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Influence of High Frequency Chest Wall Oscillation in Hospitalized Patients with COVID-19

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ABSTRACT

Background: Coronavirus disease (COVID-19) has clinical presentation that can vary with respiratory symptoms being most common such as cough, shortness of breath, and fever. Severe disease complications due to excessive pulmonary secretions as pneumonia and acute respiratory can be fatal.

Aim and objectives: To investigate the effect of high frequency chest wall oscillation (HFCWO) in hospitalized covid-19 patients on: Inflammatory markers [Neutrophil to lymphocyte ratio (NLR) and C-reactive protein (CRP)], respiratory rate (RR), arterial oxygen pressure (PaO_2), heart rate (HR), dyspnea, and hospital stay period.

Patients and methods: This randomized controlled study was conducted on seventy hospitalized Covid-19 patients at intensive care units (ICU) who were divided into two groups equally in numbers. Over two weeks, the study group received HFCWO in addition to active cycle of breathing technique (ACBT) while the control group received ACBT only.

Results: There was no significant difference concerning all measured outcomes between both groups pre-intervention. By the end of the study, there was a significant increase in PaO2 of study group compared with that of control group (p= 0.01) while CRP and NLR showed significant decrease in the study group compared with that of control one (p= 0.002, p= 0.001 respectively). Also, a significant decrease in HR, RR, and hospital stays of study group compared with that of control group was noticed (p= 0.001, p= 0.001, and p= 0.002 respectively).

Conclusion: Adding HFCWO to the traditional chest physical therapy protocol play an important role in reducing and preventing respiratory complications in COVID-19 patients.

Key words: Chest wall oscillation, COVID-19, C-Reactive Protein, Heart Rate, Length of stay

INTRODUCTION

Novel coronavirus disease 2019 (COVID-19) infections, declared by the World Health Organization (WHO) as a pandemic, had unprecedented global effects on people's daily activities and way of life **(1)**.

The clinical symptoms range from asymptomatic to severe respiratory involvement, which can lead to respiratory failure and potentially fatal pulmonary or extrapulmonary complications **(2).**

Airway mucus is an adhesive viscoelastic gel composed mostly of high molecular weight mucous glycoproteins and water, which is important in maintaining lung function and health, pathological mucus hypersecretion as in COVID-19 may cause airway obstruction and lead to respiratory distress **(3)**.

Cough is a natural defense mechanism that protects the respiratory tract from inhaling foreign bodies and by clearing excessive bronchial secretions. In COVID-19 patient, cough efficacy is impaired resulting in hypoxemia, high respiratory and heart rates**(4).**

Resting RR values also contribute to the prognosis of COVID-19 patients as ICU admission and mortality are associated with significantly higher RR values compared to non-ICU patients and survivors **(5,6)**.

Respiratory physiotherapy is considered as one of the therapeutic options for symptom alleviation in various respiratory viral infections. Active cycle of breathing techniques (ACBT) is accomplished by patients independently can also help the clearance of pulmonary secretions, improvement of lung function, and amelioration of effective cough in these patients. Three components defined for this technique are:1) breathing control, 2) deep breathing or thoracic expansion exercises, and 3) forced expiratory techniques like huff and cough **(7).**

Studies support the benefits of chest physiotherapy devices either alone or combined with other interventions, which enhance the total lung capacity, SpO2, respiratory rate, might help to alleviate the frequency and severity of pulmonary complications, and thereby reducing the risk of recurrence following COVID-19 **(8,9).**

Compared to conventional chest percussion and postural drainage methods, HFCWO is a pulmonary rehabilitation method used for the recovery of pulmonary functions and removal of secretions in the lungs. It acts on all lobes of the lungs simultaneously, independent of the patient's position. **(10).**

This leads to the question as to whether a preferred use of noninvasive respiratory therapy device in addition to the traditional chest physical therapy can improve outcome in COVID-19 patients. Based on these considerations, we aimed to investigate the effect of HFCWO in hospitalized covid-19 patients on: Inflammatory markers [NLR and CRP], RR, HR, and PaO2 and hospital stay period.

PATIENTS AND METHODS

This was a randomized controlled study conducted on seventy hospitalized Covid-19 patients at ICU in Ain Shams University Hospital.

Patients were divided into two groups: Control Group: consisted of 35 patients who received ACBT plus their traditional medications and **Study Group:** consisted of 35 patients who received HFCWO device, ACBT, and their traditional medications.

Sample size

Sample size calculation was performed using G*POWER statistical software (version 3.1.9.2) for comparative study between two groups. Based on previous research of **Çelik et al., (11)** who found a significant effect of HFCWO in patients with COVID-19 on SpO2 difference compared with conventional chest physiotherapy. The calculation revealed that the

required sample size for this study was 28 subjects per group. Calculations were made using α=0.05, power 80% and effect size = 0.77 and allocation ratio N2/N1 =1.

Eligibility criteria

Inclusion criteria: Seventy hospitalized covid-19 patients from both gender their ages ranged from 55 – 65 years old, covid-19 patients with lung fibrosis (diagnosed by the physician and confirmed by chest CT), duration of illness ranged from 1-2 weeks, all patients had resting oxygen saturation (SpO_2) from 80 – 92 % and O2 therapy delivered via Nasal cannula or face mask.

Exclusion criteria: Patients with the following conditions were excluded from the study: Hemodynamically unstable, pneumothorax (if chest tube is present), asthmatic, chest deformities, pleural effusion, diaphragmatic hernia. Cardiac / thoracic surgery mechanically ventilated and intubated, metabolic or cardiovascular diseases, (SaO2) less than 80 % and severe lung fibrosis also excluded.

Ethical consideration

The study was approved by the Ethics Committee of Faculty of Physical Therapy, Cairo University/Egypt No: **P.T.REC/012/003890** and registered under the number ID: **NCT05705661** in the Clinical Trials. gov. There were adequate provisions to maintain privacy of participants and confidentiality of the data are as follows: The patients were given the option of not participating in the study if they did not want to. We put code number to each participate with the name and address kept in a special file. The patient's name was hidden from the data assessor. The results were used only in a scientific manner and wasn't used in any other aims.

Measurements

The following parameters were assessed at baseline and at the end of the intervention, after gathering basic information (sex, age, SpO_2) and all participants were screened to ensure that they met the inclusion criteria.

Primary outcome

PaO_2

Arterial blood gases (ABG), arterial blood sample was taken by the nurse to measure PaO_2. At baseline and at the final training session, the same research member took measurements for both groups.

Secondary outcomes

Complete blood count

Blood sample was drawn to assess NLR, CRP

HR and RR

They were assessed by beside bed monitor.

Hospital stays period

It was obtained from the patient's medical record file.

Treatment Procedure

The control group: They performed ACBT (include: breathing control, deep breathing exercises, huffing) and manual percussion. **Breathing control (relaxed breathing):** The initial stage of ACBT focuses on breathlessness recovery and improving breathing quality. The patient should be in a comfortable position, with relaxed shoulders and arms, and breathe in and out through their nose and mouth, avoiding shoulder rise. Maintain relaxed breathing for one to two minutes. **Thoracic expansion exercises (deep breathing):** The second stage of ACBT aims to improve air entry to the lungs and loosen stuck secretions. Patients are

instructed to take long, slow breaths, hold them for up to five seconds, and breathe out comfortably.

Forced expiratory technique (Huff): The third stage involves moving secretions from smaller airways to easier-to-cough and clear areas. This stage requires practice and should be checked by a respiratory physiotherapist. Patients should take a slow breath, open their mouth, and huff the air out, aiming to push the secretions upwards. Huffing should be gentle and not too hard to avoid wheezing. Crackles on the breath out should be heard, and the number of huffs should be limited to reduce wheezing. The session duration was between 30 min twice/day for 15 days as guided by the patient fatigue and comfort. (According to Borg scale of dyspnea for monitoring). **Manual Techniques (percussion):** These are techniques that involve applying certain forces to the patient's chest using the hands which is a rhythmic succession of rapid and light strokes performed with cupped hands on the patient's chest wall. The technique was applied to the specific segment to be treated while the patient breathes at a tidal volume (therefore both during inspiration and during exhalation). Percussion strength was based on patient feedback (it must not create discomfort). The used frequency was between 4.6 and 8.5 Hz.

The study group: They received the same ACBT in addition to HFCWO; the patient was in a semi-recline position, with wrapped vest around the chest. The HFCWO protocol included 3–5 cycles, with a pressure range of +10 to +40 IP cmH2O and was adjusted according to the patient age, amount of secretions, tolerance of patients, and chest auscultation every session. The numbers of total sets were 3-5 with a duration of 15 min, daily, for two sessions/ day, time range according to the ability of the patient **(11).**

Data Analysis

Statistical analysis was performed through the statistical package for social studies (SPSS) version 25 for windows.

- Unpaired t test was conducted for comparison of age and hospital stay between groups while Chi-squared test was conducted for comparison of sex distribution between groups.
- Mixed MANOVA was conducted to compare the effect of time (pre versus post) and the effect of treatment (between groups), as well as the interaction between time and treatment on mean values of PaO_2, HR, RR, NLR and CRP. Post-hoc tests using the Bonferroni correction were carried out for subsequent multiple comparison.
- The level of significance for all statistical tests was set at $p < 0.05$.

RESULTS

There were no statistically significant differences between groups in participants' baseline (Table 1)

Table (1): Comparison of age between control and study groups.

	Control group	**Study group**	**MD**	**t-value**	**p-value**	**Sig**
	$\overline{X}$ **±SD**	$\overline{X}$ **±SD**				
Age (years)	60.74 ± 4.84	61.23 ± 4.48	-0.49	-0.43	0.66	**NS**
Sex						
Female	15 (43%)	13 (37%)	-	-	0.62	**NS**
Male	20 (57%)	22 (63%)	-	-		

X: mean, t value: Unpaired t value, SD: Standard deviation, p value: Probability value, MD: mean difference, NS: Non-significant.

There was no significant difference in PaO_2 between control and study groups pretreatment ($p = 0.53$). There was a significant increase in PaO_2 of study group compared with that of control group post treatment ($p = 0.01$). (Table 2)

Table (2): Mean PaO_2 pre and post treatment of control and study groups.

PaO2 (mmHg)	Pre treatment	Post treatment	MD	% of change	p-value	Sig
	$\overline{X}$ ±SD	$\overline{X}$ ±SD				
Control group	78.85 ± 5.48	84.62 ± 6.76	-5.77	7.32	0.001	S
Study group	77.94 ± 6.78	88.11 ± 5.31	-10.17	13.05	0.001	S
MD	0.91	-3.49				
p-value	0.53	0.01				
Sig	**NS**	**S**				

X: mean, t value: Unpaired t value, SD: Standard deviation, p value: Probability value, MD: mean difference, NS: Non-significant.

There was no significant difference in RR between control and study groups pretreatment (p = 0.81). There was a significant decrease in RR of study group compared with that of control group post treatment (p = 0.001). (Table 3)

Table (3): Mean RR pre and post treatment of control and study groups.

RR (breath/min)	Pre treatment	Post treatment	MD	% of change	p-value	Sig
	$\overline{X}$ ±SD	$\overline{X}$ ±SD				
Control group	24.68 ± 2.52	22.42 ± 3.10	2.26	9.16	0.01	S
Study group	24.83 ± 2.34	17.80 ± 3.92	7.03	28.31	0.001	S
MD	-0.15	4.62				
p-value	0.81	0.001				
Sig	**NS**	**S**				

X: mean, t value: Unpaired t value, SD: Standard deviation, p value: Probability value, MD: mean difference, NS: Non-significant.

There was no significant difference in neutrophils/lymphocytes ratio between control and study groups pretreatment (p= 0.52), but there was a significant decrease in neutrophils/lymphocytes ratio of study group compared with that of control group post treatment (p = 0.001). (Table 4)

Table (4): Mean NLR pre and post treatment of control and study groups.

Neutrophils/lymphocytes ratio (NLR)	Pre treatment	Post treatment	MD	% of change	p-value	Sig
	$\overline{X}$ ±SD	$\overline{X}$ ±SD				
Control group	13.77 ± 3.24	9.75 ± 3.85	4.02	29.19	0.001	**S**
Study group	14.48 ± 5.56	7.61 ± 3.24	6.87	47.44	0.001	**S**
MD	-0.71	2.14				
p-value	0.52	0.001				
Sig	**NS**	**S**				

X: mean, t value: Unpaired t value, SD: Standard deviation, p value: Probability value, MD: mean difference, NS: Non-significant.

There was no significant difference in CRP between control and study groups pretreatment (p = 0.62). There was a significant decrease in CRP of study group compared with that of control group post treatment (p = 0.002). (Table 5)

Table (5): Mean CRP pre and post treatment of control and study groups.

C- Reactive Protein CRP (mg/dl)	Pre treatment	Post treatment	MD	% of change	p-value	Sig
	$\overline{X}$ ±SD	$\overline{X}$ ±SD				
Control group	100.76 ± 38.67	51.54 ± 11.64	49.22	48.85	0.001	S
Study group	105.56 ± 42.22	43.47 ± 9.72	62.09	58.82	0.001	S
MD	-4.8	8.07				

p-value	0.62	0.002	
Sig	**NS**	**S**	

X: mean, t value: Unpaired t value, SD: Standard deviation, p value: Probability value, MD: mean difference, NS: Non-significant.

There was a significant decrease in hospital stay of study group compared with that of control groups (p = 0.002). (Table 6)

Table (6): Comparison of hospital stay between control and study groups.

	Control group	**Study group**	**MD**	**t-value**	**p-value**	**Sig**
	$\overline{X}$ **±SD**	$\overline{X}$ **±SD**				
Hospital stay (days)	11.68 ± 2.55	9.91 ± 2.0	1.77	3.19	0.002	**S**

X: mean, t value: Unpaired t value, SD: Standard deviation, p value: Probability value, MD: mean difference, NS: Non-significant.

DISCUSSION

The purpose of the present study was to investigate the effect of HFCWO in hospitalized covid-19 patients on inflammatory markers (NLR, and CRP), HR, RR and PaO2 saturation, and hospital stay period.

The symptoms of SARS-CoV-2 infection can be nonspecific. The most common clinical manifestations include pyrexia (88.7%), cough (67.8%), fatigue/tiredness (38.1%), sputum production (33.4%), dyspnea (18.6%), sore throat (13.9%), and headache (13.6%). Especially, some patients were afebrile or confirmed to have an asymptomatic infection (12).

In this study, all variables including age, sex distribution and baseline characters were matched in all patients of both groups, and all other factors may affect the treatment (e.g., asthamatic patients, patient with chest deformities, pleural effusion, diaphragmatic hernia, cardiac and thoracic surgery, mechanically ventilated and intubated patients, metabolic or cardiovascular diseases, and patients have (SpO_2) less than 80 %) were excluded from the study.

Concerning effect of treatment on PaO_2: there was a significant increase in PaO_2 in the control group by 7.32% and study group by 13.05% post treatment compared with pretreatment. However, there was a significant increase in PaO_2 in the study group compared with that of the control group post treatment (p = 0.01).

In agreement with our results, **Cheng et al.,** performed a prospective cohort study on a total of sixty-five patients with severe acute exacerbations of COPD. Patients were categorized into two groups: HFCWO intervention was given to group A and expiration with the glottis open in the lateral posture (ELTGOL) was performed to patients in group B. After treatment, HFCWO group had significantly higher PaO_2 than ELTGOL group. The differences were statistically significant (P < 0.05) **(13)**.

Concerning effect of treatment on SaO2: In the present study, there was a significant increase in SaO2 in the control group 3.47% and study group 8.39% post treatment compared with pretreatment. Additionally, there was a significant increase in SaO2 in the study group compared with that of control group post treatment (p = 0.01).

Regarding the RR, there was a significant decrease in RR in the control group by 9.16% and in the study group by 28.31% post treatment compared with pretreatment. Additionally, there

was a significant decrease in RR of study group compared with that in the control group post treatment (p = 0.001).

In agreement with our results, **Usenko and Aryayev** found that there was a significant decrease in RR of main group (received basic therapy in combination with HFCWO procedures) and control group (received basic therapy exclusively) post treatment compared with pretreatment. Additionally, there was a significant decrease in post treatment RR of main group compared with that of control group **(14)**.

About CRP: there was a significant decrease in CRP in the control group by 48.85% and study group by 58.82% post treatment compared with pretreatment. Also, there was a significant decrease in CRP in the study group compared with that of control group post treatment (p = 0.001).

Our findings agreed with **Cheng et al.,** who found that CRP significantly lower in HFCWO group who received oxygen therapy, respiratory support, relieving cough and asthma, anti-infection, or nutritional support in addition to HFCWO than in ELTGOL group who received oxygen therapy, respiratory support, relieving cough and asthma, anti-infection, or nutritional support after treatment (P < 0:05) **(13)**.

Additionally, **Sari et al.,** found that a decrease was found in the CRP value at days 2 and 3 with the difference being more prominent in the VEST™ group than ACPRC group **(15)**.

Concerning effect of treatment on NLR: In our study, there was a significant decrease in NLR in the control group by 29.19% and study group by 47.44% post treatment compared with pretreatment. Additionally, there was a significant decrease in NLR in the study group compared with that of control group post treatment (p = 0.001).

Supporting our results, **Okan,** carried out retrospective study on 23 patients with coronary artery disease and 28 patients with pulmonary disease before cardiopulmonary rehabilitation program, to evaluate a possible association between NLR levels and exercise capacity in individuals planned to be enrolled in cardiopulmonary rehabilitation program. They found that NLR could be used as a predictor to evaluate the exercise capacity in patients enrolled in cardiopulmonary rehabilitation programs **(16)**.

About the hospital stay days: there was a significant decrease in hospital stay days in the study group compared with that of the control group (p = 0.002).

In agreement with our results, **Cheng et al.,** found that the length of stay (LOS) of patients in group A who received oxygen therapy, respiratory support, relieving cough and asthma, anti-infection, or nutritional support in addition to HFCWO were significantly shorter than those of group B who received oxygen therapy, respiratory support, relieving cough and asthma, anti-infection, or nutritional support (P < 0:05) **(13)**.

Similarly, **Javanbakht et al.,** carried out prospective, randomized, controlled trial to assess the effect of Vest™ HFCWO system compared with manual chest wall physiotherapy for managing airway clearance in patients with complex neurological disorders. They demonstrated that the Vest™ system has the potential to reduce the respiratory-related hospitalizations, which is in the line with our results **(17)**.

In patients with COVID-19, pulmonary rehabilitation is believed to be effective in managing dyspnea, cough, respiratory failure, and gas exchange abnormalities during the acute illness period. In the chronic period, it is believed to be effective against fatigue, chronic respiratory symptoms, nutritional deficiency, difficulties in daily life activities due to decrease in functional status, decrease in work performance, deterioration in quality of life, and psychosocial problems **(18)**.

LIMITATIONS

Despite the improvement of the measured outcomes, there are some limitations that must be mentioned as: Relatively small sample size, lack of generally accepted physiotherapy

protocols for ICU patients in critical conditions and finally there is no Evaluation for the long term effect of HFCWO on pulmonary function and other post COVID19 persistent symptoms.

CONCLUSION

Both respiratory physiotherapy ACBT technique and HFCWO played an important role in reducing and preventing respiratory complications in COVID-19 patients. However, HFCWO in addition to traditional respiratory techniques were better than traditional respiratory techniques only in the improvement of the measured outcomes PaO_2, CRP, NLR, HR, RR and the hospital stay days.

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