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Efficacy of Inspiratory Muscles Training on Functional Capacity for Patients on Chemotherapy

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Abstract

Background: Cancer is a major public health problem that gives an economical burden on the patient and government. The incidence of different types of cell tumors are increasing nowadays.

Aim of Study: To investigate the effect of inspiratory muscles training on functional capacity for patients on chemotherapy.

Material and Methods: Forty male patients on chemotherapy from at least one cycle and their mean ages 37.1 ±4.89 years. The patients were selected from National Cancer Institute, Cairo (inpatient ward). The study lasted from March 2018 to June 2018. Patients were randomly assigned into two groups. Group A (30 patients) who received inspiratory muscles training for 4 successive weeks, 5 sessions/week; and Group B (10 patients) acted as a control group on chemotherapy only. Data obtained from both groups regarding forced vital capacity (FVC), forced expiratory volume in one second (FEV1), FEV1/FVC ratio and 2min walk test were statistically analyzed and compared.

Results: After 4 weeks of management for both groups the results showed that in FVC in the study group a significant increase by 33.44% while in control group, a significant decrease by 37.3%. FVE1 increased by 34.52% in the study group while it decreased by 34.09% in the control group. However, it was shown that no significant difference in the FEV 1/FVC ratio. Also results related to 2min walk test distance showed increase by 17.29% in group A while decrease by 15.48% in group B.

Conclusion: It can be concluded that inspiratory muscles training can be adjunctive to the rehabilitation program for patients on chemotherapy aiming for enhancing their functional capacity.

Key Words: *Chemotherapy – Inspiratory muscles training – Functional capacity.*

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Introduction

CANCER is a disease of the cells in the body, it is the name that is given to a mass of cells that grows in an abnormal, unregulated way and that ultimately overwhelms a body system or organ. Cancer is currently a major cause of morbidity and mortality internationally and poses a significant burden on both patients and their families and the health care system as a whole **[1,2]**.

There are several definitions of cancer survivors; we use the term "cancer survivor" to describe any person who has been diagnosed with cancer. This includes patients currently fighting cancer and those who may have become cancer free. Many survivors must cope with long-term effects of treatment as well as psychological concerns such as fear of recurrence. The terms "patient with cancer" and "survivor" are used interchangeably. It is important to note that not all individuals with a history of cancer identified with the term "cancer survivor" **[3]**.

Chemotherapy(CT) is one of three pillars of cancer treatment along with surgical treatment and Radiotherapy (RT). CT drugs interfere with a cancer cell's ability to divide and reproduce. It differs from surgery or radiation in that it's almost always used as a systemic treatment **[4-6]**.

Although CT is given to kill cancer cells, it also damages normal cells and cause significant side effects. Side effects vary depending on the particular CT drug, dosage, rout of administration and patient characteristics, some people have very few side effects while others may have more. Some CT side effects can be severe enough to require hospitalization **[4,6,7]**. Many chemotherapy agents can induce pulmonary toxicity, these patterns of

injury include not only parenchymal lung disease but also pleural manifestations, airway diseases, pulmonary vascular abnormalities, mediastinal changes, and neuromuscular effects [8].

Fatigue is one of the most common symptoms of cancer and its treatment, manifested in the clinic through weakness and exercise intolerance. Recent Advances: Oxidative stress, mediated by cancer or chemotherapeutic agents, is an underlying mechanism of the drug-induced toxicity. No targeted tissues, such as striated muscle, are severely affected by oxidative stress during chemotherapy. There is clinically available chemotherapy drugs that cause fatigue and oxidative stress in cancer patients, with an in-depth focus on the anthracycline doxorubicin. Doxorubicin, an effective anticancer drug, is a primary example of how chemotherapeutic agents disrupt striated muscle function through oxidative stress [9].

There is considerable evidence that respiratory muscle training improves pulmonary function and exercise performance in healthy athletic populations. As it increases respiratory muscle strength and delays respiratory muscle fatigue and the onset of breathlessness. Respiratory muscle training has proven to be beneficial for respiratory function in patients withchronic diseases [10].

Inspiratory muscle training applies a load to the diaphragm and accessory inspiratory muscles to increase their strength and endurance [11].

Patients and Methods

Forty male patients on chemotherapy from at least one cycle and their ages were ranged from 30 to 50 years. The patients were selected from National Cancer Institute, Cairo (inpatient ward). The Ethical Committee of Faculty of Physical Therapy no. P.T.REC/012/001806 and approval of the Institution Review Board of the National Cancer Institute no. 201617032.4. All patients were carefully examined and referred by their oncologist. The study lasted from March 2018 to June 2018. All patients were randomly assigned into 2 groups: Group A (study group): This group included 30 patients on chemotherapy, in addition to Inspiratory Muscle Training (IMT) in the form of threshold inspiratory muscle trainer 5 sessions per week for 4 weeks. Group B (control group): This group included only ten patients, who received chemotherapy only 4 cycle (1 per week) for 4 weeks. Inclusion criteria: All patients of this study were on chemotherapy from at least one cycle as a treatment of malignant tumor, hemodynamically stable, ambulant.

Exclusion criteria: Lung cancer, history of any pulmonary disease, metastasis of lung, ribs, mediastinal structure, pulmonary pathology (e.g. acute respiratory distress syndrome or exacerbation of chronic obstructive pulmonary disease), ruptured eardrum or any other condition of the ear, severe bronchospasm, patients with worsening heart failure signs and symptoms, bed-ridden patients.

Procedures of the study:

- *Evaluation procedures:*

Spirometric tests: Spirometric measurements (FVC), (FEV1) and (FEV1/FVC) ratios. The best value is obtained from at least three efforts and measured at 3min intervals.

2min walk test: Each patient was asked to cover as much ground as possible over 2 minutes. Continuous walking if possible, and to be concerned if he needed to slow down or stop to rest.

Therapeutic procedures:

- *Threshold inspiratory muscle training (Hs730-Eu-010/USA)* : (Group A) the patients were starting breathing at a resistance equal to 30% of their Maximal Inspiratory Pressure (MIP), measured at baseline [12]. Session duration: 15 minutes [13], frequency: Each session was performed each morning for 15 minutes [12].
- *Incrementing the training load:* The resistance was increased incrementally, based on the rate of Perceived Exertion (RPE) scored by the patient on the modified Borg Scale. The acceptable level of exertion in this study was level 4. If the RPE was less than 5, the resistance of the inspiratory threshold trainer was increased incrementally by 2cm H_2O. The resistance was not change if the level of perceived exertion was rated from 6 to 8, and the resistance was decreased by 1 to 2cm H_2O if the level of perceived exertion was rated 9 or 10 [13]. Then the load was increased rapidly over the first 7 days up to 60-80% of baseline MIP [14].
- Eventually, the patients received respiratory muscle training by threshold inspiratory muscle training each morning for 4 weeks.

They were assessed by Spirometric tests, 2min walk test before and after period of treatment.

- *Statistical producers:* Descriptive statistics and *t*-test was conducted for comparison of the mean age, weight, height, and BMI of both groups, *t*-test was conducted for comparison of FVC, FEV1, FEV1/FVC and 2min walk test between both groups, paired *t*-test was conducted for compar-

ison between pre and post-treatment mean values of FVC, FEV1, FEV1/FVC and 2min walk test in each group. The level of significance for all statistical tests was set at $p<0.05$. All statistical measures were performed through the Statistical Package for Social Studies (SPSS) Version 19 for windows.

Results

Subjects demographic data: There was no significance difference between both groups in the mean age, weight, height, and BMI ($p>0.05$) as shown in (Table 1).

FVC, FEV1 and FEV1/FVC ratio:

Pre treatment mean values of FVC, FEV1 and FEV1/FVC ratio of both groups (A and B):

FVC: The mean difference between both groups was –0.22 L. There was no significant difference pre treatment in the FVC between the group A and B ($p=0.65$) (Table 2).

FEV1: The mean difference between both groups was –0.09L. There was no significant difference pre treatment in the FEV 1 between the group A and B ($p=0.8$) (Table 2).

FEV1/FVC ratio: The mean difference between both groups was –0.07L. There was no significant difference pre treatment in the FEV1/FVC ratio between the group A and B ($p=0.98$) (Table 2).

Post-treatment mean values of FVC, FEV1 and FEV1/FVC ratio of both groups (A and B):

FVC: The mean difference between both groups was 2.02L. There was a significant increase post-treatment by 33.44% in the FVC of group A compared with that of group B ($p=0.0001$) (Table 3).

FEV1: The mean difference between both groups was 1.67 L. There was a significant increase post-treatment by 34.52% in the FEV1 of group A compared with that of group B ($p=0.0001$) (Table 3).

FEV1/FVC ratio: The mean difference between both groups was –1.34%. There was no significant difference post-treatment in the FEV1/FVC ratio between the group A and B ($p=0.68$) (Table 3).

2min walk test distance:

Pre-treatment mean values of 2min walk test distance of both groups (A and B): The mean difference between both groups was 1.66 meter. There was no significant difference pre-treatment in the 2min walk test distance between the group A and B ($p=0.87$) (Table 4).

Post-treatment mean values of 2min walk test distance of both groups (group A and B): The mean difference between both groups was 39.25 meter. There was a significant increase post-treatment by 17.29% in the 2min walk test distance of the group A compared with that of the group B ($p=0.01$). (Table 5).

Table (1): Descriptive statistics and *t*-test for the mean age, weight, height and BMI of group A and B.

	Group A X ± SD (SE)	Group B X ± SD (SE)	MD	*t*-value	*p*-value	Sig.
Age (years)	37.1±4.89 (0.9)	37.8±5.05 (1.6)	–0.7	–0.38	0.7	NS
Weight (kg)	74.06±8.08 (1.47)	72.2±8.96 (2.83)	1.86	0.61	0.54	NS
Height (cm)	171.8±5.36 (0.97)	173.1±5.36 (1.69)	–1.3	–0.66	0.51	NS
BMI (kg/m^2)	25.2±3.47 (0.63)	24.13±3.16 (1)	1.07	0.85	0.39	NS

X : Mean. MD : Mean Difference. *p*-value : Probability value.
SD : Standard Deviation. *t*-value: Unpaired *t*-value. NS : Non Significant.
SE : Standard Error.

Table (2): *t*-test for comparison between pre-treatment mean values of FVC, FEV1 and FEV/FVC ratio of group A and B.

	– Group A X ± SD (SE)	– Group B X ± SD (SE)	MD	*t*-value	*p*-value	Sig.
FVC (L)	3.05±0.59 (0.1)	3.27±1.49 (0.47)	–0.22	–0.45	0.65	NS
FEV 1 (L)	2.52±0.53 (0.09)	2.61±1.02 (0.32)	–0.09	–0.25	0.8	NS
FEV1/FVC (%)	82.36±7.81 (1.42)	82.43±10.42 (3.29)	–0.07	–0.01	0.98	NS

X : Mean. MD : Mean Difference. *p*-value : Probability value.
SD : Standard Deviation. *t*-value: Unpaired *t*-value. NS : Non Significant.
SE : Standard Error.

Table (3): *t*-test for comparison between post-treatment mean values of FVC, FEV 1 and FEV/FVC ratio of group A and B.

	– Group A X ± SD (SE)	– Group B X ± SD (SE)	MD	*t*-value	*p*-value	Sig.
FVC (L)	4.07±0.76 (0.13)	2.05±0.65 (0.2)	2.02	8.12	0.0001	NS
FEV 1 (L)	3.39±0.61 (0.11)	1.72±0.58 (0.18)	1.67	7.73	0.0001	NS
FEV1/FVC (%)	82.66±4.42 (0.8)	84±9.72 (3.07)	–1.34	–0.41	0.68	NS

X : Mean. MD : Mean Difference. *p*-value : Probability value.
SD : Standard Deviation. *t*-value: Unpaired *t*-value. S : Non Significant.
SE : Standard Error. NS : Significant.

Table (4): *t*-test for comparison between pre-treatment mean values of 2min walk test distance of group A and B.

	2min walk test distance (meter) X ± SD (SE)	MD	*t*-value	*p*-value	Sig.
Group A	115.44±29.24 (5.33)	1.66	0.15	0.87	NS
Group B	113.78±28.84 (9.12)				

X : Mean. *t*-value : Unpaired *t*-value.
SD : Standard Deviation. *p*-value : Probability value.
SE : Standard Error. NS : Non Significant.
MD : Mean Difference.

Table (5): *t*-test for comparison between post-treatment mean values of 2min walk test distance of group A and B.

	2min walk test distance (meter) X ± SD (SE)	MD	*t*-value	*p*-value	Sig.
Group A	135.41±23.7 (4.32)	39.25	3.05	0.01	S
Group B	96.16±38.2 (12.08)				

X : Mean. *t*-value : Unpaired *t*-value.
SD : Standard Deviation. *p*-value : Probability value.
SE : Standard Error. S : Significant.
MD : Mean Difference.

Discussion

The result of this study were supported by Pfalzer et al., 2008 **[15]**, who studied the effect of A 10-week inspiratory muscle training program using IMT device on lower-extremity mobility in people with Multiple Sclerosis (MS) which found significantly increase in inspiratory muscle strength, timed static standing balance scores, and a trend toward increase in distance walked on the 6MW test in ambulatory individuals with mild-to-moderate MS.

Physical and functional effects of cancer and its treatments include diminished cardiovascular function, reduced pulmonary function, decreased strength, deterioration of lean body tissue, weight change, difficulty sleeping, fatigue, nausea and vomiting, and pain **[16]**.

Moreover, this study was supported by Stephanie et al., 2018 **[17]**, who showed that high-intensity IMT was set at 80% of maximal effort which resulted in increased Maximum Inspiratory Pressure [MIP] and Sustained Maximum Inspiratory Pressure [SMIP], lung volumes, work capacity, and power output in individuals who were healthy, whereas IMT at 60% of maximal effort increased work capacity and power output only. Inspiratory muscle training intensities lower than 40% of maximal effort did not translate into quantitative functional outcomes.

Mello et al., 2012 **[18]**, stated that a simple, inexpensive, home-based in IMT program resulted in clinically relevant increments of maximal functional capacity, associated with a reduction in Muscle Sympathetic Nerve Activity (MSNA) and improvement in the quality of life. Moreover, our results show that respiratory muscle training improves exercise intolerance, neurovascular control, and cardiac sympathetic and parasympathetic regulation in patients with Chronic Heart Failure (CHF).

Conversely, Valkenet et al., 2016 **[19]**, study showed that pre-operative inspiratory muscle training decreased incidence of pneumonia and length of hospital stay in trial group but did not find any improvements in functional capacity due to the preoperative home-based inspiratory muscle training program.

Foden et al., 2010 **[20]**, study showed that in the IMT group, both MIP and maximum expiratory pressure (17% and 23%, respectively; p (0.03) were improved. Similar improvements were noted for the sham-IMT group with 23% and 33% from baseline for MIP and maximum expiratory pressure, respectively p (0.03). There were no significant changes in pulmonary function at rest and any of the performance parameters associated with the repetitive sprint test (sprint and recovery times, peak heart rate and peak blood lactate concentration). Reported experiences of using the IMT train-

ing device suggested "less breathlessness" and "less tightness in the chest during the training". Which concluded that although there was no improvement in sprint performance, an improved respiratory muscle function and quality of life were reported by participants in both the IMT and sham-IMT groups.

Finally it can be concluded that the improvement in ventilatory functions and functional capacity in patients on chemotherapy due to IMT in group A by increasing inspiratory muscle strength which overcome fatigue and cachexia (form of the side effects of chemotherapy).

Conclusion:

According to the results, it can be concluded that there is a significant effect on functional capacity which appear in 2min walk test distance results and significant increase in ventilatory function (FVC and FEV1) which overcome the chemotherapy and cancer related fatigue. Although there was no significant changes in FEV1/FVC ratio.

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فاعلية تدريب عضلات الشهيق وتأثيرها على القدرة الوظيفية لمرضى العلاج الكيميائى

يعد السرطان من المشكلات الصحية العامة التى تشكل عبئاً أقتصادياً على المريض والحكومة. تتزايد الإصابة بأنواع مختلفة من الأورام.

الهدف من الدراسة هو التحقيق من تأثير تدريب عضلات الشهيق على القدرة الوظيفية للمرضى الذين يتلقون العلاج الكيميائى.

\الطريقة: تشمل التجربة أربعون مريضاً من الذكور يتلقون العلاج الكيميائى جرعة واحدة على الأقل ومتوسط أعمارهم ٣٧.١±٤.٨٩ سنة. تم أختيار المرضى من المعهد القومى للسرطان، القاهرة (المرضى الداخلى). أستمرت الدراسة من مارس ٢٠١٨ إلى يونيو ٢٠١٨. تم توزيع المرضى عشوائياً إلى مجموعتين المجموعة (أ) (٣٠ مريضاً) التى تلقت تدريب عضلات الشهيق لمدة ٤ أسابيع متتالية، ٥جلسات/الأسبوع، والمجموعة (ب) (١٠ مرضى) كمجموعة ضابطة يتلقون العلاج الكيميائى فقط. تم تحليل البيانات التى تم الحصول عليها من كلا المجموعتين فيما يتعلق بالقدرة الحيوية القسرية (FVC)، وحجم الزفير القسرى فى ثانية واحدة (FEV1) ونسبة FEV1/FVC وأختبار ٢ دقيقة سيراً على الأقدام ومقارنة النتائج إحصائياً.

\النتائج: بعد ٤ أسابيع من التدريب لكلتا المجموعتين أظهرت النتائج أن FVC لمجموعة الدراسة زيادة كبيرة بنسبة ٣٣.٤٤٪ بينما فى المجموعة الضابطة إنخفاض كبير بنسبة ٣٧.٣٪ زاد FEV1 بنسبة ٣٤.٥٢٪ فى مجموعة الدراسة فى حين إنخفض بنسبة ٣٤.٠٩٪ فى المجموعة الضابطة ومع ذلك، فقد تبين أنه لا يوجد فرق كبير فى نسبة FEV1/FVC. كما أظهرت النتائج المتعلقة بمسافة أختبار المشى ٢ دقيقة زيادة بنسبة ١٧.٢٩٪ فى المجموعة (أ) بينما أنخفضت بنسبة ١٥.٤٨٪ فى المجموعة (ب).

\الملخص: يمكن الأستنتاج أن تدريب عضلات الشهيق من الممكن أن يرفق ببرنامج إعادة التأهيل للمرضىالذين يتلقونالعلاج الكيميائى بهدف تعزيز قدراتهم الوظيفية.