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ORIGINAL RESEARCH

Impact of Inspiratory Muscle Training and Positive Expiratory Pressure on Lung Function and Extubation Success of ICU Patients: a Randomized Controlled Trial

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Abstract: **Introduction:** Preparing patients for extubation from mechanical ventilation (MV) necessitates focused respiratory muscle strengthening. This study aimed to evaluate the effect of threshold inspiratory muscle training (IMT) and positive expiratory pressure (PEP) exercises on outcomes of patients who underwent MV in intensive care unit (ICU). **Methods:** This randomized controlled trial was conducted in 2023 at the ICUs of Imam Reza Hospital, Mashhad, Iran. Participants were allocated to either intervention or control group (each comprising 35 patients) through block randomization. The intervention group received standard daily chest physiotherapy as well as targeted inspiratory and expiratory muscle strengthening exercises using the threshold IMT/PEP device, administered twice daily over one week. The control group received standard daily chest physiotherapy alone. Finally, the outcomes (lung compliance, duration of intubation, extubation success rate, and diaphragmatic metrics) of the two groups were compared. **Results:** 70 patients with the mean age of 56.10 ± 14.15 (range: 28.00-85.00) years were randomly divided into two groups (50% male). Significant improvements were observed in the intervention group regarding pulmonary compliance values (35.62 ± 4.43 vs. 30.85 ± 6.93; p= 0.001), peak expiratory flow (PEF) (55.20 ± 10.23 vs. 47.80 ± 11.26; p = 0.002), and maximum inspiratory pressure (MIP) (33.40 ± 4.25 vs. 30.08 ± 6.08; p = 0.01) compared to the control group. Diaphragm inspiratory thickness (0.29 ± 0.03 vs. 0.26 ± 0.04; p = 0.001), diaphragm expiratory thickness (0.22 ± 0.03 vs. 0.20 ± 0.04; p = 0.006) and motion (1.61 ± .29 vs. 1.48 ± .21; p = 0.04) also exhibited significant differences between the two groups. Extubation success rate was higher in the intervention group (68.60% vs. 40%; p = 0.01). The duration of mechanical ventilation was 15.14±7.07 days in the intervention group and 17.34±7.87 days in the control group (p = 0.20). The mean extubation time was 7.00 ± 1.88 days for the intervention group and 9.00 ± 2.00 days for the control (p < 0.001). **Conclusions:** Threshold IMT/PEP device exercises effectively enhance respiratory muscle strength, diaphragm thickness, and reduce ventilator dependency. These findings support their potential for inclusion in rehabilitation programs for ICU patients.

Keywords: Breathing exercises; Pulmonary function tests; Airway extubation; Intensive care units; Respiration, artificial

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1. Introduction

Mechanical ventilation (MV) is a critical intervention in intensive care units (ICUs) for patients who are unable to breathe independently, facilitating necessary pulmonary gas exchange (1, 2). However, MV is not without side effects, notably respiratory muscle dysfunction, which is a frequent complication following prolonged use (3, 4). Medrinal et al. (2016) found that over 24 hours of MV could lead to a 54% decrease in inspiratory muscle strength (5), contributing to diaphragmatic muscle atrophy (6). The diaphragm, being the principal muscle for spontaneous breathing, becomes inactive under MV, leading to rapid atrophy and, in some cases, ventilator-induced damage (1, 3, 7).

Diaphragmatic dysfunction is reported in 53% of patients within 24 hours of intubation, complicating and prolonging the weaning process (5).

Diaphragmatic dysfunction is a significant predictor of weaning failure, leading to extended periods of MV, increased necessity for tracheostomy, and heightened mortality rates by 25-50% (8). Extubation failure, defined as the need for reintubation shortly after planned extubation, occurs in 4-13% of ICU extubations, underscoring the challenge of weaning patients from MV (6, 9-12).

Weaning, which constitutes a substantial portion of the MV

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duration, presents a significant clinical hurdle, with failure rates between 26-42% (8, 11). Successful weaning is closely tied to diaphragmatic function, where its thickness and motions are indicative of respiratory muscle strength and lung volume. With diaphragmatic thickness reducing daily in ventilated patients, interventions aimed at minimizing muscle atrophy or bolstering muscle strength are essential for improving patient outcomes (13, 14).

The role of physiotherapy, particularly respiratory muscle exercises, is pivotal in the weaning process. Such exercises, including inspiratory and expiratory muscle training, are recommended to enhance diaphragmatic strength, aerobic capacity, and cough efficiency (6, 15, 16). Inspiratory muscle training (IMT), for instance, has been shown to significantly improve maximum inspiratory pressure (MIP) in patients with respiratory muscle weakness (17). The use of devices like the Threshold IMT, which offers controlled resistance, has been acknowledged for its effectiveness in increasing inspiratory muscle strength beyond traditional methods (17-20).

Furthermore, the application of external positive expiratory pressure (PEP) with the Threshold PEP device serves as a viable alternative to conventional chest physiotherapy, reducing expiratory resistance and improving respiratory parameters (21). Despite these benefits, adherence to respiratory muscle training (RMT) remains a challenge (16), and its integration into standard ICU practices is limited (5, 22).

Limited research exists on expiratory muscle training (EMT), and few studies have investigated combined inspiratory and expiratory muscle training to strengthen both inspiratory and expiratory muscles (22). To date, most studies have focused on the separate effects of respiratory training (19, 23, 24). Therefore, this study aimed to answer the question of whether adding respiratory muscle training (inspiratory and expiratory) by Threshold IMT/PEP to physiotherapy and conventional training can help improve respiratory muscle strength, ventilator weaning indices, and extubation success. This study is one of the first attempts to evaluate the combined effect of inspiratory and expiratory respiratory muscle training using specific threshold IMT and PEP devices in ICU patients. Our study specifically evaluates the effect of this training on key extubation success criteria, such as diaphragm thickness and motion, which have been less studied.

2. Methods

2.1. Study design and setting

This investigation was structured as a single-blind, randomized clinical trial performed in the ICUs of Imam Reza Hospital, Mashhad, Iran, throughout 2023-2024, targeting individuals on mechanical ventilation. The intervention group received standard daily chest physiotherapy as well as targeted inspiratory and expiratory muscle strengthening exercises using the threshold IMT/PEP device, administered twice daily over one week. The control group received standard daily chest physiotherapy alone. Finally, the outcomes (lung compliance, duration of intubation, extubation success rate, and diaphragmatic metrics) of the two groups were compared.

This study received approval from the Ethics Committee of Mashhad University of Medical Sciences (code: IR.MUMS.NURSE.REC.1401.123) and was registered with the Iranian Registry of Clinical Trials (code: IRCT20230214057418N1). Patient information remained confidential, and written informed consent was obtained from all patients.

2.2. Participants

The inclusion criteria encompassed a mechanical ventilation requirement beyond 48 hours, a Glasgow Coma Scale score over 13, inspiratory pressures below -20 cmH2O, arterial oxygen levels surpassing 60 mmHg, a PaO2/FiO2 ratio over 200, oxygen saturation above 90%, tidal volumes exceeding 5 ml/kg, respiratory rates under 35 breaths per minute, a rapid shallow breathing index below 105 L/min, absence of fever, and hemodynamic stability. Ventilator support was administered through Pressure Support Ventilation/Continuous Positive Airway Pressure (PSV/CPAP) with an FiO2 under 60%, PEEP between 5 and 7 cmH2O, and PSV settings ranging from 12 to 15 cmH2O.

Exclusion criteria were: the inability to perform respiratory exercises for a week, hemodynamic instability, barotrauma, necessity for sedation or muscle relaxants during the study, or a history of neuromuscular disease affecting respiratory function. Patients' disease severity and eligibility were gauged using acute physiology and chronic health evaluation (APACHE)-2 and sequential organ failure assessment (SOFA) scores, with a maximum intubation-extubation interval of 20 days.

2.3. Pre-intervention assessment

A comprehensive evaluation was conducted to ascertain disease severity and consciousness level through APACHE II, SOFA, and Richmond agitation sedation scale (RASS) scores. A blinded assessor subsequently evaluated key respiratory metrics, including Maximum Inspiratory Pressure (MIP) and pulmonary compliance, across both participant groups. MIP was measured with a ventilator set to a -18 cmH2O inspiratory pressure threshold, utilizing a threshold IMT device calibrated to 40% of the patient's MIP, adjustable between 9 and 41 cmH2O for inspiratory muscle training. Expiratory muscle strength enhancement was facilitated through a Threshold Expiratory Muscle Trainer, with adjustments ranging from 5 to 20 cm H2O, affixed to the patient's tracheal tube. Peak Expiratory Flow (PEF) was evaluated using the Bellavista 1000 e device, and pulmonary compliance was determined by configuring the ventilator to sustain an inspiratory pause of at least 0.2 seconds. The duration leading to successful extubation was meticulously recorded from the intervention's on-set, defining extubation failure as unsuccessful spontaneous breathing trials, the need for reintubation within 48 hours post-extubation, or patient mortality.

2.4. Stage of intervention

Control group: During the intervention phase, participants in the control group underwent standard physiotherapy sessions designed to improve inspiratory muscle strength. These sessions began with a baseline assessment of MIP for all patients using a ventilator. The control group's regimen encompassed a combination of passive and active limb exercises, conventional chest physiotherapy techniques like vibration and percussion, and frequent changes in patient positioning, depending on the individual's cooperation level and vital signs. Each session lasted approximately 15 minutes.

Intervention group: They received the same standard physiotherapy as the control group, with the addition of specific inspiratory and Positive Expiratory Pressure (PEP) muscle training exercises aimed at further enhancing respiratory muscle strength. Threshold inspiratory muscle training (IMT) protocol included:

- Positioning: Patients were positioned at a 45-degree angle in their beds.
- Device setup: The IMT device was calibrated for each patient and connected to the endotracheal tube, with instructions to inhale until a beep indicated a successful breath.
- Breathing regimen: The protocol consisted of five sets, each with six breaths.
- Rest periods: Patients rested for one minute between sets, with mechanical ventilation support as needed.
- Training threshold: The initial training threshold was set at 40% of the patient's MIP, aiming for five sets of ten breaths over 5 minutes.
- Progressive increase: Daily increments of 10% of the patient's MIP were applied to the threshold pressure.
- Fatigue prevention: To avoid fatigue, the conventional physiotherapy sessions for the intervention group were held separately.

Threshold positive expiratory pressure (PEP) protocol included:

- Patient positioning: Patients were laid on their side to begin therapy.
- Device adjustment: The Threshold PEP device was attached to the patient's endotracheal tube.
- Expiratory efforts: Patients performed breathing exercises against a set resistance of 7 cm H2O for 30 minutes.
- Breathing guidance: Patients were instructed to take eight to ten deep breaths, exhaling against the device's resistance.
- Secretion clearance: Sessions ended with cough exercises to clear any secretions loosened by the therapy.

Training sessions continued daily until patients were deemed ready for extubation, pausing for signs of respiratory distress or hemodynamic instability. Indicators included significant changes in respiratory rate, SpO2, blood pressure, heart rate, breathing patterns, mental status, the presence of blood in sputum, arrhythmias, or excessive sweating. In such cases, the intensity for the subsequent session remained unchanged.

The initiation of Threshold IMT and PEP matched with the start of spontaneous breathing efforts, extending to the pre-extubation period. Post-intervention assessments measured diaphragmatic function, MIP, PEF, rapid shallow breathing index (RSBI), and lung compliance, facilitating a comprehensive evaluation of the interventions' effectiveness.

2.5. Equipment description and protocols

Threshold IMT is a precision-engineered device offering resistance ranging from 9 to 41 cmH2O, designed to connect to an endotracheal tube (ETT) through flexible or rigid connectors. This spring-operated, easily adjustable device is specifically designed for resistance training in ICU patients, with daily increments in resistance levels as part of the training protocol.

Threshold PEP aims to fortify expiratory muscles by attaching the Threshold Expiratory Muscle Trainer (EMT), adjustable from 5 to 20 cm H2O, to the patient's tracheal tube end. The device facilitates expiratory muscle exercises at a resistance of 7 cm H2O for sessions lasting 30 minutes.

Diaphragm ultrasound methodology involves initial measurements of diaphragm motion during tidal breathing and maximal inspiratory efforts using a low-frequency probe (3.5 to 5 MHz) placed beneath the right costal margin. High-frequency linear probes (>7–10 MHz), positioned perpendicularly on the lateral chest wall between the 9th and 10th intercostal spaces, assess diaphragm thickness. The thickening fraction (TF), indicative of respiratory effort, is calculated based on diaphragmatic thickness changes during inspiration.

Assessing patient consciousness with RASS: A 10-Point Scale evaluates patient states from aggressive to severely drowsy or unconscious, contributing to a comprehensive assessment alongside the SOFA and APACHE II systems. APACHE II examines 10 vital physiological parameters, including body temperature, mean arterial pressure, and arterial oxygen tension, integrating the Glasgow Coma Scale for neurological evaluation, with scores ranging from 0 (non-critical) to 71 (extreme severity). SOFA score, assessing six organ systems, indicates the degree of organ dysfunction, with a total score of 16 reflecting critical organ failure.

Weaning criteria checklist: Evaluates parameters crucial for weaning from mechanical ventilation, including MIP, tidal volume, RSBI, and respiratory compliance. Training is paused if respiratory distress or significant hemodynamic changes are observed, ensuring patient safety.

Statistical analyses were conducted using GraphPad Prism V9.0 (GraphPad Software, La Jolla, California, USA). Qualitative variables were expressed as percentages, and quantitative variables were presented as means ± standard deviations (SDs). Fisher's exact test was utilized for analyzing qualitative variables, while the student's t-test was employed for quantitative variables. The diagnostic accuracy of each marker was assessed by calculating the area under the receiver operating characteristic (ROC) curve (AUC), with the optimal cutoff value determined based on the maximum Youden Index. All p-values were two-tailed, and a significance level of $p < 0.05$ was considered.

2.6. Outcomes

Post-training, clinical outcomes were assessed, including pulmonary compliance, PEF, MIP, and diaphragmatic metrics. The study examined the efficacy of weaning and extubation processes, alongside secondary outcomes like the necessity for invasive ventilation, dependency on mechanical ventilation, reintubation rates, and mortality.

2.7. Data gathering

In both groups, respiratory and cardiovascular variables (respiratory rate, heart rate, SpO2, systolic and diastolic blood pressure, and mean arterial pressure), lung function indices (pulmonary compliance, rapid shallow breathing index (RSBI), Pimax, and peak expiratory flow), and diaphragm muscle thickness (measured via ultrasound every other day) were assessed daily before and after the intervention using a ventilator.

Routine exercises in both groups included daily chest physiotherapy (vibration, percussion, etc.) administered once a day by the department's physiotherapist. In the experimental group, in addition to routine exercises, inspiratory and expiratory muscle strengthening exercises were performed using the Threshold IMT/PEP device, which was connected to the end of the endotracheal tube. The inspiratory muscle exercises, consisted of 5 sets of 10 breaths at 40% of PImax intensity, and the expiratory exercises were performed at PEP:7 cm H2O for half an hour, twice daily, for one week. The extubation protocol, included the presence of spontaneous breathing via a T-tube and 5 L/min of oxygen with hemoglobin oxygen saturation above 90%. The success or failure of extubation was evaluated 48 hours after the procedure.

2.8. Statistical analyses

The sample size was determined based on a pilot study using comparison of means between two independent groups in G-Power 3.1.9.2. The mean and standard deviation of Peak Expiratory Flow in intervention and control groups were 56.20 ± 11.53 and 47.70 ± 11.75, respectively.

Therefore, with 80% power, a 0.05 type I error rate, and effect size = 0.729, the sample size was calculated as 31 patients in each group.

Sample size was adjusted for a 10% dropout rate to 35 per group. The patients were randomly divided into intervention and control groups using a randomized block procedure with a block size of four. The random sequence was generated by a statistician using Stata software version 17.

Data were presented as mean (standard deviation;SD) or median (interquartile range) for numeric variables, and as frequency (percentages) for categorical variables. The normality of the variables was evaluated using descriptive measures such as distribution, skewness (within ±1.5), and kurtosis (within ±2). For comparisons between the intervention and control groups, Chi-square and Fisher's exact tests were used for categorical variables, independent t-tests for normally distributed numeric variables, and Mann-Whitney tests for non-normally distributed numeric variables. Within-group comparisons of quantitative variables were conducted using paired t-tests. This study followed the intention-to-treat (ITT) principle, and all patients were followed until the outcome was achieved. Analyses were conducted using IBM SPSS software, version 28 (IBM Corp., Armonk, USA) with an alpha level set at 0.05.

3. Results

3.1. Baseline characteristics of studied cases

In this study, 70 patients with the mean age of 56.10 ± 14.15 (range: 28.00-85.00) years undergoing mechanical ventilation in the ICU, were recruited (50% male). Table 1 compares the patients' characteristics in intervention and control groups. No significant difference was detected between the two groups. There were no significant differences in pulmonary compliance ($p = 0.18$), PEF ($p = 0.22$), and MIP ($p > 0.99$) between the groups at the beginning of the study. In terms of diaphragmatic metrics, no significant baseline differences were noted in inspiratory thickness ($p = 0.29$), expiratory thickness ($p = 0.52$), diaphragm thickness Fraction ($p = 0.10$), and excursion ($p = 0.97$) between the groups.

The completion rate for participation in the IMT sessions was 87.5%. Fatigue affected 11.4% of participants in the intervention group, causing delays, yet not preventing the continuation of respiratory exercises. The training was executed without adverse effects.

3.2. Comparing the studied outcomes between groups

Table 2 compares the studied outcomes including lung function, duration of mechanical ventilation, and extubation success between the groups. NNT was 4 (95% confidence interval (CI): 2.4 - 7.5), absolute risk reduction (ARR)=0.286, and relative risk reduction (RRR)=0.715.

- Lung Function

A significant improvement in pulmonary compliance was observed in both groups, with the intervention group outperforming the control ($P<0.001$). Similarly, PEF ($P<0.001$) and MIP ($P=0.004$) were significantly enhanced in both groups, with more substantial improvements noted in the intervention group (Table 2 and Figure 1).

- Duration of mechanical ventilation and extubation

The duration of mechanical ventilation was 15.14±7.07 days in the intervention group and 17.34±7.87 days in the control group ($p = 0.20$).

The mean extubation time was 7.00 ± 1.88 days for the intervention group and 9.00 ± 2.00 days for the control ($p < 0.001$).

- Diaphragmatic metrics

Post-intervention, inspiratory thickness significantly increased in the intervention group ($p = 0.01$). Conversely, expiratory thickness significantly rose in the control group ($p < 0.001$). Diaphragm thickness fraction improved significantly in both groups, and there was no marked difference between them ($p = 0.87$). However, motion (excursion) decreased significantly more in the control group than in the intervention group ($p = 0.002$).

- Weaning and extubation success rates

The study's critical outcomes revealed higher weaning and extubation success rates in the intervention group ($p < 0.05$), with an 84% increased likelihood of extubation success compared to the control group. While other outcomes did not reach statistical significance, trends suggested a reduction in the need for continued invasive ventilation, reintubation rates, and mortality in the intervention group (table 2).

4. Discussion

These results emphasize the efficacy of targeted respiratory muscle training in enhancing lung function and improving outcomes for mechanically ventilated ICU patients, highlighting the importance of integrating such interventions into patient care protocols. This study explored the impact of respiratory muscle strengthening exercises, utilizing inspiratory and expiratory techniques via Threshold IMT/PEP devices, on critical factors such as lung function, diaphragm thickness, and extubation success among patients on mechanical ventilation in the ICU. The significant enhancements in lung function indices and the increased rate of successful extubation in the intervention group compared to controls highlight the pivotal role of respiratory exercises within the treatment regimens for mechanically ventilated patients. These findings provide valuable insights into refining clinical management strategies and improving treatment outcomes.

MIP, a crucial indicator of inspiratory muscle strength, was a key focus of this study. Improved MIP values signify strengthened respiratory muscles, potentially decreasing mechanical ventilation dependency and boosting extubation prospects. This study's results, mirroring research by Bisset et al., Elbouhy et al., and Khodabandeloo et al., affirm the effectiveness of IMT exercises in elevating MIP and facilitating successful extubation, underscoring the importance of respiratory exercises in patient care protocols for those on mechanical ventilation (23, 25-27).

Peak Expiratory Flow (PEF), reflecting the highest speed at which air can be expelled from the lungs, serves as another essential measure.

Improved PEF indicates better expiratory muscle function, contributing to the efficiency of the weaning process. The enhancement in PEF observed in this study aligns with findings from Jew et al. and Sasaki et al., emphasizing the comprehensive benefits of combining inspiratory and expiratory exercises on pulmonary function, particularly in improving expiratory strength (28, 29).

Lung compliance, an indicator of the lungs' elasticity, also showed improvement, reinforcing the broad spectrum of benefits provided by respiratory exercises. Such advancements in lung function facilitate the extubation process, highlighting the need for respiratory rehabilitation programs in patient care strategies.

The comparison of these outcomes with previous studies (17) demonstrates a consensus on the efficacy of respiratory muscle exercises in improving lung function and increasing successful extubation rates. This consistency supports the integration of Threshold IMT/PEP exercises into therapeutic regimens for ICU patients, potentially shortening mechanical ventilation durations and enhancing weaning processes (4, 17).

Furthermore, this research emphasizes the crucial role of diaphragm thickness and motion in the weaning and extubation processes. The observed significant improvements in these areas following respiratory muscle exercises highlight their importance in patient recovery and independence from mechanical ventilation. These findings, supported by research such as that by Yoo et al. (7), which point to the benefits of respiratory exercises in diaphragm function and extubation success, advocating for their inclusion in patient treatment plans.

Strengthening respiratory muscles using Threshold IMT and PEP can help reduce the duration of a patient's need for mechanical ventilation.

This reduction prevents complications such as ventilator-associated infections and muscle atrophy, leading to quicker patient recovery. By improving the function and strength of the diaphragm and other respiratory muscles, the chances of successfully weaning the patient off mechanical ventilation are increased, which helps reduce the length of ICU stays and lowers treatment costs. The exercises used in the study improved maximum respiratory pressures and peak respiratory flows, positively impacting the quality of life for patients after hospital discharge. These findings highlight the importance of integrating respiratory muscle strengthening exercises into rehabilitation programs for ICU patients and suggest their potential to become a standard component in the clinical management of these patients.

Conclusively, this study affirms the positive influence of targeted respiratory muscle exercises on enhancing lung function and extubation success in mechanically ventilated ICU patients. It calls for the systematic incorporation of such exercises into rehabilitation programs, potentially improving clinical outcomes and reducing healthcare costs by decreasing the duration of mechanical ventilation and ICU stays.

Future research should investigate the long-term effects of respiratory muscle training on patient outcomes post-ICU discharge, explore optimal timing and duration of interventions, and assess cost-effectiveness in diverse ICU populations. Additionally, examining the integration of these exercises into different healthcare settings and protocols can provide a comprehensive understanding of their applicability and impact.

5. Limitations

The primary limitations of this study include the subjectivity of certain outcome measures, such as diaphragm thickness, which can introduce measurement bias. Additionally, the relatively small sample size limits the generalizability (external validity) of the findings. There are also challenges associated with administering respiratory muscle training (RMT) exercises using Threshold IMT/PEP devices in patients with profound respiratory muscle weakness.

6. Conclusions

The findings revealed notable enhancements in compliance indices, MIP, PEF, and diaphragm thickness within the intervention group. The marked success in weaning and extubation rates among participants undergoing these exercises underscores the efficacy of incorporating a comprehensive range of respiratory exercises into the treatment paradigms for ICU patients. These results highlight the significant potential of respiratory muscle training in enhancing patient outcomes in critical care environments, advocating for its broader application in clinical practice to optimize the rehabilitation and recovery process of mechanically ventilated patients.

7. Declarations

7.1. Acknowledgments

We are grateful to the Research Deputy of Mashhad University of Medical Sciences for their cooperation in this research.

7.2. Conflict of interest

The authors have no conflicts of interest to declare.

7.3. Funding

We did not receive any funding for this work.

7.4. Availability of data

The data that support the findings of this study are available on request from the corresponding author.

7.5. Ethical considerations

This study received approval from the Ethics Committee of MUMS (code: IR.MUMS.NURSE.REC.1401.123) and was registered with the Iranian Registry of Clinical Trials (IRCT code: IRCT20230214057418N1). Patient information remained confidential, and written informed consent was obtained from all patients.

7.6. Authors' contributions

MK, RF, and ABM have contributed to the study on conception and design, drafting the article, revising it critically for important intellectual content. This manuscript has been read and approved by all the authors.

7.7. Using artificial intelligence chatbots

No artificial intelligence chatbots were used in this research.

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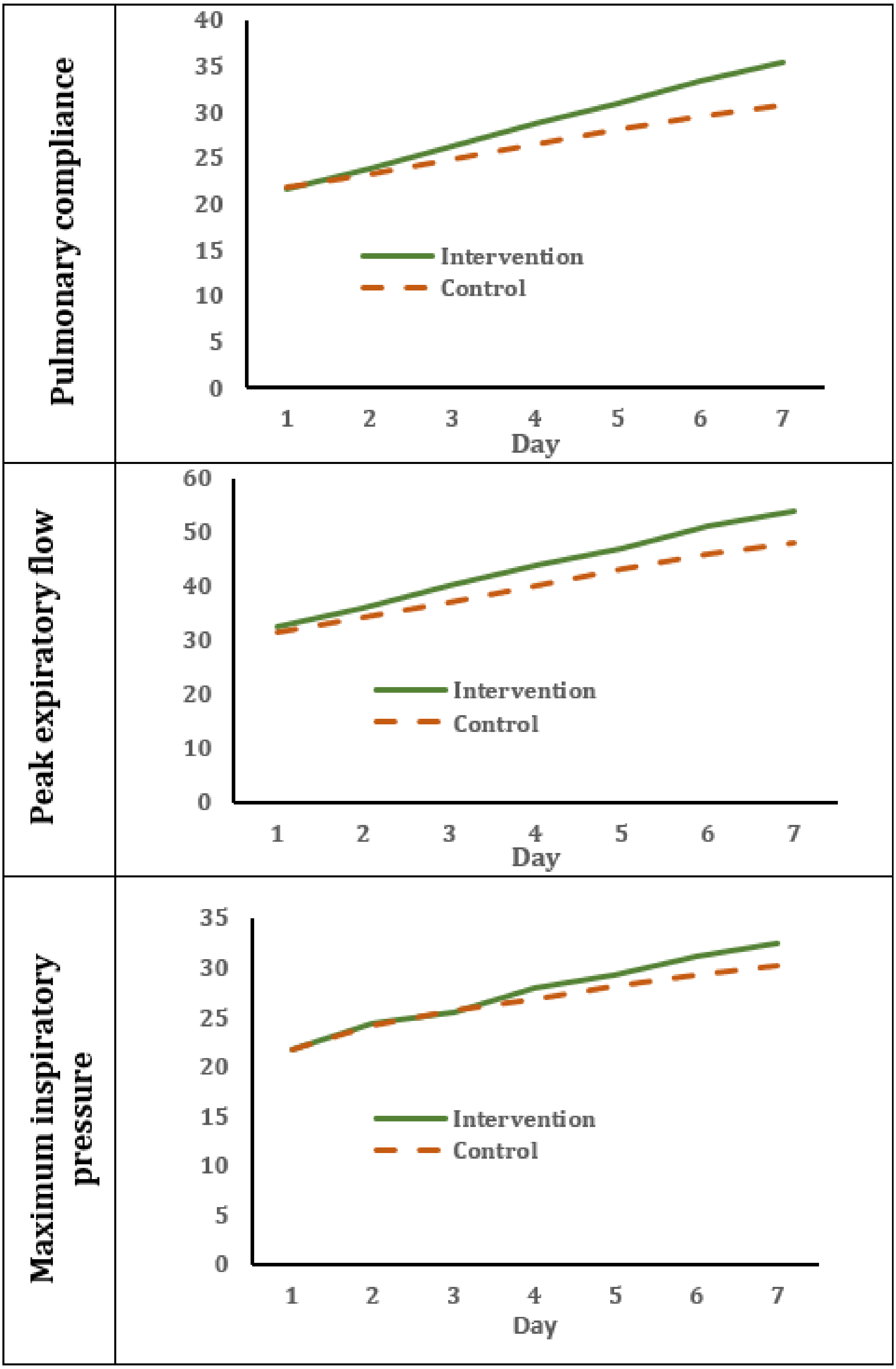

Figure 1: Pulmonary function trends during one week of mechanical ventilation in intervention and control groups.

Table 1: Comparing the baseline characteristics of patients in intervention and control groups

Variables	Intervention (n=35)	Control (n=35)	P-value
Age (year)			
Mean ± SD	52.85 ± 11.94	59.34 ± 15.56	0.05
Sex			
Male	18 (51.40)	17 (48.60)	0.81
Female	17 (48.60)	18 (51.40)	
BMI (kg/m2)*			
Mean ± SD	31.22 ± 4.21	32.25 ± 4.32	0.24
Disease severity			
APACHE II*	14.20 ± 3.42	13.08 ± 3.41	0.46
SOFA*	6.91 ± 1.48	6.68 ± 1.67	0.57
RASS*	.22 ± .68	0.22 + .84	0.84
GCS	13.51 ± .56	13.60 ± .50	0.49
Vital signs			
SBP(mmHg)	126.90 ± 12.22	123.82 ± 10.29	0.26
DBP(mmHg)	84.74 ± 6.46	85.12 ± 4.51	0.61
MAP	98.80 ± 8.05	98.02 ± 5.84	0.65
Heart rate	90.10 ± 8.76	91.48 ± 6.22	0.47
Respiratory Rate	17.62 ± 1.95	16.90 ± .88	0.25
SPO2	95.65 ± 1.12	95.64 ± .47	0.10
Laboratory findings			
Sodium (mmol/L)	138.87 ± 3.24	140.23 ± 5.62	0.29
Potassium (mmol/L)	4.24 ± .49	4.23 ± .43	0.43
Magnesium (mmol/L)	2.16 ± .40	2.15 ± .31	0.56
Creatinine (µmol/L)	1.21 ± .48	1.10 ± .31	0.76
Urea (mmol/L)	36.93 ± 7.65	34.66 ± 10.15	0.13
Blood sugar (mg/dL)	107.23 ± 9.84	107.08 ± 10.12	0.46
Smoking status			
Smoker	15 (55.6)	12 (44.4)	0.46
Non-smoker	20 (46.5)	23 (53.5)	
Drug abuse			
Positive	13 (56.5)	10 (43.5)	0.44
Negative	22 (46.8)	25 (53.2)	
Cardiac disease			
Yes	4 (57.1)	3 (42.9)	0.69
No	31 (49.2)	32 (50.8)	
Diagnosis			
COPD	11 (31.40)	7 (20.00)	0.77
Pneumonia	9 (25.70)	10 (28.60)	
Pulmonary abscess	6 (17.10)	9 (25.70)	
Septicemia	7 (20.00)	6 (17.10)	
Other	2 (5.70)	3 (8.60)	
Lung function			
PC (ml/cmH2O)	20.82 ± 1.88	21.45 ± 1.87	0.18
PEF (L/min)	31.45 ± 2.04	30.73 ± 2.38	0.22
MIP (cmH2O)	20.00 ± 4.25	20.00 ± 0.00	>0.99
Diaphragmatic metrics			
Inspiratory thickness (mm)	0.27 ± 0.02	0.27 ± 0.02	0.29
Expiratory thickness (mm)	0.23 ± 0.03	0.22 ± 0.02	0.52
Diaphragm thickness fraction	21.28 ± 7.06	19.77 ± 3.40	0.10
Excursion (mm)	1.74 ± .24	1.73 ± 0.20	0.97

Data are presented as mean ± standard deviation or frequency (%). SD: Standard deviation; BMI: Body mass index; APACHE: Acute physiology and chronic health evaluation; SOFA: Sequential organ failure assessment; RASS: Richmond Agitation Sedation Scale; GCS: Glasgow Coma Scale; SBP: systolic blood pressure; DBP: diastolic blood pressure; MAP: mean arterial pressure; COPD:Chronic obstructive pulmonary disease; PC: Pulmonary compliance; PEF: Peak expiratory Flow; MIP: Maximum inspiratory Pressure.

Table 2: Comparing the studied outcomes between intervention and control groups

Variable name	**Intervention (n=35)**	**Control (n=35)**	**P-value**
Pulmonary compliance (ml/cmH2O)			
First day	20.82 ± 1.88	21.45 ± 1.87	0.18
Last day	35.62 ± 4.43	30.85 ± 6.93	0.001
Difference	14.80 ± 3.92	9.40 ± 6.84	0.001
Within group	<0.001+	<0.001+	
Peak expiratory flow (L/min)			
First day	31.45 ± 2.04	30.73 ± 2.38	0.22
Last day	55.20 ± 10.23	47.80 ± 11.26	0.002
Difference	23.74 ± 9.84	17.05 ± 11.26	0.004
Within group	<0.001+	<0.001+	
Maximum inspiratory pressure (cmH2O)			
First day	20.00 ± 4.25	20.00 ± 0.00	>0.99
Last day	33.40 ± 4.25	30.08 ± 6.08	0.01
Difference	13.40 ± 4.25	10.08 ± 6.08	0.01
Within group	<0.001+	<0.001+	
Diaphragm inspiratory thickness (mm)			
First day	0.27 ± 0.02	0.27 ± 0.02	0.29
Last day	0.29 ± 0.03	0.26 ± 0.04	0.001
Difference	0.09 ± 0.00	-0.01 ± 0.03	0.003
Within group	0.01	0.07	
Diaphragm expiratory thickness (mm)			
First day	0.23 ± 0.03	0.22 ± 0.02	0.52
Last day	0.22 ± 0.03	0.20 ± 0.04	0.006
Difference	-0.008 ± 0.02	-0.03 ± 0.03	0.01
Within group	0.07	<0.001	
Diaphragm thickness fraction			
First day	21.28 ± 7.06	19.77 ± 3.40	0.10
Last day	28.77 ± 8.03	29.54 ± 8.04	0.87
Difference	7.48 ± 6.63	9.77 ± 6.57	0.87
Within group	<0.001+	<0.001+	
Diaphragm excursion (mm)			
First day	1.74 ± .24	1.73 ± .20	0.97
Last day	1.61 ± .29	1.48 ± .21	0.04
Difference	-0.13 ± 0.23	-.025 ± 0.11	0.002
Within group	0.002	<0.001	
Duration of mechanical ventilation (days)			
Mean ± SD	15.14±7.07	17.34±7.87	0.20
Extubation duration (day)			
Mean ± SD	7.00±1.88	9.00±2.00	0.006
Weaning			
Success	26 (74.30)	17 (48.60)	0.03
Failures	9 (25.70)	18 (51.40)	
Extubation			
Success	24 (68.60)	14 (40.00)	0.01*
Tracheostomy	2 (5.70)	6 (17.10)	0.26
Continued MV	4 (11.40)	6 (17.10)	0.49
Reintubation*	3 (8.60)	6 (17.10)	0.48
Mortality			
Yes	2 (5.70)	3 (8.60)	>0.99
No	33 (94.30)	32 (91.40)	

Data are presented as mean ± standard deviation (SD) or frequency (%). MV: mechanical ventilation. *: Reintubation within 24 hours.