

Review Paper

A Review of Effects of Inspiratory Muscle Training on Clinical and Functional Outcomes of Patients With Mechanical Ventilation

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Citation Nazir A. A Review of Effects of Inspiratory Muscle Training on Clinical and Functional Outcomes of Patients With Mechanical Ventilation. *Iranian Rehabilitation Journal*. 2023; 21(3):381-388. <http://dx.doi.org/10.32598/irj.21.3.1540.8>

doi <http://dx.doi.org/10.32598/irj.21.3.1540.8>

**Article info:**

Received: 24 Aug 2022

Accepted: 06 May 2023

Available Online: 01 Sep 2023

Keywords:

Functional ability, Inspiratory muscle strength, Inspiratory muscle training, Intensive care unit, Mechanically ventilated patients

ABSTRACT

Objectives: This review aimed to explore inspiratory muscle training (IMT) use in patients with mechanical ventilation (MV). The topics were related to its effect on the duration of MV or weaning, respiratory symptoms or lung function, inspiratory muscle strength (IMS) or endurance, functional ability, and quality of life (QoL).

Methods: Articles published in the last ten years were reviewed narratively to obtain data about how inspiratory muscle training (IMT) can affect breathing muscle strength in prolonged mechanically ventilated patients.

Results: Eleven articles were relevant to the topic, including seven original articles and four systematic reviews. We also found one practical guide on IMT in intensive care unit (ICU) patients.

Discussion: Inspiratory muscle weakness is found in most intensive care unit (ICU) patients which further causes difficulty in weaning from MV. No standard protocol exists for the use of IMT in patients who failed to wean from MV. The use of IMT was found to be safe with the incidence of side effects or unexpected events was very rare. Several studies found various effects on the success of weaning after IMT administration, such as decreased MV and weaning duration or no effect on these parameters. Studies also found various effects on IMS or endurance although most investigators found increased IMS after IMT administration. These effects vary with exercise intensity and baseline maximum inspiratory pressure (MIP). The IMT program improves lung function thereby reducing symptoms, leading to improved functional abilities and QoL. improved functional abilities and quality of life (QoL).

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Highlights

- Inspiratory muscle training (IMT) decreased mechanical ventilation or weaning duration.
- Inspiratory muscle strength (IMS) can be improved after IMT administration.
- The IMT program improved lung function, thereby reducing symptoms and improving functional abilities as well as the quality of life.

Plain Language Summary

This study aims to review the articles of the last ten years about how inspiratory muscle training (IMT) can affect breathing muscle strength in prolonged mechanical ventilation patients. The mechanical ventilation usage weakens the breathing muscle impeding patients from weaning mechanical ventilation and breathing spontaneously. Previous studies found that IMT can resolve these issues by preventing the reduction of breathing muscle mass without any adverse effects.

Introduction

Intensive care unit (ICU) treatment is associated with respiratory muscle dysfunction known as ICU-acquired weakness (ICU-AW). Factors, such as the presence of systemic inflammation, electrolyte imbalance, drug use, and immobilization have been identified as the pathogenesis of ICU-acquired weakness (ICU-AW) in addition to prolonged use of mechanical ventilation [1-3]. Prolonged use of mechanical ventilation (MV) causes proteolysis of the inspiratory muscle (diaphragm) which can be detected within 18-69 hours of using a controlled mode of MV [4]. The rate of inspiratory muscles atrophy is greater than that of the leg muscles because these muscles are more sensitive to inactivity [5-7]. Inspiratory muscle weakness can directly affect the duration of MV and ICU outcomes. Reduced diaphragm thickness is associated with the difficulty of weaning from MV, a higher rate of treatment complications, and prolonged ICU care [8].

A low inspiratory muscle strength (IMS) with maximum inspiratory pressure (MIP) less than 30 cm H₂O at the time of extubation is associated with extubation failure and 1-year mortality. Inspiratory muscle weakness is also associated with higher mortality in ICU and hospital [8].

Clinicians involved in the care of ICU patients should consider interventions for inspiratory muscle weakness [8]. The goals of clinical management are primarily to reduce the periods of inactivity of the inspiratory muscle with the use of various modalities and facilitate to wean-

ing from MV as soon as possible [5]. An early rehabilitation program is one of the interventions to facilitate weaning [9]. One study found that an early rehabilitation program in patients with respiratory failure significantly shortened the duration of MV [10].

In patients who have difficulty weaning from MV, management strategies aimed at increasing IMS. The inspiratory muscle training (IMT) program has been shown to significantly increase IMS and facilitate weaning. IMT program is safe and does not cause serious adverse events; therefore, its use in ICU patients is recommended [5]. This review was conducted to explore the use of IMT in mechanically ventilated patients. The topics were the use of IMT in mechanically ventilated patients and its effect on MV or weaning duration, respiratory symptoms or lung function, IMS or muscle endurance, functional ability, and quality of life (QoL).

Materials and Methods

Articles published in the last ten years were collected at the beginning of January 2022 through the PubMed database without limiting the type of article publications. Keywords used were “inspiratory muscle training”, “intensive care unit”, and “mechanical ventilation”. All articles written in English and accessible in full text were included.

Results

We found 38 articles relevant to the topic. After examining of the 38 articles' titles and abstracts, eleven articles were related to the topic and consisted of seven original articles (five randomized control trials, one pro-

spective cohort, and one cross-sectional survey), and two systematic reviews as well as two systematic reviews and meta-analyses. We also found one practical guide on IMT in ICU patients

Discussion

IMT in patients with MV

Rationale

The use of MV causes respiratory muscle dysfunction in the form of muscle atrophy, especially the diaphragm. It is occurred due to limited movement or inactivity. Muscle dysfunction is aggravated by age, controlled mode MV, prolonged MV, malnutrition, and use of muscle relaxants or corticosteroids [11-13].

Atrophy occurs due to loss of skeletal muscle mass resulting from increased protein degradation and decreased protein synthesis, which further causes oxidative stress. Decreased mitochondrial density, cross-sectional area of type 1 or 2 muscle fibers, and muscle strength will occur with muscle inactivity. Evidence of these pathologies was found in the diaphragm of mechanically ventilated patients. Weakness of the diaphragm can occur in up to 54% of patients which further causes difficulty in weaning [11, 12]. It is also stated that inspiratory, expiratory, and peripheral muscle strength predict prolonged extubation in mechanically ventilated patients [12].

The use of IMT in chronic respiratory disease has been shown to improve inspiratory muscle function, such as IMS and endurance. This evidence is found especially in patients with asthma, chronic obstructive pulmonary disease (COPD), and other patients with impaired diaphragmatic function [12, 13]. In COPD patients, IMT significantly increased the proportion of type 1 muscle fibers which is associated with muscle endurance, and type 2 muscle fibers size, which is associated with muscle strength [12]. Studies have shown that IMT administration for two weeks improves functions such as increased MIP and weaning duration in patients undergoing weaning trials [14, 15]. Pulmonary functions such as forced vital capacity (FVC) and forced expiratory volume in one second (FEV1), as well as shortness of breath and QoL, improved significantly after IMT administration [13]. It was stated that the IMT program increases self-confidence in patients by being aware of their ability to breathe spontaneously [14].

Indications and contraindications

The IMT program can be given to patients using MV for more than 7 days and applied since they are still on MV or after weaning [11]. It was stated that early IMT administration or within the first 24-48 hours caused only a minimal increase in inspiratory muscle strength. The severity of the disease should not prevent clinicians from considering IMT in mechanically ventilated patients for more than 7 days [16].

The requirements for giving IMT to patients still using MV include conscious and cooperative patient, positive end-expiratory pressure (PEEP) >10 cm H₂O, fraction of inspired oxygen (FiO₂) <0.60, respiratory rate less than 25 breaths per minute, and spontaneous breathing exist while still using MV. In newly weaned patients, the requirements for IMT include awake and cooperative, able to close lips around the mouthpiece well, or using tracheostomy, FiO₂ <0.60, arterial oxygen pressure (PaO₂)/FiO₂ ratio >200, and respiratory rate less than 25 breaths per minute. Since the patient must be fully aware and cooperative, consultation with the ICU physician to decrease the sedation dose is needed so that IMT administration can be initiated immediately. In addition, this collaboration is needed so that the artificial airway does not interfere with the use of IMT [11, 13].

IMT was contraindicated if the positive end-expiratory pressure (PEEP) >10 cm H₂O because it can cause derecruitment (where the lung parenchymal does not fill with air) and atelectasis. Exercise with IMT should not be administered to patients on nitric oxide therapy, nebulized with prostacyclin, or high-frequency oscillations used. Another contraindication is the respiratory rate of more than 25 breaths per minute. If the respiratory rate is high, the patient cannot hold the load for 1 s. Exercise is also contraindicated if the unstable hemodynamic status because exercise with IMT can increase intrathoracic pressure which can reduce venous return [11].

Lack of neurological, neuromuscular, and musculoskeletal functions as well as cognitive dysfunction, end-stage chronic illnesses, and a body mass index of more than 35 kg/m² are also contradictions of the IMT program [13].

The type of IMT

IMT can be performed in conjunction with other exercises or conventional physical therapy (whole-body training), or as a single IMT exercise with a resistive loading or threshold loading type. The intensity of exercise with resistive

loading IMT depends on the patient's efforts. The patient breathes according to his/her ability so that the resulting airflow varies in intensity. The intensity of exercise with threshold loading IMT is determined at a certain threshold. The patient should breathe at a defined pressure threshold to allow airflow with each breath cycle so that the inspiratory flow does not depend on the patient's effort [11].

Compared with the resistive loading type, threshold loading IMT is easier to use for load standardization and exercise prescription. The intensity of the threshold loading type gets higher and higher over time so increased muscle strength is achieved more quickly [11].

Technique for using IMT

The IMT program starts when the MV mode changes from control mode to pressure support. Before each training session, the patient was positioned in a 45° Fowler's position, and then the initial cardiorespiratory parameters such as respiratory rate, heart rate, systolic and diastolic blood pressure, and oxygen saturation were recorded. The pressure in the endotracheal tube (ETT) cuff was maintained at 30 mmHg during the exercise session. Patients perform IMT exercise according to the prescribed dose. Oxygen supplementation can be given if needed. Exercise is discontinued when signs of instability or indications for termination of exercise are observed. The cardiorespiratory parameters were recorded again 1 minute after the exercise finished [17].

In patients who experienced severe weakness, especially patients with MIP value <18 cm H₂O, it is difficult to use threshold loading IMT. With a very low MIP value, the patient cannot produce the pressure needed to open the valve at the lowest load (9 cm H₂O) with 6 breaths. In this case, the exercise starts with a sham IMT device. The patient breathes 6 times through a flexible tube connector attached to the ETT or tracheostomy, which provides little resistance. After the patient can maintain 5 sets of 6 breaths at this level for several days, the exercise can be started with the lowest load of 9 cm H₂O. The load is gradually increased several times until the patient can take 6 full breaths [11].

How to determine exercise intensity

Micro-respiratory pressure meter (micro-RPM) is a tool used to measure MIP and maximal expiratory pressure (MEP). The MIP measurement method is as follows: a) Micro-RPM is connected to the ETT or tracheostomy, b) The patient is asked to empty the lungs through a long and deep expiration, and c) The patient is asked to inhale deeply through the mouthpiece [11].

MIP and NIF measurements are not measurements of muscle strength, but these two values can describe IMS so that they can be used to determine IMT intensity [11]. The intensity of exercise can be determined by negative inspiratory force (NIF). Its value is obtained by setting the menu on MV. MIP and NIF measurements are not measurements of muscle strength, but these two values can describe IMS so that they can be used to determine IMT intensity [11].

If the MIP and NIF measurements cannot be carried out, then the exercise intensity can still be determined with the trial and error methods. Training started at a low intensity with a load of 9-15 cm H₂O and gradually increased until the patient could complete six breaths in the first set. The patient devotes all his energy to performing the first set so that it describes the best intensity that can be performed. The next day's workout should start with the intensity determined the previous day [11].

Protocol

To date, no standard protocol for the use of IMT in patients who failed to wean from MV. Treatment protocols vary depending on the population whether they are sick, healthy, or athletes. Protocols also vary in the type and intensity of exercise, whether high or low intensity and strength or resistance training [11].

In ICU patients who cannot do weight training for a certain period, interval training can be done. High-intensity interval training consists of several repetitions of exercise of high intensity (50% MIP) and short duration. This type of exercise allows for rest and recovery between sets to maximize tolerance. Exercise intensity at 50% MIP is safe and well-tolerated by the patients [11].

A low-intensity IMT program is effective in reducing weaning time by up to 30%. For this purpose, an intensity of 30% MIP is used in most programs. The repetition of the exercise varies, including 1 set of 30 repetitions, 3 sets of 10 repetitions, or 5 sets of 6 repetitions, with a rest phase of 1 minute between each set. Exercises are performed twice a day in the 45° Fowler's position [12].

In COVID-19 patients, Abodonya et al. provided IMT after weaning from MV. The exercise program started with training using an incentive spirometer in a relaxed sitting position 2 times a day for 2 weeks. After 2 weeks, the patients did an exercise with threshold loading IMT with a frequency of 2 times a day and 5 days a week for 2 consecutive weeks. Each session consists of 6 inspiration cycles. Each cycle lasts for 5 minutes consisting of

held breaths, followed by a 1-minute rest phase. The purpose of this exercise is to increase the IMS. In the fifth and sixth cycles, each patient was instructed to breathe regularly as much as possible. This exercise is intended to increase the endurance of the inspiratory muscles. The load given is 50% MIP [13].

Another study using an electronic IMT performed the exercise in a manual mode of 30 repetitions divided into three sets with a 1-minute break between sets. The exercise was performed 2 times a day with a load of 30% MIP, which was readjusted in increments of 10% daily [18].

When the patient's ability increases as indicated by the ability to achieve the predetermined intensity without complaint, the exercise intensity should be increased gradually to provide the maximum exercise load that the patient can tolerate. Increased 1-2 cm H₂O every 1-2 days is recommended. With this progression, if the patient had a baseline value of 15 cm H₂O at the beginning of the exercise, then he/she can be trained to achieve a load of 25 cm H₂O in 1 week. If the patient has complications, such as pneumonia so that pulmonary function can be impaired due to the accumulation of sputum, it may be necessary to decrease the intensity of exercise for a few days. After removing these complications, the exercise intensity should be re-determined [11].

Although no guideline for exercise discontinuation is found in ICU patients, exercise can be continued until the patient can achieve normal MIP values according to age and sex. The formula for determining the normal value of MIP is $120 - (0.41 \times \text{age})$ for men and $108 - (0.61 \times \text{age})$ for women [6].

Safety issues

Previous research showed that the incidence of side effects is very unlikely if the patient meets the eligibility criteria. Moreover, a meta-analysis found that no unexpected event found in the IMT administration [11, 19]. One study found that only 3% of participants (three participants) reported side effects requiring medical intervention, such as intravenous line and bronchoscopy detachment, a common occurrence in other rehabilitation interventions in the ICU [20]. A systematic review by Elkins and Dentice found no serious adverse event. Complications occurred during ICU care was the same between the group that received the IMT program and those that did not [21]. Another study found no side effects, no hemodynamic changes, and no required oxygen supplementation with the electronic IMT program [18].

IMT program should be discontinued if any of the following signs occur: Blood pressure changes >20% compared to resting state, systolic blood pressure >180 mmHg or <90 mm Hg, new-onset arrhythmia, decrease in oxygen saturation >10% or oxygen saturation <90%, pulmonary artery systolic pressure >60 mm Hg, heart rate >130 beats per minute, suspicion of a pneumothorax, the presence of agitation and altered level of consciousness, at risk for dislodgement of the device and intravenous line, or requiring an increase in sedation dose, and the presence of thoracoabdominal asynchrony [14].

Indication for discontinuation

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Effects of IMT on clinical and functional outcomes

The effect of IMT on clinical and functional outcomes is described as the effect on the duration of MV and weaning, symptoms of shortness of breath and lung functions, IMS and muscle endurance, as well as functional ability and QoL.

Effects of IMT on MV and weaning duration

During weaning trials, patients who exercised with IMT showed better weaning success rates than those in trialed with a T-piece over several days to several weeks [8]. A systematic review and meta-analysis found that the duration of MV and weaning was shorter in the group of patients receiving combined early mobilization and IMT programs compared to conventional physical therapy. When compared to patients receiving conventional physical therapy alone, the duration of MV was shorter in patients receiving early mobilization, while the duration of weaning was shorter in patients receiving an IMT program combined with conventional physical therapy [12]. These results were different with results found by Condessa et al. who found that the IMT program did not significantly shorten the weaning time, although the weaning duration was reduced by 8 hours in the group that received the IMT program [17].

Early mobilization improved skeletal muscle function and increased IMS, respiratory rate, tidal volume, oxygen transfer capacity, and minute ventilation which further decreased MV duration. This happens because early mobilization increases chest cavity movements. The combination of IMT and early mobilization may provide additional benefits to the duration of MV or weaning [12].

Another article review found that the IMT program did not affect the duration of MV and weaning. It was stated that compared to standard care, early mobilization decreased the duration of MV while IMT was not. The MV duration was decreased by 1.43 days with an early mobilization program. It was also stated that there was no difference in weaning duration between groups of patients given the IMT program compared to standard care [19]. Other advantages of the early mobilization program were the prevention of muscle damage and joint contracture, as well as the increase or maintenance of leg muscle strength. Early mobilization could also improve consciousness [12]. Another study found that compared to a group of patients receiving a standard care program, the electronic IMT program shortened the total weaning time [18].

Effect of IMT on shortness of breath and lung functions

One study found no change in the dyspnea scale in the group received the IMT program, but no further explanation for this result [21]. Another study conducted by Abodonya et al. that assessed the efficacy of IMT in COVID-19 patients after weaning from the MV found that the forced vital capacity (FVC), forced expiration volume in 1 second (FEV1), and dyspnea severity index scores significantly increased after 2 weeks of IMT program [13]. Condessa et al. also found an increase in tidal volume after the administration of the IMT program [17].

Effect of IMT on in IMS and muscle endurance

Bissett et al. administered a 2-week IMT program in mechanically ventilated patients at seven days after weaning. They found a greater increase in IMS in patients who received the IMT program compared to those who did not. Increased IMS was obtained in the IMT program starting with a minimum intensity of 50% MIP with five sets consisting of six breathing cycles and performed every day except on weekends [11]. Consistent with Bissett et al., Condessa et al. also obtained a significant increase in MIP after administering the IMT

program with an intensity of 40% MIP, five sets consisting of 10 breathing cycles, two times a day and seven days a week [11, 17]. Bissett et al. found that inspiratory muscle endurance did not increase significantly because the exercise episode length was not sufficient to increase endurance. Previous studies found that in patients with lung disease, healthy people, or athletes increase in muscle endurance was achieved with IMT administration for four to eleven weeks [16, 22].

Another study conducted by Bissett et al. found that patients benefitting from the IMT program are patients with inspiratory muscle weakness with the MIP value ≥ 28 cm H₂O. Increased IMS was not associated with age, gender, disease severity, and physical function, therefore it is advisable to offer the program IMT to men and women of all ages [16]. Compared to the intermittent nebulization program, the electronic IMT program did not cause a significant difference in MIP scores after the intervention [18].

Effect of IMT on functional ability and QoL

Research conducted by Bissett et al. obtained the same increase in physical function between the group given the IMT program and the control group given standard care. This is thought to be due to the influence of other programs, such as whole-body training and walking pattern exercises that can speed up recovery of physical function. Improved QoL occurred as a secondary impact of clinical improvement after weaning from mechanical ventilation [11, 21].

Patients benefitting from the IMT program are the group of patients with a moderate to high QoL score based on the 5-dimensional European QoL scale (>40) at the time of weaning from MV [16].

In COVID-19 patients after weaning from MV, a significant increase was observed in QoL scores after participating in the IMT program for two weeks [13]. The minimum dose to increase QoL was also 50% MIP [11].

Conclusion

Prolonged use of MV causes inspiratory muscle dysfunction which is exacerbated by the medical conditions and complications of treatment and medications used in the ICU. Inspiratory muscle weakness was found in most ICU patients, causing difficulty in weaning from MV. The IMT program can be administered to patients on MV or after weaning with consideration to its indications and contraindications. These conditions must be

met to ensure the safety and success of the program. To date, no standard protocol exists for the use of IMT in patients who failed to wean from MV. Different protocols for using IMT also caused different effects on the duration of MV and weaning. The effect on muscle strength or endurance and other functions vary. The use of IMT was found to be safe with the incidence of unexpected events was very low.

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Ethical Considerations

Compliance with ethical guidelines

There were no ethical considerations to be considered in this research.

Funding

This research did not receive any grant from funding agencies in the public, commercial, or non-profit sectors.

Conflict of interest

The author declared no conflict of interest.

Acknowledgments

The author acknowledge Faculty of Medicine **Padjajaran University** for the opportunity to write this article.

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