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The Effect of Early Mobilization on Respiratory Parameters of Mechanically Ventilated Patients With Respiratory Failure

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The effect of early mobilization on hemodynamic parameters of patients under mechanical ventilation has been associated with positive results and yet its effect on specific respiratory parameters is less well appreciated. This article reports the results of a study of a randomized clinical trial of intensive care unit patients receiving mechanical ventilation. The findings of this study confirmed that a 4-step protocol for early mobilization can improve PaO_2, O_2 saturation, PaO_2/FIO_2 (fraction of inspired oxygen) ratio, and pulmonary compliance. The value of interdisciplinary collaboration supporting early mobilization was confirmed. **Key words:** *early mobilization*, *mechanical ventilation*, *respiratory failure*, *respiratory parameters*

RESPIRATORY FAILURE is caused by a wide range of diseases. In this disease, the lungs lose their ability to exchange gases, which leads to serious disorders in arterial blood gases and the respiratory status of patients.[1] Patients in the acute stage of respiratory failure are forced to rest in bed and if the duration of complete bed rest is prolonged, it will have many side effects for patients, including muscle fatigue and atrophy, numbness of the limbs, and mental disorders such as depression, anxiety, and delirium following long-term use of ventilation.[2,3] These complications may accompany patients for months or years after their discharge from the hospital and are known as the intensive care syndrome. This syndrome can affect the quality of life, the rate of return to work, the probability of readmission, and the cost of treatment for patients.[4] According to available statistics, 84% to 95% of patients discharged from the intensive care unit (ICU) suffer from neuromuscular disorders for an average of more than 5 years.[5]

Immobility of patients under mechanical ventilation also has negative effects on the strength of respiratory muscles because mechanical ventilation reduces the patient's spontaneous respiratory effort.[6] There are few studies conducted on methods of

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muscle weakness prevention among patients in ICUs.[7] However, early mobilization in the ICU can play an important role in preventing the known adverse effects of immobility, which include atrophy and muscle weakness, and it can change muscle function as well.[8,9] Recent studies show that for every day of complete bed rest, 3% to 11% decrease in muscle strength occurs.[10] In general, early mobilization is made by 2 words of "early," which means the first time patient's physiological condition stabilizes, which usually takes about 2 to 5 days after admission, and the word "mobilization," which refers to performing physical movements with appropriate intensity, which causes a significant improvement in respiratory system, blood circulation, nervous system, and even the patient's state of consciousness.[11,12]

Early mobilization in the ICU is determined by factors such as the patient's physical strength and functional ability, the patient's cooperation, patient-connected equipment (endotracheal tube, venous catheters, etc), and the patient's mobilization culture.[13] Despite the importance of early mobilization, different effects of early mobilization on the patient's respiratory outcomes have been reported in the literature.[14-16] Impaired patient consciousness, electrolyte disturbances, and unstable hemodynamics are factors that limit the ability of mechanically ventilated patients to mobilize.[17] The aim of this study was to determine the effect of early mobilization on respiratory parameters of mechanically ventilated patients with respiratory failure.

METHODS

Study design and research setting

This study utilized a randomized clinical trial to evaluate the effects of early mobilization on respiratory parameters of mechanically ventilated patients within a 10-bed thoracic unit. Diagnoses included pneumonia, chronic airway obstruction, asthma, and lung mass. The annual admission of study unit is approximately 250 patients.

Sample

The study population included all patients with respiratory failure under mechanical ventilation who were admitted to the thoracic ICU. Patients who met the inclusion criteria were included in the study. Inclusion criteria for the patients were as follows: being intubated for at least 48 hours and using mechanical ventilation, being older than 18 years and younger than 65 years, having Richmond Agitation and Sedation Scale (RASS) score of more than −3 and less than 2, having stable hemodynamic conditions with the minimum dose of supportive drugs, and having positive end-expiratory pressure (PEEP) less than 8, fraction of inspired oxygen (FIO_2) less than 60%, SpO_2 less than 89%, and respiratory rate of more than 12 and less than 30 per minute. Also, patients with any mobilization disorder before admission, cognitive impairment and psychosis, neuromuscular disorders, acute stroke, body mass index of above 40, femoral or spinal fracture, and undergoing cardiopulmonary resuscitation did not enter the study. Any disturbance in hemodynamic conditions in the form of unstable conditions and death, being discharged, and being weaned off the ventilator were among exclusion criteria. The sample size of this study was calculated to be 60 (30 patients in each group) using GPower software. To select the samples, convenience sampling was used as the primary method. Then, patients were divided into the control and intervention groups by random allocation in blocks of 4. In this study, the online randomization service (https://www.sealedenvelope.com/simple-randomiser/v1/lists) was used for random allocation (Figure).

Tools and measurements

Data collection tools in this study consisted of 2 questionnaires. The first questionnaire was used to collect demographic and clinical information including age, sex, marital status, level of education, occupation, weight, cause of hospitalization, history of hospitalization, underlying diseases, history

of drugs/sedatives received, ventilator mode, and risk factors. The second questionnaire was used to collect information on respiratory parameters including arterial blood gas levels (PaO_2, $PaCO_2$, O_2 saturation [O_2 sat]), PaO_2/FIO_2 ratio, PEEP values, FIO_2 level, lung compliance, respiratory rate, duration of mechanical ventilation, and length of hospital stay in the ICU. The RASS and the Muscle Resistance Capacity (MRC) tool of the Medical Research Committee were also used in this study.

The RASS determines the agitation/sedation level of patients admitted to the ICU. The score on this scale varies from +4 to −5. On this scale, a score of zero means that the patient is alert, a score of +1 expresses that the patient is in a state of restlessness, a score of +2 means the patient is agitated, a score of +3 means the patient is very agitated, and a score of +4 means that the patient is aggressive. Also, score of −1 means that the patient is sleepy, −2 lightly sedated, −3 moderately sedated, −4 deeply sedated, and −5 means that the patient is nonresponsive.[18]

The MRC tool is a simple tool, with a score range of 1 to 5. In this scale, a score of zero is given when there is no movement in the limbs. A score of 1 refers to slight movement in the limbs and sometimes muscle tremor. A score of 2 is given when there is movement in the limb without resistance and gravity. A score of 3 is given when there is limb movement against the force of gravity. A score of 4 is given to the patient when there is muscular strength against gravity and resistance, and finally a score of 5 is given when there is normal muscle strength against full resistance.[19] This scale was used in this study to determine the patient entry to levels 3 and 4 of limb movement in the early mobilization protocol.

Intervention

The intervention designed for this study was a standard 4-level protocol.[20] In the first level, limited joint movement exercise was performed on unconscious patients 5 times for each joint. At the second level, the physiotherapy protocol was started, by which the patient had to answer 3 of the commands until the researcher knew he or she was ready to enter the next stage. The commands included the following: open your eyes, look at me, open your mouth and stick out your tongue, bring your head up and down, and raise your eyebrows when you hear the number 5. If the patient responded to 3 of the researcher's 5 commands, his or her condition was appropriate for initiating physiotherapy. When the patient gained sufficient strength and alertness to participate in occupational therapy, he or she was directed to either active supporter approach or active limited joint movement approach and moved from level 2 to level 4. Measures performed at this level included changing the position every 2 hours, inactive movement of the joint range 3 times a day, and being placed in a full sitting position at least 2 times for 20 minutes. All measures in the second level were also performed in levels 3 and 4. Upgrading from level 2 to level 3 and from level 3 to level 4 depended on the patient's score on the MRC tool in terms of muscle strength in one attempt. A score of 3 out of 5 for biceps was required to enter level 3, and a score of 3 out of 5 for quadriceps was required to enter the level 4. As the patient progressed, the activities focused on a variety of functions such as sitting on the edge of the bed, getting out of bed, balance activity in a sitting position, and prewalking exercises such as weight transfer on the legs, walking in a same spot, and moving. The early mobilization protocol is presented in the Figure. The protocol was implemented in an interdisciplinary and team manner with the cooperation of team members including the researcher, a physiotherapist, an ICU physician, and a nurse. In this study, the control group received routine ICU care, which was to change patient position once or twice in each shift.

Ethical considerations

The present study was approved in May 2016. All participants or their legal guardian

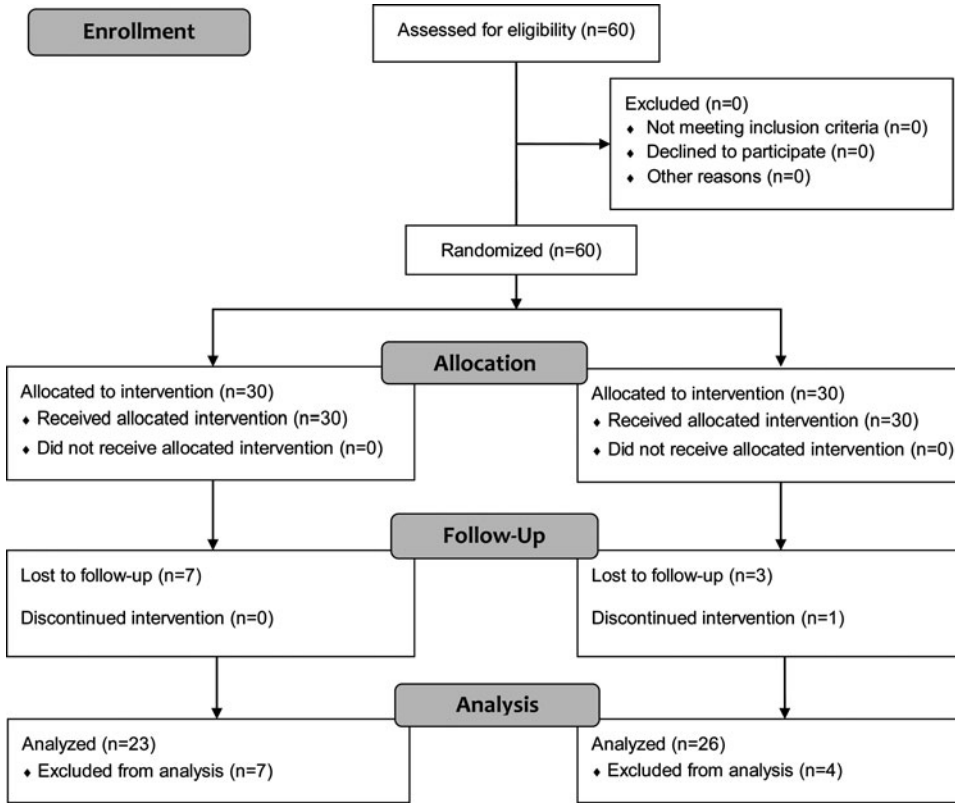

Figure. CONSORT 2010 flow diagram.

gave informed consent for the research, and their anonymity was preserved. Ethics approval was obtained on April 28, 2020, from the Ethics Committee of Tehran University of Medical Sciences with code: IRB.1399.007. Also, this research has been registered in the Clinical Trial Study Registration Center with code IRCT20161124031068N4.

Data analysis

In this study, continuous variables were expressed as mean (standard deviation [SD]) and categorical variables as frequency (percentage). Demographic characteristics between the control and treatment groups were compared using *t* tests for continuous variables and the chi-square test for categorical variables. Analysis of covariance (ANCOVA) was used to compare the groups after controlling for pretest scores. In addition, repeated-measures analysis of variance (ANOVA) was used to examine trend over time for study variables. Because of non-normality of the duration of mechanical ventilation and the duration of hospitalization in the ICU, the Mann-Whitney test was used to compare the control and treatment groups. Furthermore, effect sizes were reported in partial eta squared (η^2_p) for ANCOVA and *r* for the Mann-Whitney test. η^2_p values of 0.01, 0.06, and 0.14 were considered as low, moderate, and high effect sizes, respectively. For *r*, values of 0.1, 0.3, and 0.5 were considered as low, moderate, and high effect sizes, respectively. Data analysis was undertaken using SPSS for Windows, version 16.0 (SPSS Inc, Chicago, Illinois), and error bar graphs were depicted using GraphPad Prism, version 8.0.1 (GraphPad Prism Software Inc, San Diego, California). For all analyses, a value of $P < .05$ was considered statistically significant.

RESULTS

Findings of this study showed no significant difference between the 2 groups in terms of demographic and clinical variables (age, sex, underlying disease, cause of hospitalization, weight, history of hospitalization in the ICU, smoking, and alcohol consumption) (Table 1).

Comparison of respiratory parameters by group: Primary outcomes

According to the repeated-measures ANOVA, throughout the 3-day intervention,

Table 1. Comparison of Demographic and Clinical Characteristics of the Control and Treatment Groups[a]

	Control	Intervention	*P*
Age, mean (SD), y	54.83 (10.89)	53.92 (13.09)	.903
Sex			.851
Male	13 (56.5)	14 (53.8)	
Female	10 (43.5)	12 (46.2)	
Marital status			
Single	2 (8.7)	4 (15.4)	
Married	21 (91.3)	22 (84.6)	
Education			.262
Illiterate/primary	7 (30.4)	6 (23.1)	
Secondary/diploma	9 (39.1)	16 (61.5)	
University	7 (30.4)	4 (15.4)	
Occupation			.798
Employed	11 (47.8)	10 (38.5)	
Retired	4 (17.4)	5 (19.2)	
Housewife/unemployed	8 (34.8)	11 (42.3)	
Weight, mean (SD), kg	78.70 (10.21)	77.38 (11.76)	.681
Cause of hospitalization			.000
Pneumonia	13 (56.5)	15 (57.7)	
Altered LOC	0 (0)	1 (3.8)	
PE	2 (8.7)	3 (11.5)	
Asthma	2 (8.7)	1 (3.8)	
COPD	1 (4.3)	0 (0)	
PTE	4 (17.4)	3 (11.5)	
RF	1 (4.3)	3 (11.5)	
Underlying disease			
No	4 (17.4)	8 (30.8)	
Yes	19 (82.6)	18 (69.2)	
Smoking			.850
No	19 (82.6)	22 (84.6)	
Yes	4 (17.4)	4 (15.4)	
Alcohol consumption			.342
No	0 (0)	1 (3.8)	
Yes	23 (100)	25 (96.2)	
History of hospitalization			.026
No	17 (73.9)	25 (96.2)	
Yes	6 (26.1)	1 (3.8)	

Abbreviations: COPD, chronic obstructive pulmonary disease; LOC, level of consciousness; PE, pulmonary edema; PTE, pulmonary thromboembolism; RF, respiratory failure.

[a]Values are presented as n (%).

subjects in both groups showed a significant increase in Pa_{O_2}, O_2 sat, and compliance (all *P*s < .001) and a significant decline in Pa_{CO_2} and F_{IO_2} (all *P*s < .001).

The trend was decreasing for both PEEP and Pa_{O_2}/F_{IO_2} ratio in the treatment group during the 3-day intervention ($P < .001$ and $P < .001$, respectively), whereas in the control group, there was no significant reduction in PEEP and F_{IO_2} ($P = .211$ and $P = .078$, respectively).

Results of the ANCOVA showed a significantly higher Pa_{O_2} for the treatment group ($M = 67.73$, SE = 0.69) than for the control group ($M = 64.40$, SE = 0.74) at the posttest assessment ($F_{1,56} = 10.81$, $P = .002$, $\eta^2_p = 0.190$). The same results were found for O_2 sat ($F_{1,46} = 10.63$, $P = .002$, $\eta^2_p = 0.188$), Pa_{O_2}/F_{IO_2} ratio ($F_{1,46} = 6.74$, $P = .013$, $\eta^2_p = .128$), RR ($F_{1,46} = 10.70$, $P = .002$, $\eta^2_p = 0.189$), and compliance ($F_{1,46} = 14.46$, $P < .001$, $\eta^2_p = 0.239$). Both F_{IO_2} ($F_{1,46} = 13.56$, $P < .001$, $\eta^2_p = 0.228$) and PEEP ($F_{1,46} = 10.69$, $P = .002$, $\eta^2_p = 0.189$) in the treatment group were lower (ie, better) than in the control group at the posttest assessment. There was no difference between the control and treatment groups on Pa_{CO_2} at the posttest assessment ($P = .769$) (Table 2).

Comparison of duration of mechanical ventilation by group: Secondary outcomes

As presented in Table 3, duration of mechanical ventilation in the treatment group was higher than that in the control group, although this difference was not statistically significant ($P = .059$). The same result was found for duration of hospitalization in the ICU ($P = .082$).

DISCUSSION

The findings of this study showed that the implementation of the early mobilization protocol can improve Pa_{O_2}, O_2 sat, Pa_{O_2}/F_{IO_2} ratio, and pulmonary compliance in patients with respiratory failure under mechanical ventilation. Also, early mobilization reduced the need for higher level of F_{IO_2} and PEEP in patients. The intervention had no effect on Pa_{CO_2}.

Comparing the findings of other studies, the results of a study showed that early mobilization improves the Pa_{O_2} index in patients after coronary artery bypass graft surgery.[1] In another study, the researchers concluded that the implementation of the early mobilization protocol had no effect on the minute volume of patients in different positions. In this study, the minute volume parameter was used as a study outcome, which could indirectly affect respiratory parameters.[21]

The results of another study conducted on ICU patients showed that early mobilization had no effect on increasing O_2 sat, which is inconsistent with the results of our study.[4] It seems that the difference in the early mobilization protocol in the study of Sandoran et al is the reason for different results. In the Şenduran et al[22] study, the early mobilization protocol (patient sitting, standing, and sitting on the bed) was performed in 1 day. The findings of another study that examined the implementation of early mobilization among obese patients showed that early mobilization improved O_2 sat and Pa_{O_2}/F_{IO_2} indices, which improve oxygen delivery and outcome in patients.[14] Frequent position change and sitting position are predicted to improve alveolar ventilation and adjustment of ventilation to perfusion, which ultimately increase oxygen delivery in patients.[23]

In another study that evaluated the effect of passive joint movement exercise on hemodynamic parameters and pain intensity in mechanically ventilated patients, the researchers concluded that the exercise reduced O_2 sat at 5 and 20 minutes after the intervention, although these changes were in the normal range and probably occurred because of increased oxygen consumption by the tissues and increased need for supplemental oxygen.[5] Also in this study, only a passive movement program was used in the range of joints, which is different from the early mobilization protocol used in the present study.

Table 2. Results of Analysis of Covariance Examining Group Effect on Posttest Scores for Respiratory Parameters

	Day 1–Initial, Mean (SD)	Day 3–End, Mean (SD)	Adjusted Day 3–End, Mean (SE)	Adjusted Mean Difference Between Groups (95% CI)	$F_{1,46}$	*P*	ES (η^2_p)
PaO_2							
Control	60.47 (2.18)	64.40 (3.23)	64.40 (0.74)	3.23 (1.29 to 5.37)	10.81	.002	0.190
Treatment	60.50 (1.36)	67.73 (3.81)	67.73 (0.69)				
$PaCO_2$							
Control	45.46 (4.83)	41.68 (3.05)	41.87 (0.57)	0.23 (−1.36 to 1.82)	0.09	.769	0.002
Treatment	46.80 (4.15)	42.28 (2.87)	42.11 (0.54)				
O_2 sat							
Control	90.35 (1.64)	92.35 (2.17)	92.35 (0.38)	1.69 (0.65 to 2.74)	10.63	.002	0.188
Treatment	90.08 (1.23)	94.04 (1.37)	94.04 (0.36)				
PaO_2/FIO_2 ratio							
Control	120.01 (10.77)	136.97 (22.14)	135.41 (4.04)	14.51 (3.26 to 25.76)	6.74	.013	0.128
Treatment	115.66 (22.75)	148.55 (18.81)	149.92 (3.79)				
FIO_2							
Control	50.65 (3.47)	48.26 (3.57)	48.70 (0.69)	− 3.52 (−5.44 to −1.60)	13.56	<.001	0.228
Treatment	52.31 (3.80)	45.58 (3.83)	45.18 (0.65)				
RR							
Control	20.57 (2.73)	21.43 (2.50)	21.64 (0.43)	1.96 (0.75 to 3.16)	10.70	.002	0.189
Treatment	21.54 (2.77)	23.77 (2.10)	23.59 (0.41)				
PEEP							
Control	5.74 (0.75)	5.48 (0.67)	5.49 (0.10)	− 0.45 (−0.73 to −0.17)	10.69	.002	0.189
Treatment	5.77 (0.82)	5.04 (0.53)	5.03 (0.10)				
Compliance							
Control	41.37 (6.87)	45.42 (7.05)	44.86 (0.77)	4.04 (1.90 to 6.18)	14.46	<.001	0.239
Treatment	40.15 (5.26)	48.39 (5.89)	48.89 (0.73)				

Abbreviations: CI, confidence interval; ES, effect size; FIO_2, fraction of inspired oxygen; O_2 sat, oxygen saturation; PEEP, positive end-expiratory pressure; RR, respiratory rate; SD, standard deviation; SE, standard error.

Table 3. Comparison of Duration of Mechanical Ventilation and Duration of ICU Hospitalization in the Control and Treatment Groups

	Control	Treatment	*z*	*P*	ES (*r*)
Duration of mechanical ventilation					
Median (IQR)	11 (9-14)	7.5 (6-12.5)	1.89	.059	0.269
Mean (SD)	13.74 (9.79)	10.50 (6.37)			
Duration of hospitalization in the ICU					
Median (IQR)	15 (11-17)	11.5 (8-16.25)	1.74	.082	0.248
Mean (SD)	16.48 (9.05)	13.46 (6.89)			

Abbreviations: ES, effect size; ICU, intensive care unit; IQR, interquartile range; SD, standard deviation.

In another study, the authors concluded that early active exercise had no effect on patient O_2 sat and the changes occurred in the normal range and were not statistically significant.[11] The different results of this study can be due to the different protocol and study population used in the study. Also in this study, early mobilization was focused on movement of lower extremities for 20 minutes a day. The effect of early mobilization on respiratory parameters of patients after coronary artery bypass graft surgery showed that the early mobilization protocol increased the inhalation capacity of patients in the intervention group. However, this study did not examine pulmonary compliance.

We could not find a similar study in the field of early mobilization to examine the effect of intervention on pulmonary compliance, so further studies are needed to examine this parameter as one of the important respiratory criteria.

The findings of present study also showed that the mean duration of mechanical ventilation and the length of patient stay in the ICU in the intervention group were 3 days less than those in the control group, but this difference was not statistically significant ($P = .05$ and $P = .082$, respectively). Also, according to the effect size of 0.269 for the duration of mechanical ventilation and the effect size of 0.248 for the duration of patient stay in the ICU, the two groups were relatively different in terms of the duration of mechanical ventilation. The difference in significance level between the two groups was very small and marginal. However, the findings showed that this difference, although not statistically significant, could be clinically significant. Reducing the duration of mechanical ventilation reduces the patient's treatment costs, muscle weakness caused by ICU stay, and ventilator infection. Also, reducing the length of patient stay in the ICU reduces the patient's treatment costs and makes the highly needed ICU beds available for other critically ill patients.[10] Thus, further studies with accurate and complete elimination of influential underlying factors as well as higher sample size can help achieve richer scientific evidence.

Study limitations

One of the limitations of this study was the resistance by the treatment team, especially nurses, to perform the early mobilization protocol in mechanically ventilated patients. However, by reporting credible scientific evidence and repeated training, we were able to moderate the attitude of the treatment team toward the use of the early mobilization protocol. Another limitation of this study was the lack of blinding method.

CONCLUSION

The implementation of a 4-step protocol for early mobilization can improve the respiratory parameters of mechanically ventilated patients with respiratory failure admitted to the ICU, and nurses can use this protocol in collaboration with the multidisciplinary team.

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