease in pain intensity in (PT) group more than (CG) group with the percentage of improvement 44.4% versus 11%, (p value <0.05).

Table 2: Comparative analysis of pain intensity measurements in both groups

Variables	*PT group (n=27)*	*(CG) group (n=27)*	*P-value compared between groups post-treatment.*
VAS (0wk) median(range)	9(2)	9(2)	
VAS (8wk)) median(range)	5(3)	8(4)	
Percentage of reduction	44.4%	11%	
p-value compared with baseline within group	0.001†	0.036†	0.001*

†P-value within group *P-value between groups.

Comparative analysis of Pulmonary functions measurements in both groups

Pulmonary functions measurements were summarized in Table (3), There was a significant increase in pulmonary functions(FVC, FEV1, DLCO) in (PT) group more than (CG) group (p value <0.05).

Table 3: Comparative analysis of pulmonary functions measurements in both groups

Variables	**PT group (n=27)**		**Control group (n=27)**		**P-value compared between groups post-treatment.**
	pre	**post**	**pre**	**post**	
FVC (Mean ±SD)	75.40±5.38	82.25±3.94	76.33±5.25	76.59±5.18	
p-value within group	0.001†		0.148†		0.001*
FEV1 (Mean ±SD)	58.59±5.5	85.00±3.9	60.29±5.1	61.81±5.4	
p-value within group	0.001†		0.690†		0.001*
DLCO (Mean ±SD)	55.82±0.89	63.03±4.5	55.65±1.27	56.11±1.89	
p-value within group	0.001†		0.163†		0.001*

†P-value within group, *P-value between groups.

Table 4: Comparative analysis of QOL scores measurements in both groups

Variables	*PT group (n=27)*		*Control group (n=27)*		*P-value compared between groups post-treatment.*
	pre	**post**	**pre**	**post**	
Physical domain median(range)	42(27)	75(16)	44(18)	45(20)	
p-value compared with baseline within group	0.001†		0.093†		0.001*
Psychological domain median(range)	49(19)	79(32)	44(12)	44(16)	
p-value compared with baseline within group	0.001†		0.061†		0.001*
Social domain median(range)	37(19)	78(24)	38(19)	39(19)	
p-value compared with baseline within group	0.001†		0.073†		0.001*
Environment domain median(range)	40(20)	79(17)	38(21)	39(21)	
p-value compared with baseline within group	0.001†		0.098†		0.001*

*†P-value within group, *P-value between groups.*

Comparative analysis of (QOL) *scores measurements in both groups*

Quality of life scores for both groups were summarized in Table (4).There were significant improvement in (QOL) scores of all domains; physical, psychological, social, environmental domains post-treatment in (PT) group, (p value <0.05) while non-significant improvement of (QOL) in control group (p value > 0.05).

DISCUSSION

Sickle cell anemia is a genetic disorder that produces varying degrees of functional incapacity or even death. According to previous studies, the life expectancy of patients with sickle cell anemia has improved dramatically over the last century. Although this longer span, the disease results in many complications and progressive organ damage that may affect patients and QOL. [30,31]

Pain crises are the first and main manifestations of SCA and are the primary reason for the high rates of hospitalizations of sickle cell patients. [32] Pain is considered a serious public health problem, which negatively affects the QOL of individuals. Taking into consideration that its treatment requires a multi-action therapeutic plan, specifically physiotherapy, could help decrease pain, and improve mobility and the ability to perform self - care activities that positively impacting on the QOL. [33,34]

Physiotherapy is noticeably ignored from the general medical literature and from the current health education programs which relate to this disease as there are very few studies document the role of physical therapy in treating this condition. To the best of our knowledge, there is no known previous study introduced physical therapy program for improving QOL of those patients. This study was therefore carried out to fit this vacuum. The principal concerns of physiotherapy in treating sickle cell patients are relieving pain, prevent respiratory problems and the enhancement of efficient and adequate movement, aimed directly at improving functional ability and QOL.

The results of the present study showed that there was a significant difference between (PT) group and (CG) group after interventions. The percentages of pain reduction in (PT) were significant when compared with (CG) group. There was also a decline in the analgesic drug dosage in physical therapy group more than control group. The higher percentage of reduction of pain intensity and analgesic drug dosage in (PT) group may be due to the application of TENS. The proposed mechanism of TENS is that it activates a complex neuronal network to result in a reduction in pain. TENS activates a large diameter afferent fiber that is sent to the central nervous system to activate descending inhibitory systems. [35,36]

Only one previous study [37] evaluated effectiveness of TENS in (SCA) patients. A randomized, double-blind, cross-over study was done to compare TENS versus placebo. The results of this study showed that pain ratings and analgesic requirements at 1 and 4 h from onset of study were similar in the TENS and placebo groups but the patients' assessments of overall treatment efficacy indicated that TENS was more frequently helpful.

The SCD is a painful condition wherein breathing often is compromised. The pulmonary complications of SCD are a major cause of morbidity and mortality in affected patients. The findings of previous studies [38-42] reported that lung function parameters (FVC, FEV1, PEFR) are impaired in SCA patients.

The results of the our study showed that there were significant increase in pulmonary functions (FVC, FEV1, DLCO) in (PT) group when compared with (CG) group (p value <0.05). These improvements may be due to reduction of pain intensity and also due to application of incentive spirometry for patients in (PT) group.

Incentive spirometry likely neutralizes the impact of splinting in patients with sickle cell disorders who are

incapable to take a deep breath because of chest pain and helps retard the development of atelectasis or infiltrates and prevent development of acute chest syndrome (ACS).A number of studies [43-47] evaluated the benefits of using incentive spirometry to encourage deep Inspiratory efforts and prevent pulmonary complications. The results of these studies were in consistent with the results of our study.

Bellet et al [43] conducted a prospective, randomized trial in 29 patients with sickle cell diseases who had acute chest or back pain above the diaphragm and were hospitalized. Patients with normal or unchanged chest radiographs on admission were randomly assigned to treatment with spirometry or to a control non spirometry group. The results of their study detected that thoracic bone infarction is common in patients with sickle cell diseases who are hospitalized with acute chest pain and application of incentive spirometry can prevent the incidence of pulmonary complications (atelectasis and infiltrates) among those patients.

Ong [44] replicated a study of Bellet et al, [43] and applied incentive spirometry to twenty children between eight and 16 years of age with sickle cell disorder who were admitted with episodes of acute chest or back pain above the diaphragm and concluded that incentive spirometry is a facilitative children's cooperation and is used now in our in-patient services for children with sickle cell disorder.

Other study of Alotaibi and Waked [45] who divided forty patients with homogenous sickle anemia into IS and control group. IS group received IS in addition to medical treatment while control group received only medical treatment. The result of their study reported increase in FVC, FEV1, MMV in IS group more than control group.

Adeniyi andSaminu [46] divided randomly forty-nine SCA teenagers Forty-nine SCA teenagers into either the SCA spirometry or the SCA control groups. The SCA spirometry group went through a six-week, thrice-daily local incentive spirometry while the control did not go through the exercise. The results of their study showed that PEFR of the SCA spirometry group improved significantly over that of the SCA control group.

A retrospective cohort study [47] was done to detect incidence of ACS among SCA patients who admitted with no respiratory problems and received mandatory IS. They concluded that Mandatory IS for sickle cell disease patients admitted without respiratory complaints reduces transfusions and ACS, particularly for those presenting with back pain.

Regarding the effects of exercises on SCA, There were few studies [48-50] investigated the effects of exercise on the biological parameters involved in vaso-occlusive events in (SCA) and their results confirmed the beneficial effects of exercises. Chirico et al [48] study the effects of exercises on trained SCT carriers compared with their untrained counterparts. They reported that the overall oxidative stress and nitric oxide response is improved in exercise-trained SCT carriers compared with their untrained counterparts. In addition they suggest that physical activity could be a viable method of controlling the oxidative stress.

Debevec et al [49] provide an evidence by their study that 2 h of moderate daily exercise training can attenuate the oxidative stress induced by continuous hypoxic exposure. Cones et al [50] highlighted the basic principles that are used for exercise practice and could be used for exercise prescription and rehabilitation in patients with sickle cell anemia. They reported that SCA patient should advised to exercise slowly and progressively, to maintain adequate hydration during and after exercise, to avoid cold exposure or sudden change in temperature.

There are many factors affecting (QOL) of SCA patients such as pain crises, use of medications, hospitalizations and lost working capacity. Kater et al [51] found that SCD is associated with limitations in

different aspects of health related quality of life (HRQL), particularly physical, social, emotional and school aspects. This negative impact, particularly in the physical aspect, is painful crises. Pain is the complication that has the greatest impact on HRQL of patients with SCD and their families. [52] Improving perceived health status and maximizing physical and psychological functioning are important principles of disease management applicable to the (SCD) population. [53]

The current study was the first study evaluated the efficacy of physical therapy on (QOL) of (SCA) patients. The results of the present showed that there were significant improvements in quality of life scores for patients in (PT) group (p-value <0.05) while there were no improvement in (QOL) scores for patients in (CG) group (p-value>0.05). This improvement may be due to the reduction of pain intensity and improvement of pulmonary functions in addition to the effect of aerobic exercises that lower pain and improves social functions and vitality.

Regarding side effects, the results of this study showed that patients in (PT) group were able to do the planned physical therapy program without any side effects reported more than mild fatigue in some patients that resolved by minimal rest. Limitations of study were small sample size, lack of follow up and home program for those patients. Further studies are needed including large sample size, follow up and home program.

CONCLUSION

Our study justifies that this suggested physical therapy program is effective for improving quality of life of sickle cell patients so we recommend it as treatment program to improve health status of sickle cell patients.

ACKNOWLEDGEMENT

First of all, I thank Allah who provided me with essential power and patience to complete this work. I am very thankful to my patients for their active participation in this work.

SOURCE OF FUNDING

This research received no specific grant from any funding agency in the public, commercial, or not / for profit sectors.

CONFLICTS OF INTEREST

We certify that there is no conflict of interest with any financial organization regarding the material discussed in the manuscript.

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How to cite this article: Waked IS. Recommended physical therapy program for improving quality of life for patients with sickle cell anemia. Int J Health Sci Res. 2017; 7(1):163-173.

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