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Mobilization in the Intensive Care Unit: systematic review

Mobilização na Unidade de Terapia Intensiva: revisão sistemática

Movilización en la Unidad de Cuidados Intensivos: revisión sistemática

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ABSTRACT | Prolonged stay in the Intensive Care Unit and mechanical ventilation are associated with functional decline, increased morbidity and mortality, and healthcare costs. The early mobilization seems to have beneficial effects on these factors. The aim of this study was to systematize knowledge about early mobilization in the Intensive Care Unit. This is a systematic review, with inclusion of clinical trials published between 1998 and 2012. We used the scale Physiotherapy Evidence Database (PEDro) to assess the methodological quality of the studies. Eight studies were included and analyzed. It was concluded that early mobilization in the Intensive Care Unit has a significant impact on patients' functional outcomes.

Keywords | Early Ambulation; Exercise; Intensive Care Units; Rehabilitation; Physical Therapy Modalities.

RESUMO | Permanência prolongada na Unidade de Terapia Intensiva e ventilação mecânica estão associadas com declínio funcional, aumento da morbidade e mortalidade e custos assistenciais. A mobilização precoce parece ter efeitos benéficos sobre estes fatores. O objetivo do presente estudo foi sistematizar o conhecimento sobre a mobilização precoce na Unidade de Terapia Intensiva. Trata-se de uma revisão sistemática, com inclusão de ensaios clínicos publicados entre 1998 e 2012. Utilizou-se a escala *Physiotherapy Evidence Database* (PEDro) para avaliação da qualidade metodológica das investigações. Oito estudos foram incluídos e analisados. Concluiu-se que a mobilização precoce na Unidade de Terapia Intensiva apresentou um impacto significativamente positivo nos resultados funcionais dos pacientes.

Descritores | Deambulação Precoce; Exercício; Unidades de Terapia Intensiva; Reabilitação; Modalidades de Fisioterapia.

RESUMEN | La permanencia prolongada en la Unidad de Cuidados Intensivos y la ventilación mecánica están asociadas a la caída funcional, al aumento de morbidad y mortalidad y a los costos asistenciales. La movilización precoz parece tener efectos benéficos en esos factores. El objetivo del presente estudio fue sistematizar el conocimiento acerca de la movilización precoz en la Unidad de Cuidados Intensivos. Se trata de una revisión sistemática, con la inclusión de ensayos clínicos publicados entre el 1998 y el 2012. Se utilizó la escala *Physiotherapy Evidence Database* (PEDro) para evaluación de la cualidad metodológica de las investigaciones. Ocho estudios fueron inclusos y analizados. Se concluye que la movilización precoz en la Unidad de Cuidados Intensivos presentó un impacto significativamente positivo en los resultados funcionales de los pacientes.

Palabras clave | Ambulación Precoz; Ejercicio; Unidades de Cuidados Intensivos; Rehabilitación; Modalidades de Fisioterapia.

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INTRODUCTION

The technological and scientific evolution of advanced life support and health care, with subsequent improvement in the treatment, has played an important role in the conversion of mortality in longer survival of patients[1-3]. There are, increasingly, survivors of critical illness whose complications of prolonged stay in the intensive care unit (ICU) contribute to neuromuscular disorders, worsening of functional abilities, increased healthcare costs and decreased quality of life after hospital discharge[4,5].

The muscular dysfunction can be aggravated by the consequences of disease, sedation and immobility in bed, as well as inadequate intensity and duration of physical rehabilitation[5,6]. The frequency and severity of neuromuscular weakness and its symptoms can be alleviated, using alternatives, such as early mobilization (EM) for the prevention and treatment of such complications[7].

Early physical therapy, including during intubation and mechanical ventilation, can be carried out safely improving the functional outcomes of patients[2,4,8]. Given the need for knowledge about the effects of mobilization in the ICU, this study aimed to systematize knowledge about the EM in an intensive care environment and its impact, especially on the functional aspects and stay on mechanical ventilation (MV) and ICU.

METHODOLOGY

A systematic review and literature survey was conducted in the Medline, LILACS, SciELO and Cochrane databases, in the English and Portuguese languages, of studies published between 1998 and 2012. The keywords used were "early ambulation" OR "exercise" OR "rehabilitation" OR "physical therapy modalities" AND "Intensive Care Units" with correlates in Portuguese. Only trials with control group (CG) and full availability of access which evaluated the effect of EM in the ICU in adult humans above 18 years old were included. Studies using other resources, such as orthostatic board and electrostimulation not associated with Physical therapy were excluded. Analysis of titles and abstracts of investigations were carried out by two independent evaluators, and a third was triggered in the absence of consensus.

The selected clinical trials were assessed by the Physiotherapy Evidence Database (PEDro)[9] scale to evaluate the methodological quality using 11 pre-selected items, with scores from 0 to 10. The trials not indexed on this scale were rated by two evaluators that applied in a independent way. In the absence of consensus, a third reviewer undertook the analysis. These were physical therapists, being an expert, one graduate student and one Post Doctor with extensive experience in the studied area. The scale score was not used as a criterion for inclusion/exclusion of articles, but as an indicator of scientific evidence.

RESULTS AND DISCUSSION

There were found 875 studies, and, in the final selection, eight trials were included as shown in the diagram that can be seen in Figure 1, whose characteristics are found in Chart 1.

All investigations achieved a score ≥ 4 in the PEDro scale. Six addressed the influence of EM on the functionality[10-15], five on peripheral muscle strength (MS)[10,11,13,14,16], four on respiratory MS[3,15-17] and seven over the duration of MV and of ICU and hospital permanence period[10-13,15-17]. Five dealt with aspects such as feasibility and safety of mobilization in the ICU[12], dyspnea[15,17], muscle fatigue[17], mortality[11] and hospital costs[12]. The sample size ranged from 24 to 330 individuals of both genders, with a mean of 50 to 79 years, admitted in European[11,14,15,17], US[10,12], Asian[13], and Brazilian[16] ICUs.

Generalized weakness, decreased functional status and its impacts on quality of life represent complications of prolonged stay in ICU[4]. The present study analyzed the outcomes of MS, functionality, and length of hospital stay in MV related to EM in the ICU, and favorable responses were observed.

Muscular strength

Reviewed studies indicate gain of peripheral MS measured by the dynamometer[10,11,13] or manual muscle test (Medical Research Council – MRC)[10,14,16] in chronically ventilated patients after a rehabilitation program. One trial found an increase in the scale of strength (MRC) in the Treatment Group (TG), with an average gain of 6.6 (49±11 to 55±4, p=0.04), whereas the Countrol Group (CG) obtained 1.0 (39±14 to 40±10, p=0.82)[16]. Another study of critically ill patients who used the cycle ergometer in the lower limbs (LL) as a resource rehabilitation, beyond the normal physical interventions, demonstrated increased quadriceps MS between ICU and the hospital, discharges more relevant in TG (1.8 *versus* 2.3 N/kg^{-1}, p<0.01) than in CG (1.8 *versus* 2.0 N/kg, p<0.11)[11]. The literature suggests that the immobilization is an important cause of muscle weakness in mechanically ventilated patients, whose physical training could reverse and prevent this effect, as demonstrated in a clinical trial in which MS continued to deteriorate for six weeks in the CG[13]. The lack of a random distribution of patients and the lack of analysis of the intention to treat were negative aspects related to the quality of this study.

In relation to the amount and intensity of mobilization in the ICU, studies report frequency of once or twice a day, five to seven days per week for up to six weeks, and individual progression of intensity by the Borg scale for perceived exertion, ranging from 10 to 13 points[10,11,13,16]. In a study of deconditioned and ventilated for long periods individuals, the intensity of the effort ranged from 10 to 11 in the first week, progressing to 12 to 13 until the fifth week[13]. Another analysis with vented and more acute patients progressed the activity levels (bed, sedestation, orthostasis, ambulation and walked distance), doing physical therapy for 0.3 hours/day until discharge from the ICU[10]. The reviewed studies do not report the resistance imposed on exercises, the number of sets and repetitions performed, making the comparison between them and a possible standardization difficult.

Functional electrical stimulation (FES) has been used as a resource for the preservation of muscle mass in critically ill patients and for the recovery of MS during rehabilitation[14,17]. By comparing the effects of active mobilization with and without FES in patients with chronic obstructive pulmonary disease (COPD), there was MS improvement in both groups (p<0.05), though higher in the TG (p=0.02), demonstrating additional effects in the rehabilitation of FES[14]. One study found no significant difference between the TG and CG, respectively, on peripheral MS (MRC of 52 and 48, p=0.09) and handgrip (39 and 35 kg-force, p=0.67) on hospital discharge[10]. However, its intervention focused on the performance of functional tasks until the return to an independent status (Barthel>70) or hospital discharge, and did not use resistance exercises, which may have influenced the low gain in the MS. Another study also

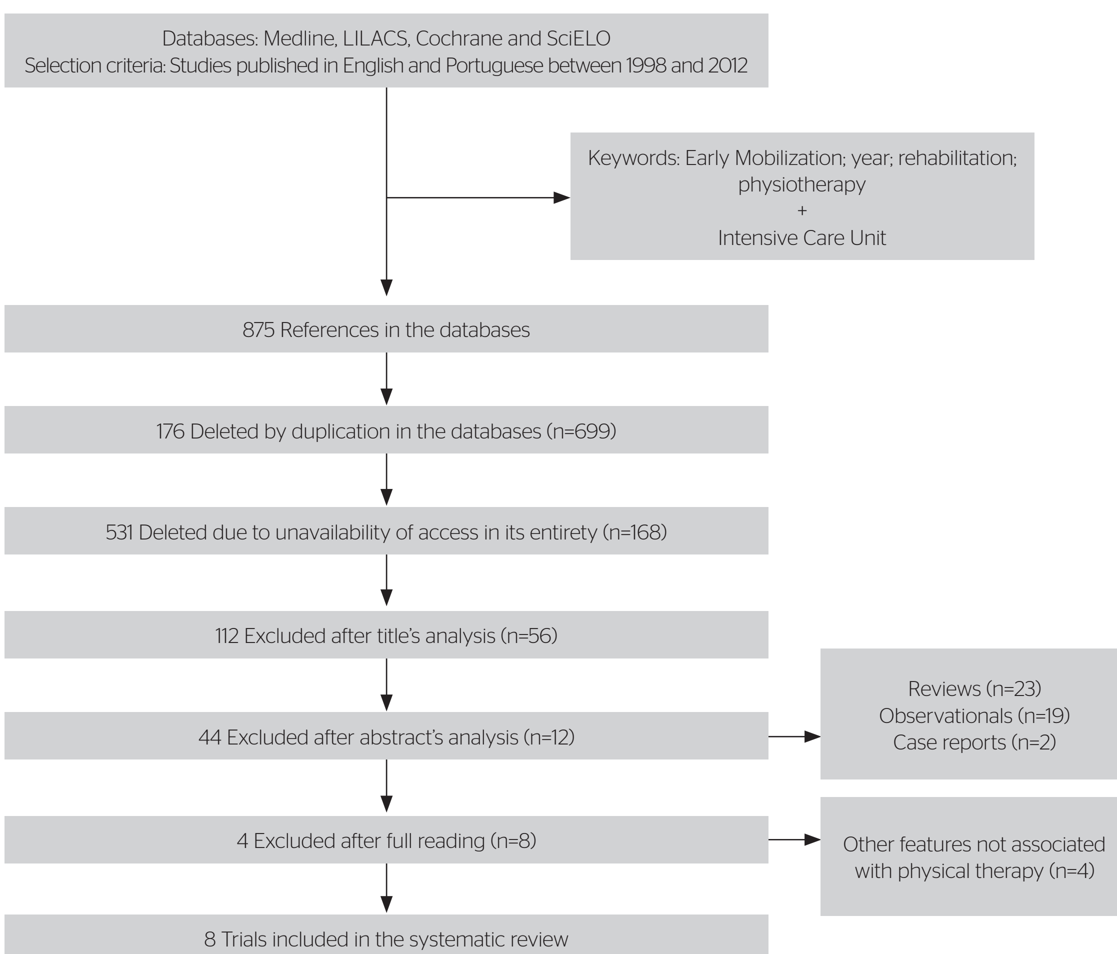

Figure 1. Diagram of the selection of articles

Chart 1. Description of selected studies

Author/Year	Study Type	PEDro Scale	Sample	Interventions	Variables evaluated	Results
Dantas et al. (2012)[16]	Controlled randomized prospective	6/10	n=28 – IG: 14 (59±15,2 years) and CG: 14 (50,4±20,4 years). Patients on MV for less than seven days .	IG: Stretching, Passive, active and resisted exercises, transfers, cycle ergometer of the lower limbs, balance training, and deambulation, 2 times/day, every day until ICU discharge. CG: Passive and active-assisted exercises 5 days/week.	Peripheral MS (MRC) and respiratory (MIP and MEP), duration of MV and hospitalization.	IG: Increased MIP and peripheral MS. There was no significant gain in MEP in both groups and no difference in duration of MV and hospitalization.
Schweickert et al. (2009)[10]	Controlled randomized prospective	8/10	n=104 – IG: 55 (54,4 years) and CG: 49 (57,7 years). Patients on MV <72 hours with the expectation of another 24 hours and functional independence two weeks before admission (Barthel≥70).	IG: Progressive Exercises for upper and lower limbs, sedestation, trunk control, functional tasks, training transfers and ADLs, stationary gait and deambulation 7 days/week, with daily interruption of sedation in both groups. CG: Physical therapy only after medical clearance.	FIM, Barthel Index, ADL, free fan days, distance traveled, MS (MRC and hand grip), hospitalization time.	IG: Higher scores on the Barthel number of independent ADLs and walking distance in discharge, with most previous functional return; shorter duration of delirium, and more ventilator-free days. There was no difference in MS and time stayed in ICU and in the hospital.
Burtin et al. (2009)[11]	Controlled randomized prospective	4/10	n=67 – IG: 31 (56±16 years) and CG: 36 (57±17 years). Patients with critical illness with an expected ICU stay≥7 days.	IG and CG: Respiratory physiotherapy, passive or active mobilization of upper and lower limbs and deambulation, 5 days/week. IG also performed lower limb cycle ergometer for 20 minutes, 5 days/week.	6MWT, SF-36, handgrip, quadriceps strength (dynamometer), functional status, time of weaning, hospitalization and mortality.	IG: Increased isometric quadriceps MS, functionality (6MWT) and functional status (SF-36). There was no difference in grip strength, mortality 1 year after discharge and time of weaning and time stayed in ICU and hospital.
Morris et al. (2008)[12]	Prospective cohort	4/10	n=330 – IG: 165 (54±16,8 years) and CG: 165 (55,4±16,8 years). Patients with ARF, three days of admission and intubation≥48h.	IG: Protocol on 4 levels (passive, active and resisted exercises, sedestation for 20 minutes 3 times/day, transfers and deambulation, 7 days/week. CG: passive exercise and repositioning every 2 hours, 5 days/week.	Hospitalization and MV time, hospital costs, and number of days for the first leaving the bed.	IG: Reduced length of stay in ICU and hospital, hospital costs and fewer days for first leaving the bed. There was no difference in duration of MV.
Chiang et al. (2006)[13]	Controlled randomized prospective	4/10	n=32 – IG: 17 (mean: 75 years) and CG: 15 (mean: 79 years). Patients on MV via TQT for more than 14 days.	IG: Exercises for upper and lower limbs, diaphragmatic breathing, functional workout in bed, transfers and walking, 5 times/week for 6 weeks. CG: Encouraging verbal to physical mobilization, not routinely.	Respiratory MS (MIP and MEP) and peripheral (grip strength), functionality (FIM, Barthel, 2 minute walk test), time off of MV.	IG: Increased peripheral and respiratory MS and free time on the MV, improvement in FIM and Barthel. At the end, 53% of IG were able to ambulate and 0% GC.
Porta et al. (2005)[18]	Controlled randomized prospective	5/10	n=66 – IG: 32 (70±5,6 years) and CG: 34 (72±5,2 years). Patients recovering from ARF weaned at 48 to 96 hours after intubation.	IG: Exercises for upper and lower limbs, respiratory therapy, deambulation, functional exercises, trunk control and transfers for 6 weeks with daily 45 minute sessions and load progression in the cycle ergometer of the upper limbs (15 days for 20 minutes). CG: Kinesiotherapy.	Inspiratory MS, dyspnea and muscle fatigue.	IG: Reduced muscle fatigue and dyspnea and improvement in inspiratory MS.
Zanotti et al. (2003)[14]	Controlled randomized prospective	4/10	n=24 – IG: 12 (66,2±8 years) and CG: 12 (64,5±4 years). Patients Confined to bed (≥30 days) in MV with CRF, hypercapnic COPD, atrophy and hypotonia.	IG: Kinesiotherapy and FES in lower limbs for 30 minutes (5 minutes at 8 Hz and 250 ms and 25 minutes at 35 Hz and 350 ms), 5 days/week for 4 weeks. CG: Just kinesiotherapy.	Peripheral MS, cardiorespiratory function (oxygen saturation, RR and HR) and bed-chair transfer.	RR reduction in IG, and improved peripheral MS in both groups, being higher in IG. There was no difference in HR and oxygen saturation. IG moved from bed to chair in fewer days.
Nava (1998)[15]	Controlled randomized prospective	4/10	n=80 – IG: 60 (65±6 years) and CG: 20 (67±9 years). COPD patients recovering from ARF	IG and CG: 2 daily sessions of 30-45 minutes sedestation, Passive, active and resisted exercises and deambulation. IG: TMR (threshold, 10 minutes, 2 times/day, 50% of MIP), stationary bike (20 minutes, 15 watts), stairs (25 steps 5 times) and treadmill (30 minutes, 2 times/day) for 3 weeks.	Length of stay in ICU, distance walked during the 6MWT, dyspnea and inspiratory MS (MIP).	IG: Improvement in 6MWT with lower HR at rest and after 6MWT increased MIP and reducing the degree of dyspnea. There was no significant difference regarding the length of stay in ICU.

IG: Intervention Group; CG: control group; MV: mechanical ventilation; LL: lower limbs; ICU: Intensive Care Unit; MS: muscular strength; MRC: Medical Research Council; MIP: maximal inspiratory pressure; MEP: maximal expiratory pressure; UL: upper limbs; ADL: activities of daily living; FIM: Functional Independence Measure; 6MWT: the six-minute walk test; SF-36, Short Form Health Survey; ARF: acute respiratory failure; TQT: tracheostomy; CRF: chronic respiratory failure; COPD: chronic obstructive pulmonary disease; FES: Functional electrostimulation; RR: respiratory rate; HR: heart rate; TMR: respiratory muscle training found no difference in grip strength between the groups ($p=0.83$), probably because of its intervention was centered on the lower limbs[11].

Association between strength and function was observed in some studies[11,14]. Positive correlation between the six-minute walk test (6MWT) with quality of life (SF-36) ($p<0.001$; $r=0.55$) and quadriceps MS ($p=0.002$; $r=0.40$), and the last one with the SF-36 ($p<0.001$; $r=0.46$) at discharge, was identified by a study that used the LL cycle ergometer in critically ill patients. This correlation suggests that the quadriceps MS can contribute to the performance of the walk and the feeling of functional well-being[11]. In this study[11], the quadriceps MS variable showed greater gains in TG compared to CG, between ICU and hospital discharges (1.83±0.91 *versus* 2.37±0.62 N/kg^{-1} and $p<0.01$ in TG; 1.86±0.78 *versus* 2.03±0.75 N/kg^{-1} and $p=0.11$, in the CG). The TG also had higher values on the 6MWT compared to CG at discharge (196 [126-329] *versus* 143 m [37-226], $p<0.05$) and the SF-36 (21 [18-23] *versus* 15 points [14-23], $p<0.01$). However, these values can not be considered different due to the intersection of the confidence intervals[11]. Another study in patients with COPD bedridden that received MV and used FES observed gain of MS compared to CG (2.16±1.02 *versus* 1.25±0.75, $p=0.02$) and reduced the number of days required for bed-chair transfer compared to individuals who did not use the technique (10.75±2.41 *versus* 14.33±2.53, $p=0.001$)[14].

Additionally, studies have observed an improvement in inspiratory MS represented by the increase in maximal inspiratory pressure (MIP) after the exercise program associated with diaphragmatic breathing[13] (46 to 60 cmH_2O, $p<0.05$), respiratory muscle training with linear load[15] (45±1 to 61±1 cmH_2O, $p<0.05$), lower limb cycle ergometer[16] (52±1 to 66±2 cmH_2O, $p=0.02$) and upper limb (UL)[18] (43±1 to 52±2 cmH_2O, $p<0.001$). A possible limitation of these studies, for ethical reasons, it was the lack of a real CG, in which no rehabilitation program was conducted.

Functionality

Clinical trials demonstrated increased functional independence through the Barthel Index and the Functional Independence Measure (FIM) after rehabilitation in patients on MV[10.13]. One study reported that FIM appears to be more sensitive to detect changes that the Barthel, however few have reported what constitutes a clinically significant change on these scales[13].

Increased number of daily life activities and walked distance at hospital discharge were observed by a study in which a return to the pre-independent morbidity was observed in 59% of TG compared to 35% in the CG ($p=0.02$; OR=2.7; 95%CI 1.2–6.1)[10]. Another study with individuals unable to walk on admission showed, after six weeks of physical training, that 53% of TG regained their ability to walk, with average distance traveled in two minutes 42.9±12.7 m (n=9), unlike CG, which remained bedridden and unable to walk at the end of the study[13]. A third analysis in patients with COPD in the ICU for respiratory care showed that 87% regained their walking independence after the rehabilitation program[15]. Despite improvement in the studies cited, the discrepancy in the values of the treatment effect is due, probably, the heterogeneity of the populations studied and the percentage of ventilated patients.

Delayed onset of physical rehabilitation during MV was associated with worse performance after ICU discharge[19]. A significant improvement in the supine-sedestation-orthostasis transfer activities after EM program[14,19,20], as well as gains in the time necessary to first leaving the bed in the TG (5 *versus* 11 days, $p<0.001$)[12] have been observed in patients on MV. One study showed shorter time to bed-chair transfer (10 *versus* 14 days, $p=0.001$) in COPD patients mobilized with the addition of FES of the lower limbs, reflecting improved functional capacity and quality of life[14].

The use of the cycle ergometer in the lower limbs in addition to standard intervention resulted in improved self-perceived functional status (SF-36) compared to CG at discharge (21 *versus* 15 points, $p<0.01$). In this study[11], the authors found no difference between groups on the ICU and the hospital discharges in the ability to orthostasis through the Berg scale ≥ 2 ($p=0.4$; $p=0.7$), and independent ambulation through functional classification ≥ 4 ($p=0.72$; $p=0.18$)[11]. In contrast, the TG patients had greater distance walked at hospital discharge (196 *versus* 143 m, $p<0.05$) independently (73 *versus* 55%), with a trend towards greater need for rehabilitation after discharge in the CG (17 *versus* 10%), although not significantly[11]. Some limitations of this study are the small sample size and the lack of rigorous standardization during time on emergency, in which TG had higher time on the ICU before inclusion in the study (14 *versus* 10 days, $p<0.05$), with longer period of intravenous sedation (11 *versus* 8 days, $p<0.05$). These, added to the fact that TG has had the application of cycle ergometer in the lower limbs as the unic differentiated conduct of the CG, may have influenced their statistical significance.

Ambulation increase after transfer of ventilated patients to the ICU, where the activity is the care's goal, was verified by a study (p<0.001). The authors reported that sedatives, even if intermittent, reduced the likelihood of ambulation and showed that the ICU can contribute to unnecessary immobilization, with consequent physical dysfunction (p=0.009; OR=1.9; 95%CI 1.1-3 1)[19]. Another study observed increased in mobility after improving the quality of physical therapy and rehabilitation services in the ICU, resulting in reduction of sedatives and greater alert state of patients (p=0.03)[20]. Clinical trials that conducted rehabilitation program in the ICU observed an increase in walked distance and ambulation ability at discharge, suggesting that the MV does not prevent the acquisition of mobility[10,11,13,15].

Internment/ventilation

Shorter ICU (5.5 *versus* 6.9 days, p<0.025) and hospital (11.2 *versus* 14.5 days, p<0.006) stay were observed in a study in patients with acute respiratory failure (ARF), without an increase in costs[14]. Although other studies[11,15,16] observed fewer hospital days in the TG, this difference was not significant relative to the length of stay in ICU and hospital, probably because of the small sample size of these studies.

The time of weaning was analyzed only for a clinical trial, which found no difference between the TG (exercises and cycle ergometer) and the CG (exercises) of critically ill patients (6 *versus* 6 days p=0.40)[11]. Significant reduction in the time of weaning after the rehabilitation program was noted by a study in a multidisciplinary unit, in which 30% of patients were weaned within seven days, showing inverse correlation between UL MS and weaning time (r=0.72 and p<0.001), in which, for each point gained in the range of MS (MRC), there was a decreased in seven days of the time of weaning[21]. The discrepancy between the findings may be due to the longer period of sedation in ICU before the TG inclusion in the study, and the differentiation of CG only through the use of cycle ergometer. However, despite no significant improvement in the weaning time, the trial identified improvement in the 6MWD, in quadriceps MS and the quality of life.

An analysis found that daily interruption of sedation combined with physical therapy and early occupational in mechanically ventilated patients resulted in more ventilator free days (23.5 *versus* 21.1 days, p=0.05)[10]. Another trial with patients undergoing prolonged MV (52 and 46 days in the TG and CG, respectively) also showed increased in MV free time in the TG (8.9 *versus* 4.8 hours, p<0.01), with greater removal capacity of the ventilator during at least 12 hours/day (47 *versus* 20%)[13]. This study[13] found correlations between the VM free time and functional outcome (r=0.66), suggesting that the prolonged MV is associated with worsening functional performance, so physical training should not be underestimated in these patients.

Other aspects

Low occurrence of adverse events after exercise protocol was observed by a clinical trial demonstrating safety and feasibility without increasing costs[12]. As for symptoms, studies show a reduction in dyspnea[15,18] and muscle fatigue[18] after early training in patients recovering from ARF.

Although prolonged period on MV is associated with a greater decline in physical function compared to cognitive, one study found an increase in the cognitive domain scores in the TG, with significant deterioration in the CG, after physical training in patients undergoing prolonged MV[13]. Another study found that the daily interruption of sedation and early physical and occupational therapies in critical patients on MV resulted in shorter duration of delirium (2 *versus* 4 days; p=0.02)[10]. These findings demonstrate the relation between neuromuscular and cognitive functions and the EM importance for the preservation of these systems.

Additionally, studies found higher hospital mortality in CG (25 *versus* 18%, p=0.530[10] and 18.2 *versus* 12.1%, p=0.125[12]) compared to TG that made EM, although not significantly. Another study evaluated the mortality rates during hospitalization (24 *versus* 16%) and one year after discharge (10 versus 8%), whereas they were higher in the TG, but with no significant difference between groups (p=0.29) and no association of the causes of death reported by intensivists with proposals interventions[11].

The key factors that influenced the quality of the studies reviewed were: lack of randomisation, blindiness of the evaluators, adequate monitoring and analysis of the intention to treat[11-16,18].

CONCLUSION

EM in the ICU seems to minimize the loss of functional abilities, with favorable results for the prevention and treatment of neuromuscular disorders resulting from increased survival of patients and prolonged permanence in bed, as demonstrated by studies of this review. Its use in clinical practice seems to be feasible and safe, being able to promote improvement in functional capacity, quality of life, peripheral and respiratory MS, and reduced length of stay and MV. It is suggested the realization of clinical trials with greater standardization for description and comparison of different treatment protocols in order to identify the frequency, dose, intensity and types of therapeutic exercises needed to improve outcomes associated with physical therapy.

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