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Influence of early mobilization on respiratory and peripheral muscle strength in critically ill patients

Influência da mobilização precoce na força muscular periférica e respiratória em pacientes críticos

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ABSTRACT

Objective: To evaluate the effects of an early mobilization protocol on respiratory and peripheral muscles in critically ill patients.

Methods: A randomized controlled clinical trial was conducted with 59 male and female patients on mechanical ventilation. The patients were divided into a conventional physical therapy group (control group, n=14) that received the sector's standard physical therapy program and an early mobilization group (n=14) that received a systematic early mobilization protocol. Peripheral muscle strength was assessed with the Medical Research Council score, and respiratory muscle strength (determined by the maximal inspiratory and expiratory pressures) was measured using a vacuum manometer with a unidirectional valve. Systematic early mobilization was performed on five levels.

Results: Significant increases were observed for values for maximal inspiratory pressure and the Medical Research Council score in the early mobilization group. However, no statistically significant improvement was observed for maximal expiratory pressure or MV duration (days), length of stay in the intensive care unit (days), and length of hospital stay (days).

Conclusion: The early mobilization group showed gains in inspiratory and peripheral muscle strength.

Keywords: Breathing exercises; Respiratory muscles; Intensive care units

INTRODUCTION

Advances in intensive care and mechanical ventilation (MV) in the past two decades have increased critically ill patient survival. However, some patients require prolonged MV (PMV) and are deconditioned due to respiratory insufficiency caused by underlying disease, adverse effects of medications, and prolonged immobilization.[1-3]

Patients in the intensive care unit (ICU) are often confined to their beds, which results in inactivity, immobility, and severe osteomyoarticular system dysfunction.[4,5] These changes are predisposing factors for polyneuropathy and/or myopathy in critically ill patients and lead to a 2- to 5-fold increase in MV duration and time for ventilatory weaning.[6]

Immobility disproportionately affects respiratory muscles because the mechanical ventilator performs a large amount of the respiratory effort, decreasing the spontaneous ventilation effort. This results in the partial or complete absence of neural activation and muscle

This study was conducted at the Hospital Agamenon Magalhães - HAM - Recife (PE), Brazil.

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mechanics, thereby reducing the diaphragm's ability to generate strength.(5) This atrophy is more pronounced in the respiratory muscles than in the peripheral muscles, even though both are inactive.(2) Respiratory muscle function impairment contributes to exercise intolerance, dyspnea, and hypercapnia; however, it can be improved with adequate physical training.(7)

Electrophysiological studies have demonstrated diffuse neuromuscular abnormalities in limbs of 50% of ICU patients after 5 to 7 days of MV, and the main clinical symptom is physical deconditioning due to muscle weakness.(3)

Mobilizing critically ill patients confined in the ICU and positioning them in order to prevent joint contractures is an early rehabilitative mechanism that has significant effects on oxygen transportation, maintenance of muscle strength and joint mobility, and lung function and respiratory system performance. All of these factors can facilitate MV weaning, which reduces the length of ICU and overall hospital stays and improves quality of life after hospital discharge.(8-11)

Rehabilitating patients with respiratory diseases is a well-established way to alleviate symptoms and optimize function, regardless of disease stage.(8,12) However, there are currently no standard protocols to guide physical therapy in critically ill patients. This lack is important because these patients have high rates of morbidity and mortality, impaired respiratory function, consequent reduction of quality of life, and high health care costs.(13)

The aim of the present study was to assess the effects of a mobilization protocol on the peripheral and respiratory muscles of critically ill patients in order to assist in treatment guideline designs.

METHODS

A randomized controlled clinical trial with concealed allocation was conducted in the general ICU of the Hospital Agamenon Magalhães - HAM between February 2009 and February 2011. The study was approved by the HAM Research Ethics Committee under protocol number CAE 0039.0.236.000-08.

Patient recruitment was performed by a researcher who made daily visits to the HAM ICU and selected patients who fit the population profile intended for the study using a checklist. When the researcher identified a patient who met the eligibility criteria, their legal guardian was informed of the aims of the study and an invitation to participate was extended. All volunteers and/or patient guardians included in the study were informed about the purpose of the project and signed an Informed Consent Form (ICF) according to Resolution 196/96 of the Brazilian Ministry of Health.

The study included male and female individuals on MV who met the following inclusion criteria: adequate cardiovascular reserve, demonstrated by <50% variation in resting heart rate (HR)(14) and systolic blood pressure (SBP) <200 mmHg or >90 mmHg; adequate respiratory reserve, demonstrated by peripheral oxygen saturation (SpO_2) >90% with fraction of inspired oxygen (FiO_2) <60%, no signs of respiratory distress and respiratory rate (RR) <25 breaths per minute; and no physical exercise program prior to study enrollment.(15)

Patients with signs of intracranial hypertension, inability to walk without assistance before acute illness in the ICU, cognitive impairment before being admitted to the ICU, neuromuscular disease, stroke, body mass index (BMI) >40, unconsolidated fracture, MV for more than 7 days, or postoperative recurrence or cancer therapy in the previous 6 months were excluded from the study.

The volunteers were randomly divided into two groups. Conventional physical therapy group (CPTG) patients received passive mobilization of the four limbs five times a week and active-assisted exercises according to patient improvement and cooperation. The early mobilization group (EMG) patients received a systematic early mobilization protocol, twice a day, every day of the week, as depicted in figure 1.

Patient data collection was initiated after these procedures. Recruited patients' clinical records, demographic information, clinical history, diagnosis, BMI, blood gas data, and Acute Physiology and Chronic Health Evaluation Classification System II (APACHE II) scores were compiled and compared.

Respiratory and peripheral muscle strength was assessed in both groups once sedation was withdrawn, and peripheral muscle strength was measured for all four limbs every day using the Medical Research Council (MRC) score, with values ranging from 0 (tetraplegia) to 60 (normal muscle strength). Respiratory muscle strength was indirectly assessed every 3 days, and the values obtained for maximal inspiratory pressure (PImax)

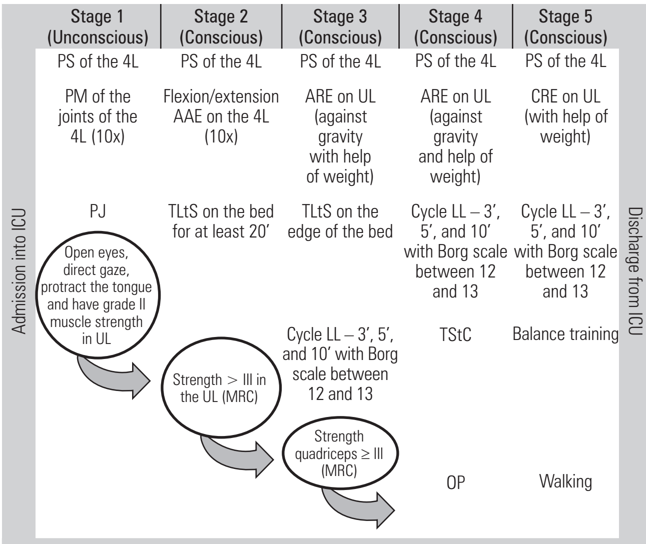

Figure 1 – Early mobilization protocol for critically ill patients on mechanical ventilation. ICU - intensive care unit; PS - passive stretching; 4L - four limbs; PM – passive mobilization; PJ - positioning of the joint; UL - upper limbs; AAE – active-assisted exercise; TLtS – transfer from lying to sitting position; MRC – Medical Research Council; ARE – active-resistive exercise; LL - lower limbs; Cycle LL – cycle ergometry for lower limbs; TStC - transfer from sitting to chair; OP – orthostatic posture; CRE - counter-resistance exercise. Source: Adapted from Morris PE, Goad A, Thompson C, Taylor K, Harry B, Passmore L, et al. Early intensive care unit mobility therapy in the treatment of acute respiratory failure. Crit Care Med. 2008;36(8):2238-43.[29]

and maximal expiratory pressure (PEmax) at the time of ICU discharge (T_{ICU}) were considered as the final measurements.[13]

PImax and PEmax were assessed based on residual volume and total lung capacity, respectively, in stable patients who were being weaned from MV using a vacuum manometer (Comercial Médica®, São Paulo, Brazil) with a unidirectional valve for 40 seconds.[16]

The early mobilization protocol was interrupted in patients with tachycardia or bradycardia; signs of respiratory distress, as evidenced by accessory muscle use, flaring of nostrils (FN), or an increase in RR >25 breaths per minute; changes in SpO_2 to <90%; and an increase or decrease in mean arterial pressure (MAP) by 20 mmHg.

The Kolmogorov-Smirnov test was used to verify the normal distribution of the study variables. Fisher's exact tests and chi-squared tests were used to assess differences between proportions, and independent and paired sample Student's t tests were used to analyze continuous variables. Correlation analyses were performed using Spearman's correlation test. All conclusions were based on a 5% level of significance, and Microsoft Office Excel 2007 (Manaus, Brazil) and GraphPad Prism, version 4.0 (La Jolla, USA) were used.

RESULTS

Four hundred and thirty-one patients were admitted to the ICU during the study period. Among these, 372 patients were ineligible based on the inclusion and exclusion criteria. The 59 remaining patients were randomly divided into the CPTG (n=33) and EMG (n=26). Nineteen and 12 deaths occurred in the CPTG and the EMG after the study protocol was initiated, respectively, resulting in a final sample of 14 patients in each group.

Table 1 shows the overall characteristics of the study sample regarding age, gender, APACHE II score, prevalence of diabetes mellitus, and primary clinical diagnosis. There were no significant differences between the studied groups. None of the patients received neuromuscular blocking agents or corticosteroids following study allocation.

Table 1 - Patient characteristics

	Conventional physical therapy group (N=14)	Early mobilization group (N=14)	p value
Age (years)	50.43±20.45	59.07±15.22	0.21*
Female gender	10 (71.43)	7 (50.00)	0.75**
APACHE II	21.07±7.23	23.71±8.51	0.38*
Diabetes mellitus	1 (7.14)	1 (7.14)	1.51**
Primary diagnosis			
Acute respiratory failure	7 (50.00)	6 (42.86)	1.00**
Pneumonia	3 (21.43)	1 (7.14)	0.60**
Cardiomyopathy	0 (0.00)	0 (5.88)	1.00**
Collagenosis	1 (7.14)	0 (0.00)	1.00**
Postoperative period of thoracoabdominal surgery	1 (7.14)	2 (14.28)	1.00**
Acute myocardial infarction	1 (7.14)	1 (7.14)	1.00**
Leptospirosis	0 (0.00)	1 (7.14)	1.00**
Acute renal insufficiency	0 (0.00)	1 (7.14)	1.00**
Pulmonary tuberculosis	1 (7.14)	1 (7.14)	1.00**
Neoplasia	0 (0.00)	1 (7.14)	1.00**

APACHE II - Acute Physiology and Chronic Health Evaluation Classification System II. Age and APACHE II parameters are expressed as the mean ± standard deviation, while the other parameters are shown as absolute values (%). * Student's t test for independent samples; ** Fisher's exact test.

Table 2 shows the PImax, PEmax, and MRC values and variations obtained before and after study protocol implementation. We observed a significant increase in PImax after the study period in the EMG (52.71±12.69 before versus 66.64±26.44 after; p=0.02). This phenomenon was not observed for patients in the CPTG (67.86±33.72 before versus 73.86±34.26 after; p=0.60). When analyzing expiratory muscle strength, no significant gains were observed for PEmax values in either group. No significant increase in peripheral muscle strength was observed after the study period in the CPTG (39.21±14.63 before versus 40.29±10.51 after; p=0.82); however, a significant gain in peripheral muscle strength was observed for the EMG (49.29±11.02 before versus 55.86±4.40 after; p=0.04). When comparing both groups, MRC values before (49.29±11.02 versus 39.21±14.63; p=0.00) and after (55.86±4.40 versus 40.29±10.51; p=0.00) were significantly higher in the EMG patients. No significant differences were observed for total MV duration ($T_{MV,}$ p=0.60), ICU stay length ($T_{ICU,}$ p=0.77), or and hospital stay length ($T_{Hosp,}$ p=0.25) between the two groups.

Table 2 – Assessment of muscle strength variables in the conventional physical therapy and early mobilization groups

	Conventional physical therapy group (N=14)	Early mobilization group (N=14)	p value*
$PImax_{before}$ (cmH_2O)	67.86±33.72	52.71±12.69	0.12
$PImax_{after}$ (cmH_2O)	73.86±34.26	66.64±26.44	0.53
p value**	0.60	0.02	
$PEmax_{before}$ (cmH_2O)	61.71±27.83	47.14±19.14	0.11
$PEmax_{after}$ (cmH_2O)	62.79±21.50	59.07±23.95	0.66
p value**	0.90	0.07	
$MRC_{initial}$	39.21±14.63	49.29±11.02	<0.001
MRC_{final}	40.29±10.51	55.86±4.40	<0.001
p value**	0.82	0.04	

PImax – maximal inspiratory pressure; PEmax - maximal expiratory pressure; MRC - Medical Research Council. The results are expressed as the mean ± standard deviation. Values of PImax are expressed in module. *Student's t-test for independent samples; **Student's t-test for paired samples.

DISCUSSION

The present study showed that the EMG exhibited significant increases in PImax and MRC when compared to the CPTG, although no differences were observed in T_{MV} (days), T_{ICU} (days), and T_{Hosp} (days).

Immobility, physical deconditioning, and muscle weakness are problems often found in patients on MV. These complications inherent to prolonged ventilation are multifactorial, and age, female gender and chronic diseases, such as congestive heart failure, diabetes mellitus, and chronic obstructive pulmonary disease, are independent predictors of ICU-acquired weakness.[17,18]

These complications may lead to delayed weaning from MV and pressure ulcer development with consequent reduction in quality of life after ICU discharge, progressing to physical deconditioning.[19] Immobility results in functional muscle loss, which is roughly a 1.3 to 3% loss in muscle strength per day and up to 10% over 1 week of inactivity.[4] Epidemiological data show that over 5 million people are admitted to ICUs each year, and many develop complications associated with prolonged bed rest, which significantly affects morbidity, mortality, and hospitalization costs.[20]

The data in table 1 list the characteristics of the studied sample and their primary clinical diagnosis. There were no differences in the distribution, demonstrating the homogeneity of both groups at the beginning of the study. Similarities were also observed when the sample was assessed for T_{ICU}, T_{MV}, and T_{Hosp}, as shown in table 2.

In a randomized study conducted in 458 patients with pneumonia treated at 17 hospitals, Mundy et al.[21] used a protocol in which patients were transferred from the bed to a chair or urged to walk for at least 20 minutes during the first hours of admission. They found that early mobilization reduced the T_{ICU} without complications from the primary disease.

Atrophy resulting from disuse and innervation loss in some diseases promotes decreased muscle mass, affecting the musculoskeletal system through myosin fiber changes (primarily caused by oxidative stress), decreased protein synthesis, and increased proteolysis. Muscle activity is anti-inflammatory, which plays an increasingly beneficial role in severe diseases, such as acute respiratory dysfunction syndrome (ARDS) and sepsis. In contrast, just 5 days of bed rest can be sufficient for the development of increased insulin resistance and vascular dysfunction in healthy individuals. All of these factors contribute to increased risks and complications, resulting in prolonged T_{ICU}.[19,22] By biopsying the human diaphragm, Levine et al.[23] showed that 18 to 69 hours of controlled MV is sufficient to reduce the cross-sectional area of types I and II muscle fibers, resulting in increased diaphragmatic proteolysis during inactivity, which leads to muscle fiber atrophy and increased risk for muscle fatigue. These processes also delay MV weaning.

Table 2 shows a significant gain in inspiratory muscle strength only in the EMG. These results may be associated with the upper limb (UL) training performed in patients subjected to early mobilization compared to the control. Some of the muscle groups worked during UL mobilization are inserted and stabilized in the rib cage, and this may have contributed to the recruitment of accessory inspiratory muscles, thus resulting in increased inspiratory muscle strength, as represented by the higher PImax value. Regarding expiratory muscle strength, although no significant gain was observed in any of the groups, a tendency for gain in expiratory strength was observed in the EMG when compared to the CPTG. This may have been due to the small size of the sample, as indicated by the p-value. Our findings are consistent with the gain in PImax but differ from the gain in PEmax observed by Chiang et al.[1] in a study that evaluated physical training effects on 32 patients on prolonged MV who were subjected to strength and resistance exercises, transfers from lying to sitting and sitting to standing, and diaphragmatic exercises. These patients showed significant improvements in the PImax, PEmax, and limb strength on the third and sixth weeks of the study period. These results suggest that physical training could actually attenuate and partially reverse the effects of immobilization.

Peripheral muscle dysfunction, often observed in patients on prolonged MV that is due to immobilization on the bed combined with other factors leads to ICU-acquired weakness, which is defined by an MRC score <48. This functional marker allows for the prognosis of a longer hospital stay and increased risk of mortality after hospital discharge.[3]

Dysfunction was evident in the studied population at the first evaluation; the CPTG had a mean MRC value of 39.21, whereas the EMG value was 49.29 ($p<0.001$). After the first assessment, a significant increase in MRC scores was observed in the EMG, with a mean gain of 6.57 ($p=0.04$), and this significant increase did not occur in the CPTG, for which the gain in MRC was only 1.08. The study by Martin et al.[13] showed that exercising the muscles inserted in the rib cage, such as the pectoralis major, results in the improvement of ventilatory mechanics, inspiration, and expiration. The authors assessed 49 patients subjected to an early mobilization program directed at the ULs and found a correlation between peripheral muscle strength score and weaning time.

In the present study, we were able to observe a gain in peripheral muscle strength in the EMG as assessed by the MRC score. This result affirms that mobilization in the ICU is feasible and safe when applied early and systematically. In addition, this procedure reduces the effects of immobilization, maintains functional capacity, and reduces the loss of muscle fibers that deteriorate with immobility. Our findings corroborate those reported by Burtin et al.[24], who showed gains in capacity and functional status, as well as quadriceps strength, in a randomized controlled study conducted with 90 patients on MV for more than 7 days who were subjected to early exercises through passive ergometry of the lower limbs (LL) for 20 minutes. Schweickert et al.[25] conducted a randomized controlled study in which one group of patients was subjected to passive, active-assisted, and free active exercises, including transfer from lying to sitting on the bed, transfer to the chair, balance training, and walking. We found that 59% of the patients returned to functional independence upon hospital discharge, compared to only 35% in the control group. Accordingly, patients in the intervention group had 2.4 fewer days of ventilatory support when compared to the control group. In this study, the systematic mobilization program did not influence T_{MV}, T_{ICU}, or T_{HOSP}.

Some authors have demonstrated that early mobilization is an important component in the care of critically ill patients who require prolonged MV; it facilitates improved lung and muscle function, accelerates the recovery process, and decreases T_{MV} and T_{ICU},.[1,7,22,26-30]

The present study has several limitations. First, there was a difference between the initial values of PImax between the CPTG and the EMG. However, these groups were selected at random, and the difference was not significant. Another limitation of the study was the small number of patients, which is reflected in the low power of the current study. Sample size calculation performed after the assessment of the initial data indicated that 50 patients per group would have been necessary to achieve a 95% confidence level and a type II error (β) of 80%.

CONCLUSION

We were able to verify that compared to patients who underwent the standard mobilization program, patients subjected to a systematic early mobilization protocol showed gains in inspiratory muscle strength and peripheral muscle strength.

RESUMO

Objetivo: Avaliar os efeitos de um protocolo de mobilização precoce na musculatura periférica e respiratória de pacientes críticos.

Métodos: Ensaio clínico, controlado e randomizado realizado em 59 pacientes de ambos os gêneros, em ventilação mecânica. Os pacientes foram divididos em grupo fisioterapia convencional - grupo controle, n=14, que realizou a fisioterapia do setor, e grupo mobilização precoce, n=14, que recebeu um protocolo sistemático de mobilização precoce. A força muscular periférica foi avaliada por meio do *Medical Research Council* e a força muscular respiratória (dada por pressão inspiratória máxima e pressão expiratória máxima) foi mensurada pelo manovacuômetro com uma válvula unidirecional. A mobilização precoce sistemática foi realizada em cinco níveis.

Resultados: Para os valores de pressão inspiratória máxima e do *Medical Research Council*, foram encontrados ganhos significativos no grupo mobilização precoce. Entretanto, a pressão expiratória máxima e o tempo de ventilação mecânica (dias), tempo de internamento na unidade de terapia intensiva (dias), e tempo de internamento hospitalar (dias) não apresentaram significância estatística.

Conclusão: Houve ganho da força muscular inspiratória e periférica para a população estudada quando submetida a um protocolo de mobilização precoce e sistematizado.

Descritores: Exercícios respiratórios; Músculos respiratórios; Unidades de terapia intensiva

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