Original Article

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Inspiratory Muscle Trainer Versus Diaphragmatic Breathing Exercise on 6-Minute Walk Test in Adolescent Girls with End-Stage Renal Disease

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Abstract:

Objective: Inspiratory muscle weakness (IMW) is very common among adolescents with end-stage renal disease (ESRD). Untreated IMW in ESRD adolescents induces acute and chronic pulmonary complications, low physical performance, and impairment in quality of life (QoL). This was a 12-week breathing-retraining trial that compared the effects of threshold inspiratory muscle trainer (TIMT) versus the diaphragmatic breathing exercise procedure (DBEP), on ESRD adolescent girls' maximal inspiratory pressure (MIP) and QoL, which was assessed by the Child Health Questionnaire (50-item parent form) (CHQ/PF_{50}), pulmonary functions, and six-minute walk test (6MWT).

Material and Methods: This breathing-retraining trial enrolled forty adolescent girls with ESRD. The girls were randomly divided into two groups: one group contained twenty girls that were trained by TIMT, while the other group contained 20 girls whom were trained by DBEP. The 20-minute rehabilitation of IMW by TIMT or DBEP was applied 3 times weekly. Adolescent girls' forced vital capacity (FVC), CHQ/PF_{50}-related score of physical summary, MIP, 6MWT, CHQ/PF_{50}-related score of psychosocial summary, forced expiratory volume in the first second of girls' expiration (FEV1), and 6MWT-associated physiological data (blood pressure, heart rate, and rate of perceived exertion) were assessed.

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Results: All outcomes of adolescent girls with ESRD in the first group that were trained by TIMT showed significant improvements, whereas the other group's girls did not show the same reported significant improvements.

Conclusion: Compared to DBEP, the 12-week training by TIMT significantly improved ESRD adolescent girls' FVC, CHQ/PF50-related score of physical summary, MIP, 6MWT, CHQ/PF50-related score of psychosocial summary, FEV1, and 6MWT-associated physiological data.

Keywords: Threshold inspiratory muscle trainer, diaphragmatic breathing exercise, six-minute walk test, pulmonary functions; end-stage renal disease.

Introduction

The presence of structural and/or functional renal abnormalities for ≥12 weeks is the description of chronic kidney disease (CKD). Besides various histopathological/laboratory tests and imaging procedures, a glomerular filtration rate (GFR) below 60 ml/min/1.73m^2 for ≥12 weeks is mandatory for the diagnosis of CKD. CKD is globally prevalent among children and adolescents; as Per one million children, there are 82 CKD cases[1].

Due to the absence of an Egyptian CKD registry, not only is the number of CKD children not well known, renal failure in children/adolescents may also only be diagnosed when the disease reaches its end stage[2].

End-stage renal disease (ESRD) is the permanent deterioration of renal functions. In ESRD, for sustaining a sufferer's life, renal replacement therapies (peritoneal dialysis, hemodialysis, or kidney transplantation) are strongly needed/prescribed[3].

ESRD not only affects the daily activities of adolescents and/or their parents/caregivers but also deteriorates adolescents' physical performance[4]. In CKD or ESRD patients, physical performance is usually and periodically tested by the low-cost, valid, and reliable six-minute walk test (6MWT)[5]. To perform the 6MWT (walking for 6 minutes in a 30-meter corridor), the concurrent presence of strong peripheral circulation, good balance, and high mobility/endurance are required from CKD or ESRD patients[6].

Unfortunately, CKD or ESRD patients' performance during 6MWT is expected to be low. Besides fatigue, physical deconditioning, skeletal muscle disuse/atrophy, sedentary behavior, back pain, subclinical pro-inflammatory status, and compromised functions of the cardiopulmonary/cardiovascular system[7], the presence of ESRD-induced impairment of respiratory muscle strength is the cause of low values for the 6MWT in ESRD patients[8].

ESRD-induced impairment of respiratory muscle strength is explained by the hemodialysis (HD) process, accumulation of uraemic toxins (uraemic syndrome), electrolyte and/or acid/base imbalances, loss of respiratory muscular mass, and respiratory myopathy. ESRD-induced impairment of respiratory muscle strength decreases partial pressure of blood oxygen and lowers ESRD patients' cardiopulmonary conditioning; hence, ESRD patients' exercise capacity, well-being, physical performance, quality of life (QoL) as well as independence are negatively affected[9].

Little attention has been paid to the treatment of impairment of respiratory muscle strength during rehabilitation programs for ESRD patients. Respiratory muscle training (RMT) is a common strategy/treatment used to improve respiratory muscle functions, strength, and endurance in patients with chronic illnesses[10].

It is documented/reported that the diaphragmatic breathing exercise procedure (DBEP) is one of the breathing techniques that is simple and easily used to improve patients' hypoxemia, ventilation/oxygenation, and work of breathing[11].

On the other hand, the threshold inspiratory muscle trainer (TIMT) – a device used during inspiratory muscle training (IMT) – has been recently suggested as an alternative to DBEP in the last few years in CKD[12]. This study aimed to compare the response of 6MWT, pulmonary functions, and QoL to TIMT versus DBEP in adolescent girls with ESRD.

Material and Methods

Design

This was a randomized comparative breathing-retraining study in adolescent girls with ESRD.

Settings

Adolescent girls (n=40) with ESRD were recruited from El-Demerdash Hospital.

Ethics

Local ethical committee approval was gained to compare the efficacy of TIMT versus DBEP in adolescent girls with ESRD (Approval No. P.T.REC/012/004627). Adolescents' parents/caregivers signed the participation consent. In this ESRD study, Helsinki recommendations were applied.

Inclusion criteria

All eligible ESRD adolescents received extensive assessment of their physical status and their medical history/records from their primary care physician. Girls that were ESRD adolescents were included in this breathing retraining study. ESRD was diagnosed by their adolescents' primary care physician for at least six months. Adolescents' ages ranged from 13-18 years of age. Adolescents' and parents' agreements were the conditions for participation in this breathing retraining study.

Exclusion criteria

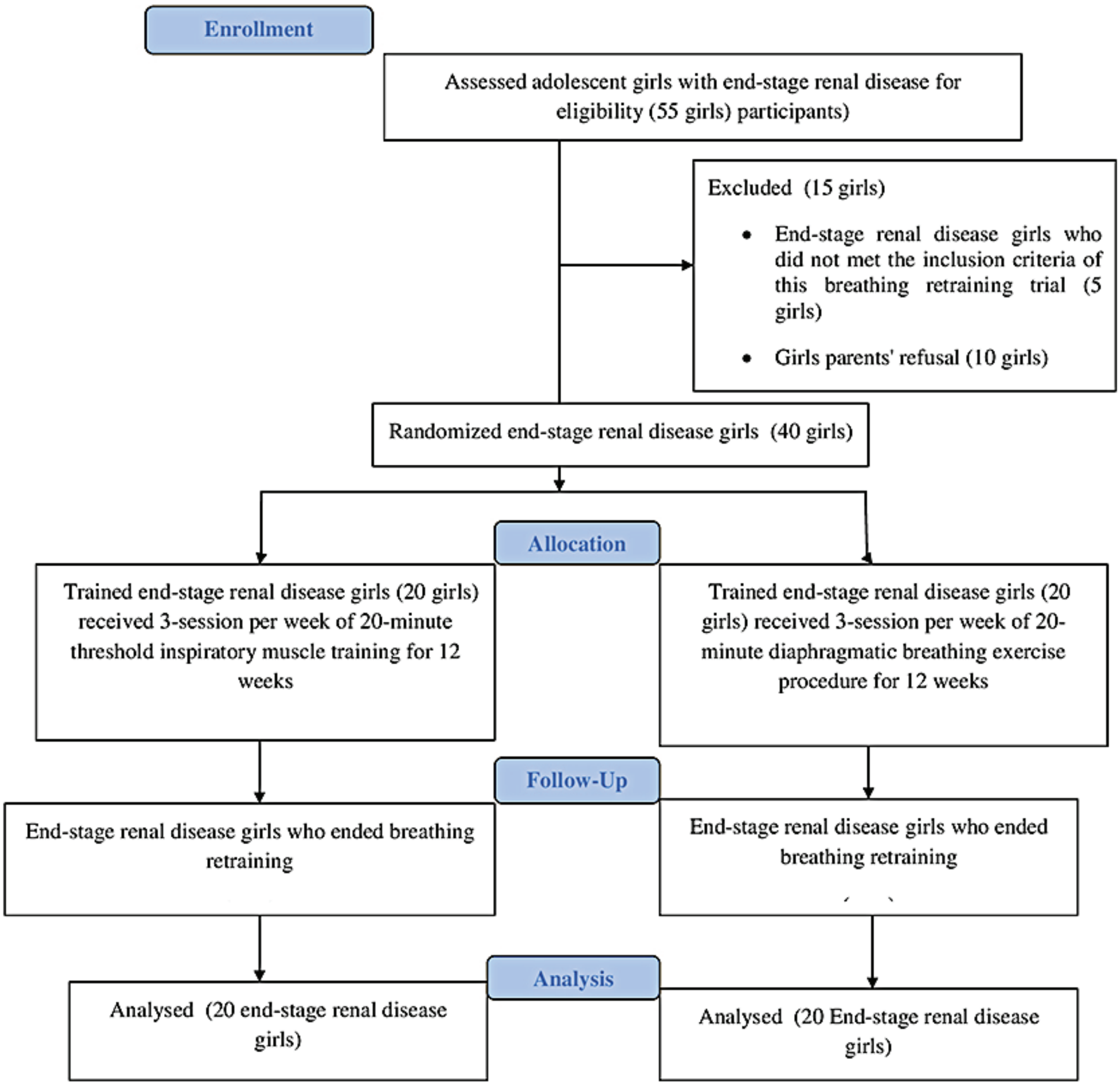
Adolescents with smoker parents and adolescents with unstable general/medical conditions; such as anemia, adolescents with respiratory diseases/infections, heart/liver disease, musculoskeletal/neurological disorders/issues, intellectual/mental disorders, metabolic/autoimmune issues, visual/hearing impairments, psychological disorders and malignant masses, were excluded.

Randomization

Via the closed envelop technique; from July to December 2023, 40 adolescent girls with ESRD were randomly divided into the TIMT (n=20 ESRD girls) or DBEP group (n=20 ESRD girls) (Figure 1). Randomization was carried out by a nursing specialist, to whom the identity of the treatment (TIMT or DBEP) provided to the girls was not revealed. All the treatments (TIMT or DBEP) were performed under the supervision of the authors in the hospital of recruitment.

Program of diaphragmatic breathing exercise

Firstly, in the supine position, girls with ESRD were instructed to lay down for 5 minutes on their back, on a plinth, with one pillow placed under their head and another one placed under their knees for extra support/relaxation. Girls with ESRD were instructed to place one hand on their abdomen, with the other hand resting on their chest wall's upper part. When performing inspiration, the girl's on-abdomen hand moved upward, while the other on-chest-wall hand remained as still as possible. When performing expiration, the girl's on-abdomen hand moved downwards, while the on-chest-wall hand remained as still as possible again. Inspiration was performed slowly, deeply, and without inducing tiredness for all girls. All girls with ESRD were ordered to breath from both nostrils with deep inspiration. In all girls with ESRD, the expiration was performed by slowly letting all of the air out from the girls' mouths with a sigh. At the start of every inspiration, girls with ESRD



ESRD=end-stage renal disease

Figure 1 Flow chart of participating ESRD adolescent girls during this breathing retraining study

were instructed to relax their upper shoulder and neck muscles to avoid the action/movement of their accessory inspiratory muscles. Also, to avoid hyperventilation, five respiratory cycles were followed by a 1-minute rest. In the DBEP group, one session of DBEP was continued for 20 minutes, and this DBEP session was repeated 3 times weekly for 12 weeks.

Program of inspiratory muscle training by TIMT

TIMT, training sessions were scheduled to execute a supervised training for 20 minutes, three times a week, for 12 successive weeks. The used device was the Philips Respironics TIMT Model, which was made in the United Kingdom. The training was performed in an upright sitting position, while using the device's nasal clip. The inspiratory load of TIMT was adjusted to 40% of the girl's previously measured/assessed maximal inspiratory pressure (MIP). Five repetitions of inspiratory muscle training via TIMT were considered as one set of training, which was repeated for 20 minutes, with one-minute intervals between sets[13].

Outcomes

Six-minute walk test

6MWT was performed/executed in a corridor, being thirty meters in length and 1.5 meters in width, according to popular/published guidelines/recommendations of the American Thoracic Society[14]. The girls' longest walked distance was computed in meters. During the evaluation of the 6MWT test, ESRD vital signs (oxygen saturation levels, heart/pulse rate, and blood pressure) were continuously monitored/assessed. Also, the authors utilized 6MWT-standardized phrases of encouragement for all tested ESRD girl; such as: "My little clever girl, you are doing well" and "My little clever girl, keep up good work". A Modified Borg Scale was utilized to assess/monitor ESRD sensation/perception of breathlessness and fatigue during the 6MWT.

Changes of physiological data in response to 6MWT

The following 6MWT-associated physiological data were assessed immediately at the end of the 6MWT in both HD groups: systolic blood pressure, heart rate, diastolic blood pressure (physiological data were assessed by Omron digital sphygmomanometer device), and the rate of perceived exertion, which was measured using or utilizing the Borg Scale; with scores ranging from 6 (no perception/sensation of dyspnea) to 20 points (maximum perception/sensation of dyspnea).

Pulmonary functions

ESRD girls' forced vital capacity (FVC) was monitored. Additionally, the ESRD forced expiratory volume at the first second of expiration (FEV1) was monitored by a Jaeger-MS-IOS Spirometer.

Maximal inspiratory pressure

For all ESRD girls, MIP was monitored/assessed using a micro-respiratory Pressure Meter (MICRORPM™, American Manufacturing). MIP is an indicator of inspiratory muscle strength, and his indicator was monitored before and after the breathing-retraining trial in both ESRD groups.

Girls' QoL

The Child Health Questionnaire (50-item parent form/proxy) (CHQ/PF_{50}) is used to assess QoL that is affected by the presence of different chronic illnesses, including ESRD. The CHQ/PF_{50} was introduced and/or filled out by the adolescent girls' parents/caregivers so as to assess/evaluate thirteen CHQ/PF_{50}-related physical and psychosocial domains: status of general health, adolescent physical functioning, ESRD role/social physical functioning, reported self-esteem, reported mental health, ESRD general behavior, perception of bodily pain, by-parent reported role/social behavioral/emotional functioning of ESRD, parent/caregiver impact – time, parent/caregiver impact – emotional, reported ' in-family activities, reported girls-associated family cohesion, and at least change/variation in health status over the last year before the evaluation. Parents' answers/responses covered the last 4 weeks before the evaluation of ESRD, except change/variation in health status that covered the last year before the evaluation. This was calculated/rated with a response ranging from: 1 (it means now much worse) to 5 (it means now much better). Every girl's raw score for each CHQ/PF_{50}-related domain was transfigured on a 0–100 scale. Two weighted/standardized CHQ/PF_{50}-related summary scores (physical and psychosocial summary scores) were calculated/rated. After ending this breathing-retraining trial in both groups of ESRD girls, a higher CHQ/PF_{50}-summarized score of physical or psychosocial summary reflected an improvement in QoL[15].

Sample size calculation of adolescent girls with ESRD

The statistician of this breathing-retraining trial confirmed the inclusion of 16 ESRD adolescent girls in every group; according to the 80%-power-analysis results of G*power calculation (effect size of ESRD girls' FVC was 1.04 calculated/analyzed from 16-pilot-test ESRD adolescent girls). According to the statistician's estimated dropout (25%) of ESRD girls during the performance of this breathing retraining trial, the number of ESRD adolescent girls was elevated to 20 girls in every group.

Statistical analysis

All data of ESRD girls were normally distributed. The statistician of this breathing-retraining trial confirmed this point using the Smirnov test. The statistician applied paired and unpaired tests in the statistical analysis of ESRD girls' data at a significance<0.05. The statistician used the licensed version of SPSS 18.

Blinding

The assessors of adolescent girls' outcomes (6MWT-associated physiological data, FVC, CHQ/PF_{50}-related score of physical summary, MIP, 6MWT, CHQ/PF_{50}-related score of psychosocial summary, and FEV1) were not informed of the identity of the treatment (TIMT or DBEP).

Results

Regarding the between-group comparison of ESRD girls' pre-training demographic data, pre-training main clinical laboratory data (presented in Table 1), and pre-training outcomes (presented in the trial's Table 2) showed a non-significant variation/difference.

As presented in the trial's Table 2, within-group comparison of ESRD girls' pre-and post-values of 6MWT-associated physiological data (blood pressure, heart rate, and rate of perceived exertion), FVC, CHQ/PF_{50}-related score of physical summary, MIP, CHQ/PF_{50}-related score of psychosocial summary, and FEV1 showed a significant improvement in the group receiving TIMT only, while the adolescent girls with ESRD in the group receiving DBEP did not show the same improvements.

As presented in the trial's Table 2, between-group comparison of ESRD girls' post-FVC, CHQ/PF_{50}-related score of physical summary, 6MWT-associated physiological data (blood pressure, heart rate, and rate of perceived exertion), MIP, CHQ/PF_{50}-related score of psychosocial summary, and FEV1) showed a significant improvement in favor of the group receiving TIMT.

Table 1 Basic/clinical data (mean±S.D.) of adolescent girls

Adolescent girls' basic/clinical data	TIMT group	DBEP group	p-value
Age of adolescent girls (years)	15.10±1.41	15.35±1.46	0.585
Body mass index of adolescent girls (kg)	19.53±2.80	20.56±3.41	0.303
Adolescent girls' duration of end stage renal disease (year)	5.70±1.45	6.25±1.51	0.247
Adolescent girls' hemodialysis duration (month)	35.25±5.80	36.90±6.69	0.409
Adolescent girls' estimated glomerular filtration rate (ml/min/1.73 m^2)	19.10±2.44	18.70±3.27	0.663
Adolescent girls' hemoglobin (g/dL)	12.11±1.13	12.06±1.13	0.889
Adolescent girls' serum creatinine (mg/dL)	8.05±1.56	8.82±1.31	0.099
Adolescent girls' albumin (g/dL)	3.54±0.71	3.75±0.75	0.368

TIMT=Threshold inspiratory muscle trainer; S.D.=standard deviation, DBEP=diaphragmatic breathing exercise procedure, kg=kilogram, dL=deciliter, ml=milliliter
Note: all adolescent girls' p-values are non-significant (adolescent girls' p-value>0.05)

Table 2 Adolescent girls' results

Adolescent girls' parameters	TIMT group	DBEP group	p-value (between groups of adolescent girls)
Adolescent girls' forced vital capacity	Mean±S.D.	Mean±S.D.	
Before breathing retraining	1.23±0.23	1.11±0.28	0.146
After breathing retraining	1.35±0.21	1.15±0.27	0.012*
p-value (within groups of adolescent girls)	<0.001*	0.075	
Adolescent girls' forced expiratory volume (in 1st second)	Mean±S.D.	Mean±S.D.	
Before breathing retraining	1.46±0.37	1.38±0.29	0.451
After breathing retraining	1.71±0.31	1.45±0.26	0.006*
p-value (within groups of adolescent girls)	<0.001*	0.058	
Adolescent girls' maximal inspiratory pressure (cm H_2O)	Mean±S.D.	Mean±S.D.	
Before breathing retraining	63.49±8.69	58.87±7.17	0.074
After breathing retraining	101.29±7.70	62.90±10.61	0.0001*
p-value (within groups of adolescent girls)	<0.001*	0.057	
Adolescent girls' child-health questionnaire "parent form, 50 questions" (physical summary)	Mean±S.D.	Mean±S.D.	
Before breathing retraining	43.55±6.94	46±8.11	0.311
After breathing retraining	54.75±7.21	48.25±6.98	0.006*
p-value (within groups of adolescent girls)	<0.001*	0.241	
Adolescent girls' child-health questionnaire "parent form, 50 questions" (psychosocial summary)	Mean±S.D.	Mean±S.D.	
Before breathing retraining	42.70±6.75	44.40±6.45	0.420
After breathing retraining	55.15±7.01	46.35±7.82	0.0006*
p-value (within groups of adolescent girls)	<0.001*	0.127	
Adolescent girls' systolic blood pressure (mmHg)	Mean±S.D.	Mean±S.D.	
Before breathing retraining	130.40±4.50	133.35±4.90	0.054
After breathing retraining	126.15±4.28	132.10±5.40	0.0004*
p-value (within groups of adolescent girls)	< 0.001*	0.199	
Adolescent girls' diastolic blood pressure (mmHg)	Mean±S.D.	Mean±S.D.	
Before breathing retraining	90.65±3.37	92.65±3.43	0.070
After breathing retraining	85.55±3.45	91.55±3.60	0.0001*
p-value (within groups of adolescent girls)	<0.001*	0.138	
Adolescent girls' heart rate (beat/minute)	Mean±S.D.	Mean±S.D.	
Before breathing retraining	88.60±3.57	90.10±3.75	0.202
After breathing retraining	83.70±3.55	88.60±4.93	0.0009*
p-value (within groups of adolescent girls)	<0.001*	0.067	
Adolescent girls' rate of perceived exertion	Mean±S.D.	Mean±S.D.	
Before breathing retraining	13.10±1.80	14.10±2.26	0.129
After breathing retraining	9.50±1.53	13.60±2.60	0.0001*
p-value (within groups of adolescent girls)	<0.001*	0.428	

TIMT=Threshold inspiratory muscle trainer, S.D.=standard deviation, DBEP=diaphragmatic breathing exercise procedure, mmHg=millimeter mercury

*Note: all adolescent girls' p-values are significant (adolescent girls' p-value<0.05)

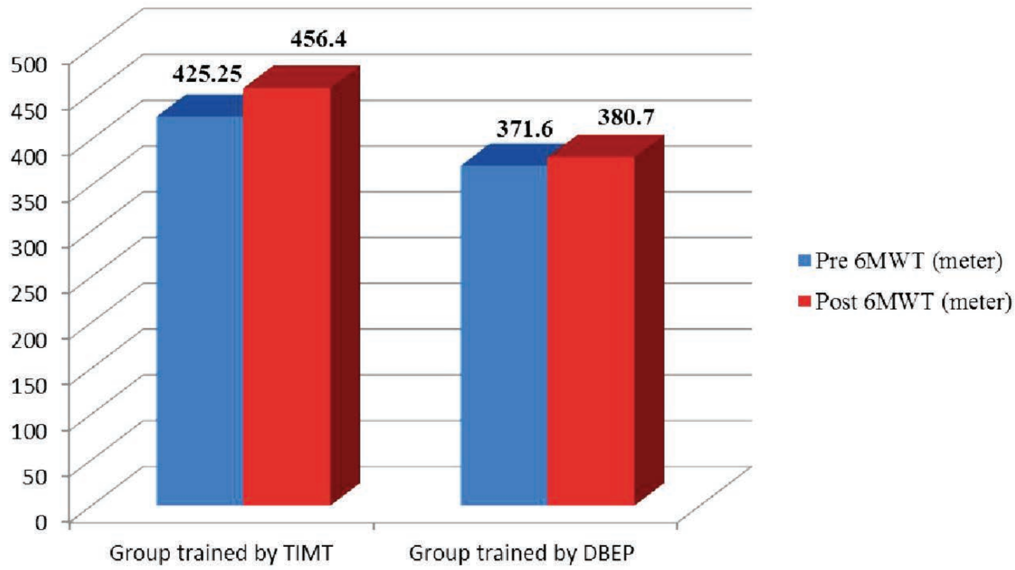
Regarding the pre-value of 6MWT, no significant difference was reported between the group that received TIMT and the group that received DBEP (425.25±91.71 versus 371.60±79.68 meters, respectively. Besides the significant improvement of 6MWT that occurred only in the group trained by TIMT, the post-value comparison of 6MWT between groups showed a significant difference toward the group trained by TIMT (post value of 6MWT in the first group was 456.40±87.76 meters versus 380.70±73.18 meters) (Figure 2).

Discussion

This breathing retraining trial, executed on adolescent girls with ESRD, showed a great, significant improvement in ESRD girls' FVC, CHQ/PF50-related score of physical summary, MIP, 6MWT, CHQ/PF50-related score of psychosocial summary, and FEV1 after using TIMT for 12 weeks. The mechanism of TIMT-induced improvement in ESRD girls' outcomes is not fully explained in ESRD literature.

The morphological/functional adaptations of inspiratory muscles resulting from physical training techniques/devices; including TIMT, enhances the body's capacity/response to stressful situations; including exercise situations. The increase in ESRD patients' cardiac output, proportional to the applied levels of exercise intensity/load, is very important to provide huge amounts of oxygen/nutrients necessary to the active, working, and contracting muscles during different body activities. Hence, patients' 6MWT or physical performance improves[16].

During the assessment of physical performance in patients with inspiratory muscle weakness, blood flow is increased in the patient's respiratory muscles, with a simultaneous decrease in blood flow to the patient's muscles of locomotion; hence, patient's complain of limited physical performance and early fatigue perception. The regular use



TIMT=Threshold inspiratory muscle trainer

Figure 2 Pre and post mean values of six-minute walking test in both groups of TIMT can correct the imbalance of blood flow to working muscles of locomotion, and therefore the patients' fatigue lessens and physical performance improves[17]. The reported improvement in physical performance is usually associated with reported improvement in physical and mental aspects of patients' lives; hence, the patients' QoL improves

Regular use of TIMT at a fixed MIP strongly activates the patient's weak inspiratory muscles and delays the loss of muscular mass. These effects produce phenotype modification of the patients' inspiratory muscles, and therefore strength and endurance of inspiratory muscles increases[18]; this may explain improved MIP after the regular use of TIMT.

ESRD girls' pulmonary functions improved significantly after the regular use of TIMT. According to Elsisi et al.[19], the regular use of TIMT improves the perception of dyspnea, lowers the rib cage's dynamic hyperinflation, promotes gas exchange, maximizes the performance of good thoracoabdominal motion/pattern, and improves respiratory muscles' strength/endurance, thus, HD patients' pulmonary functions improve.

The involvement of the hyper-activated sympathetic nervous system and ESRD-induced respiratory complications help in the development of ESRD-associated clinical manifestations of ESRD, HD-associated poor quality of life, and 6MWT-associated increases in the patient's physiological data (blood pressure, heart rate, and rate of perceived exertion).

Respiratory training ameliorates the over-activation of the sympathetic nervous system and control respiratory system; hence, the subjects' quality of life and physiological data improves[20].

Regarding TIMT effects' on the measured outcomes in the presented breathing retraining trial, scarce studies have been conducted on ESRD adolescents or children. The majority of respiratory training trials have been conducted on ESRD adults.

Supporting us, the 12-week training by TIMT significantly improved 15 sedentary HD patients' FEV1, MIP, and FVC (the mean±standard deviation of HD patients' age was 50.3±6.6 years old)[21]. Again, HD adult patients' FEV1 and FVC significantly improved after 12 weeks of training by TIMT[22].

In agreement with this study's results, 12 weeks of training by TIMT significantly improved 40 HD patients' 6MWT, MIP, FEV1, and FVC (the HD patients' ages ranged from 30 to 40 years old)[23]. Again, in HD adult patients, another Egyptian trial reported a significant improvement in 6MWT after regular adherence to 8 weeks training by TIMT[9].

Also, the 12 week training by ITMT in Egyptian HD adults. aged 45-55 years of age. significantly improved their FVC and FEV1[19]. A reported improvement in MIP, QoL, and 6MWT was detected after the 10-week training by TIMT in HD patients. aged 18-70 years of age[24].

In contrast to this study's breathing retraining trial's results, despite the improvement in respiratory muscle strength, the non-supervised/home-based 6-week training by TIMT did not improve pediatric pulmonary functions or functional capacity after kidney transplantation[13]. Additionally, in disagreement with this study, despite improvement in HD adults' FVC, 10-week training by TIMT did not show significant improvement in FVC[24]. Furthermore, the 8-week training by IMT did not significantly improve twelve HD patients' FVC, FEV1, 6MWT, and QoL (assessed by Kidney-Disease QoL-36 questionnaire) in participants aged 18-65 years of age[25].

Limitations of this ESRD study

Comparing the effects of different types of respiratory muscle training devices or different intensities of TIMT on adolescent girls' assessed outcomes was the main limitation of this ESRD study that must be faced in future ESRD studies. Also, tracking adolescent girls' outcomes after ending the 12-week training by TIMT was another limitation of this ESRD trial, which again must be faced in future breathing retraining in ESRD trials.

Conclusion

Compared to DBEP, the 12-week training by TIMT significantly improved ESRD adolescent girls' FVC, CHQ/PF50-related score of physical summary, MIP, 6MWT, CHQ/PF50-related score of psychosocial summary, FEV1, and 6MWT-associated physiological data.

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This breathing retraining trial, conducted on forty adolescent girls with ESRD, did not receive any internal or external funding.

Conflict of interest

The authors of this breathing retraining trial, conducted on forty adolescent girls with ESRD, report no conflict of interest.

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