

Good tolerance and benefits should make early exercises a routine in patients with acute brain injury

Boa tolerância e benefícios de exercícios precoces devem fazer parte da rotina em pacientes com lesão cerebral aguda

Rayssa Bruna Holanda Lima*
Flávia Manhani Muzette
Karla Luciana Magnani Seki
Gustavo Christofoletti

Universidade Federal de Mato Grosso do Sul (UFMS), Campo Grande, MS, Brazil

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*** Correspondence:** rayssa.lima_@hotmail.com

Abstract

Introduction: The negative impact of prolonged immobilization results a physical decline during hospitalization in patients with acute brain injury. **Objective:** To investigate the benefits of early exercises on the mobility of patients with acute brain injury assisted at an Intensive Care Unit (ICU). **Methods:** This is a prospective, single-blind, controlled clinical trial. A total of 303 patients were assessed. Due to eligibility criteria, exercise protocol was applied in 58 participants, 32 with brain injury caused by traumatic event and 26 with brain injury caused by cerebrovascular event. Exercise began 24 hours after patients' admission at the ICU. Participants were submitted to passive and active mobilization protocols, performed according to level of sedation, consciousness and collaboration. Statistical analysis was conducted with repeated measures analysis of variance. Significance was set at 5%. **Results:** The group of patients with traumatic brain injuries was younger (p = 0.001) and with more men (p = 0.025) than the group of patients with clinical events. Most exercise sessions were performed in sedated patients. By the end of the protocol, participants with traumatic and clinical brain injury were able to do sitting and standing exercises. Both groups were similar on ICU discharge (p = 0.290). The clinical group presented better improvement on level of consciousness than the traumatic group (p = 0.005). **Conclusion:** Participants with an acute brain injury presented at the time of discharge from the ICU good mobility and improvement in the level of consciousness.

Keywords: Brain injuries. Critical care. Exercise therapy. Intensive Care Units. Neurological rehabilitation.

Resumo

Introdução: *O impacto negativo da imobilização prolongada resulta em declínio funcional durante a hospitalização em pacientes com lesão cerebral aguda.* ***Objetivo:*** *Investigar os benefícios dos exercícios precoces na mobilidade dos pacientes com lesão cerebral aguda atendidos em uma Unidade de Terapia Intensiva (UTI).* ***Métodos:*** *Trata-se de um estudo clínico prospectivo, controlado e cego. Foram avaliados 303 pacientes. Devido aos critérios de elegibilidade, o protocolo de exercício foi aplicado em 58 participantes, 32 com lesão cerebral causada por evento traumático e 26 com lesão cerebral causada por evento cerebrovascular. O exercício começou 24 horas após a admissão dos pacientes na UTI. Os participantes foram submetidos a protocolos de mobilização passiva e ativa, realizados de acordo com o nível de sedação, consciência e colaboração. A análise estatística foi realizada com análise de medidas repetidas de variância. A significância foi estabelecida em 5%.* ***Resultados:*** *O grupo de pacientes com lesão cerebral traumática foi mais jovem (p = 0,001) e com mais homens (p = 0,025) do que o grupo de pacientes com eventos clínicos. A maioria das sessões de exercícios foi realizada em pacientes sedados. Ao final do protocolo, os participantes com lesão cerebral traumática e clínica foram capazes de fazer exercícios de sentar e ficar em pé. Ambos os grupos foram semelhantes na alta da UTI (p = 0,290). O grupo clínico apresentou melhor ganho no nível de consciência do que o grupo traumático (p = 0,005).* ***Conclusão:*** *Os participantes com lesão cerebral aguda apresentaram no momento da alta da UTI boa mobilidade e melhora do nível de consciência.*

Palavras-chave: *Lesões cerebrais. Cuidados intensivos. Terapia por exercício. Unidades de Terapia Intensiva. Reabilitação neurológica.*

Introduction

Brain injuries constitute a public health issue. Commonly related to head trauma and cerebrovascular events, brain injuries present high levels of morbidity and they are responsible for impacting patients' cognitive, motor and psychosocial functions.[1,2]

Advances in intensive care unit (ICU) have led to higher survivals rates of people with brain injuries. Contrasting with that, physical decline is devastating during hospitalization.[3-5] Its negative effects are extensively reported in ICU patients. The benefits of early mobilization have been shown recently, but only a few studies have addressed exercises in neurocritical patients.[6,7]

Hospitalized patients are subject to risks of sepsis, multiple organs failure, prolonged mechanical ventilation, use of corticosteroids and neuromuscular blocking-drugs – all factors that collaborate for the development of a syndrome called ICU Acquired Weakness (ICU-AW).[8] The ICU-AW have incidence rates from 25% to 100% of patients under mechanical ventilation, leading to an increase in hospitalization length.[9] Interventions that shorten patients' recovery brings potential to improve life expectancy and reduce hospital costs.

In the case of neurocritical patients, motor rehabilitation during the initial phase of the disease prevents pneumonia, contractures and thromboembolisms.[10] The literature, however, is scarce in relation to the safety of application of early mobilization protocols in patients with acute brain injuries. Moreover, the factors that may determine patients' functional recovery in ICU are still controversial.[11] Due to that, the present study investigated the benefits of an early exercise program regarding mobility in patients with acute brain injury and analyzed factors associated to patients' functional recovery in the ICU environment.

Methods

This is a clinical study carried out at the adult ICU of a high complexity hospital in the city of Campo Grande/MS, Brazil. The study was approved by the Institutional Ethics Committee (protocol number 2,170,031) and it was performed in accordance with the Declaration of Helsinki. Written informed consent from human subjects was obtained prior the assessments. The project was registered prospectively in the Brazilian Registry of Clinical Trials (RBR-6tps79 registry), prior to patient enrollment. This study conforms to all CONSORT guidelines.

The inclusion criteria comprised adult patients diagnosed with acute brain injury by traumatic event or caused by cerebrovascular event (confirmed by clinical history and brain tomography), hospitalized for more than 48 hours and whose parents have given written consent to participate in this research. Exclusion criteria involved patients with brain tumor, those with pre-existing brain diseases, subjects admitted to the ICU under suspicion or already in brain death protocol, individuals with previous motor sequelae, in use of orthopedic external fixators, musculoskeletal traction or with lower limb amputation. Subjects that had been through previous surgery, open abdominal wound or spine cord lesion were also excluded from this study.

Participants were included in the first 24 hours of admission in the ICU. The first step was to collect (and daily update) sociodemographic characteristics, personal history, cause of brain injury, type of treatment, disease severity (assessed with the Acute Physiology and Chronic Health Evalution II, APACHE-II),[12] brain tomography, sedation time, orotracheal intubation time and hospital stay. APACHE II score is a form of assessment and classification of the disease severity index, and its main objective is to quantitatively describe the degree of organic dysfunction in critically ill patients.[12]

The sample size was estimated assuming a power of 95%, with a 5% type I error and an effect size of 0.31 – based on previous study that assessed effects of exercise on ICU length of stay.[13] Participants were divided into two groups according to the cause of brain injury: group of traumatic brain event and group of clinical (cerebrovascular) event. After the first 24 hours of admission, the presence or absence of sedatives, vasoactive drugs, hemodynamic aspects and clinical conditions were re-assessed in order to evaluate if the application of the exercise program could be initiated.

The sedation level of the participants was evaluated with the Richmond Agitation and Sedation Scale (RASS).[14] The Glasgow Coma Scale (GCS) was used to assess the level of awareness of the participants.[15] The instrument was applied in the first 24 hours of suspension of sedation and in the last day before discharge from the ICU. Functionality was scored using the ICU Mobility Scale (IMS), measured in the awake patient on the day of discharge of the ICU.[16] This scale measures in a simple, fast and objective way the highest level of propagation by the patient during the performance of the proposed activities, developed based on ten levels of mobility. Patients able to walk independently, without a mobility aid, are considered to have higher scores.[16]

The exercise program was performed 24 hours after patient's admission at the ICU, once a day, with a 30 minutes session, five times a week (except on weekends), and respecting the following contraindications or interruption of mobilization upon reaching these parameters: systolic blood pressure < 90 mmHg, intracranial pressure > 22 mmHg, heart rate < 50 bpm or > 140 bpm, vasoactive drugs > 5 mg/min, PEEP > 12 cm H_2O, peripheral oxygen saturation < 90%, respiratory rate > 40 breaths per minute, and axillary temperature > 39 °C.

The exercise program was divided into two levels. The first level was performed in sedated patients, from which passive exercises were applied in the following muscle groups: shoulder abductors and adductors, elbow, wrist, hip, knee and ankle flexors and extensors. The second level was performed in patients without sedation or 24 hours after sedation suspension. This level was subdivided into 2A and 2B, according to the participant's collaboration. Level 2A was applied in non-sedated patients without collaboration and/or understanding. Level 2B was applied in collaborative patients who understood the commands.

The exercises program of the second level was performed in the seating position. In sublevel 2A, the patient should perform cervical and trunk exercises, with weight discharge in the upper limbs and passive exercises in the main muscles of the body. In sublevel 2B, the subject should perform pro-active exercises, trunk and cervical training, and weight discharge in upper and lower limbs with evolution to standing and gait training. For safety reasons, a second researcher assisted in the transfer of the patient from the sitting to standing position.

Statistical analysis

Data characterization was performed by number of events for the categorical variables, mean ± standard deviation for the continuous parametric variables and median (25% - 75% quartiles) for the continuous non-parametric variables. The comparison between the trauma and clinical groups for the variables age, APACHE II, sedation time, orotracheal intubation time, length of hospital stay and sedation, number of sessions performed at each level and functionality were assessed using the unpaired t-test or Mann-Whitney test. Regarding the variables comorbidity, sex, treatment, outcome and total number of sessions performed according to the levels of mobilization, contraindicated sessions and interrupted sessions were assessed using the chi-square test. At the level of initial and final ICU awareness in the trauma and clinical group, represented by the Glasgow variable, they were assessed using two-way ANOVA for the repeated measures model followed by the Tukey post-test. Significance level was set at 5%.

Results

Figure 1 shows the flowchart regarding the selection of the participants. A total of 303 patients were admitted at the ICU during eight months of assessments. Two hundred and forty-five participants were excluded for not meeting the eligibility criteria.

The anthropometric and clinical aspects of the participants are presented in Table 1. Groups were similar for orotracheal intubation time, sedation time and length of stay at ICU. Groups were different for age, sex and APACHE-II.

Twenty-two participants of the traumatic group (68.7%) and seventeen subjects of the clinical group (65.4%) were submitted to surgical procedures. Hospital deaths were seen in five patients of the traumatic group (15.6%) and in eight patients of the clinical group (30.7%). Groups were homogeneous for surgery ($p = 0.992$) and death incidence ($p = 0.290$).

Data about the exercise protocol used in the traumatic and clinical groups are described in Table 2. The majority of exercises was carried out in sedated patients. Groups were similar for number of sessions and for sessions per patient ($p > 0.05$ in all analyses).

Table 3 highlights the level of consciousness of the participants at the beginning and at the end of ICU admission. Repeated measured Anova pointed out that groups were similar at baseline, both improved at the ICU but the clinical group improved more than the trauma group.

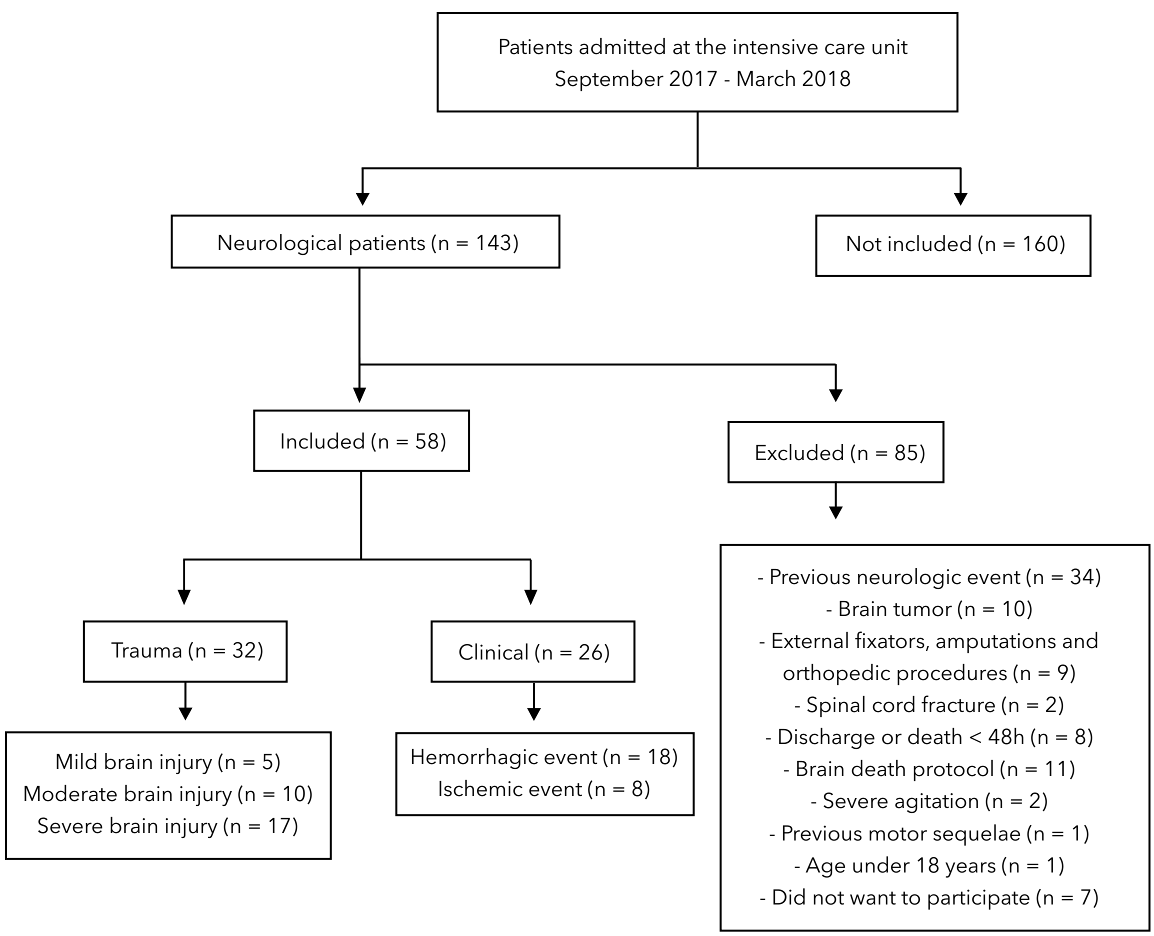

Figure 1 - Flowchart of the participants.

Table 1 - Clinical and anthropometric predictors in the traumatic and clinical groups

	Groups		p-value
	Trauma	Clinical	
Age, years	36.0 (24.5 - 59.5)	63.0 (59.0 - 69.0)	0.001
Sex (Female:Male)	7:25	14:12	0.025
APACHE-II, points	21.0 ± 7.0	25.0 ± 5.0	0.028
Sedation time (days)	5.0 (2.5 - 7.50)	5.0 (2.0 - 8.0)	0.962
Orotracheal intubation (days)	9.0 ± 4.3	9.0 ± 4.0	0.733
Length of stay at the ICU (days)	11.5 ± 6.3	12.5 ± 7.0	0.584

Note: Data are described in number of events for sex, mean ± standard deviation for APACHE-II, orotracheal intubation and length of stay at the ICU, and median (25-75% quartiles) for age and sedation time; p-values in the qui-square test for sex; p-values in the independent Student t-test for APACHE-II, orotracheal intubation and length of stay at the ICU; p-values in the Mann Whitney U-test for age and sedation time.

Table 2 - Exercise protocol and Intensive Care Unit (ICU) Mobility Scale for the trauma and clinical groups

Exercise protocol		Groups		p-value
		Trauma	Clinical	
Level 1	Number of sessions	108	82	0.993
	Sessions per patient	3.0 (2.0 - 5.0)	3.0 (2.2 - 5.0)	0.903
Level 2A	Number of sessions	61	49	0.091
	Sessions per patient	2.0 (1.5 - 4.5)	3.0 (2.0 - 3.5)	0.661
Level 2B	Number of sessions	21	8	0.682
	Sessions per patient	2.6 (0.9 - 3.0)	2.0 (0.8 - 4.0)	0.277
ICU Mobility Scale	Points	7.0 (7.0 - 7.0)	6.0 (3.2 - 8.0)	0.622

Note: Data are described in frequency of events for number of sessions and median (25-75% quartiles) for sessions per patient and mobility; p-values in the qui-square test for number of sessions; p-values in the Mann Whitney U-test for sessions per patient and functional independence.

Table 3 - Level of consciousness at the beginning and end of the exercise protocol

Groups	Time		p-values		
	Baseline	Final	Group	Time	Interaction
Trauma	8.0 ± 3.0	10.0 ± 3.0	0.359	0.001	0.005
Clinical	6.0 ± 3.0	10.0 ± 2.0			

Note: Data are described in mean ± standard deviation; p-values in repeated measures Anova.

Discussion

Neurocritical patients often require ICU monitoring and treatment. It is known that admission to the hospital, whatever the patient's profile is, leads to physical decline.[11] Due to that, our study investigated the benefits of early exercises in patients with acute brain injury at an ICU environment. Results showed that most sessions were carried out in sedated patients. By the end of our mobilization protocol, participants with traumatic and clinical injuries presented good tolerability to exercise and mobility progression at ICU discharge (both groups with good IMS scores). These findings are promising, although they should be analyzed in face of some particularities.

Previous studies showed that men usually have high risk of developing brain injuries due to traumatic accidents, and women, differently, are more likely to suffer brain injuries as a consequence of cerebrovascular events (ischemic or hemorrhagic).[17,18] Such pattern was found in this study and it is detailed in Table 1.

The authors originally recruited 303 participants. Eligibility and feasibility criteria, however, ended up with 80% of sample losses. Although a representative sample size is important to control type 1 and 2 statistical errors, the inclusion of heterogeneous participants could create bias and corrupt the results. In this sense, the authors opted to restrict the sample size and exclude potential bias. As a consequence of the rigid selection criteria, both traumatic and clinical groups were similar on several variables that compromise patients' health, such as sedation time ($p = 0.962$), orotracheal intubation time ($p = 0.733$) and length of stay at the ICU ($p = 0.584$).

As presented in Table 2, most of the exercise sessions were carried out in sedated patients. This happened because sedoanalgesia is common in neurocritical patients.[19] Although early mobilization promote benefits to patients and it decrease hospital length, professionals should be aware and constantly check the use of central nervous system depressors before beginning the sessions.[20-22]

For this study, the assessment of patients' sedation was performed through RASS and with cranial tomography images. Since there are several instruments assessing sedation and consciousness at ICUs, authors suggest more discussions and a proper guideline detailing sedation strategies in neurocritical environment.

Morris et al.[23] were one of the first in describing motor protocols in ICU. These authors used exercises progression according to patients' neurological function. In the present study, we performed a systematic exercise protocol as a strategy to facilitate the progression of mobilization and to assess patients' gains. This aspect was important to show benefits of early exercises in acute brain injuries, and to corroborate results from previous studies.[23-26]

Patients in the neurological ICU participating in an early mobility program consisting of a progression from head of bed elevation to outof-bed activity and walking not only demonstrated improved physical function and also to reduce the complications associated with immobility in the ICU.[7] Early mobility programs have been shown participants initiated early rehabilitation with higher frequency but shorter duration of sessions.[7,27]

However, intensive care environment are multiple factors that can limit the performance of rehabilitation in the neurological profile. Some of them involve the complexity of injuries, risk of iatrogenic neurological damage, presence of external fixation devices, movement range restrictions, intracranial pressure and the risk of rupture of external ventricular drains.[27,28]

Moreover, in traumatic brain injury, scientific data is still not clear as to the benefit of early mobilization, although other neurological disorders indicate that early mobilization positively influences the improvement of functionality[29] and a recent large rehabilitation trial (AVERT) on stroke patients suggested that very early mobilization protocol started within 24 hours, from the acute event was associated with a reduction in the odds of a favorable outcome at three months.[27]

Therefore, despite intensive rehabilitation of patients after severe traumatic brain injury is feasible[30] and safe,[28] more research is needed in the area of early mobilization for severe brain injury, especially in subgroups of participants, patients with traumatic brain injury, stroke and hypoxic brain injury, for example.[30,31]

Increased intracranial pressure (ICP) may be a determining factor for the progression of mobilization. Neurosurgery patients with an external ventricular drain (EVD) due to increased intracranial pressure often remain on bed rest and was reported reasons for delaying mobilization in these patients: fear of dislodging the EVD, raised ICP during mobilization when the EVD is closed to drain, causing intracranial vasospasm, accidentally over-draining cerebral spinal fuid from the patient's EVD due to improper clamping during mobilization, and lack of therapist experience with an EVD and working in a neurosurgical ICU.[27,32] Rehabilitation therapists must have full understanding of treatment precautions and contraindications and continuously remain alert to patient signs and symptoms indicating the need to modify or terminate treatment.[27]

The exercise program improved the level of consciousness of patients from both groups. Repeated measures Anova, however, showed that improvement in the clinical group was higher than in the traumatic group. The authors attribute this finding to patients' disease severity, where APACHE-II scores of the traumatic group showed higher commitment and risk of death than the score of the clinical group ($p = 0.028$).

The originality of this study upon others is that this protocol included three levels of exercises (1, 2A and 2B) and, at the end, subjects should be able to stand up and walk safely with help of physicians and physical therapists. Readers should be aware that the profiles of brain injuries are wide and this exercise protocol may not be suitable to all patients.

The authors encourage readers to take in consideration the following limitations. First, the absence of a control group makes impossible to affirm that the improvement seen in this study was restricted to the exercise program. Other therapies applied concomitantly likely affected the results. The authors opted for not including a control group with no therapy assuming that they would encounter ethical barriers for such a proposition. Second, the final sample size of this study was relatively small when compared to the initial recruitment. Even though, it must to be highlighted that this research exceeded the minimum of participants stipulated in the sample size calculation. Finally, participants were not followed up after hospital discharge. Due to that, it is not possible to affirm that benefits found at ICU remained in patients' home.

Conclusion

The proposed exercise program could be fully applied (all levels) in both groups of studied participants, and at the time of discharge from the ICU, good mobility and improvement in the level of consciousness in the neurocritical profile. Studies with more protocols must be carried out to isolate the effect of exercise in relation to other therapies applied concomitantly in the neurocritical patient.

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Authors´ contributions

RBHL, KLMS, GC were responsible for the research idea, study design, and data analysis and interpretation. RBHL and FMM were responsible for the data acquisition. All the authors contributed to the article writing and editing.

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