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EFFECTS OF EARLY MOBILIZATION ON THE INCIDENCE OF DELIRIUM IN THE ICU. REVIEW OF SYSTEMATIC REVIEWS

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ABSTRACT

INTRODUCTION: Delirium is understood as an acute change in mental state, with a wide variety of neuropsychiatric signs and symptoms, with a fluctuating course and explained by disorders in cerebral homeostasis. Early mobilization (EM) is defined as an energy-consuming activity that aims to maintain or support the patient's mobility through passive or active movement exercises. Objective: to review knowledge about the effects of EM on delirium in critically ill patients in hospital. Methods: a literature review, with research in the PubMed database, using meta-analyses published between 2014 and 2024, in English, using the terms: delirium, intensive care units and rehabilitation. Results: 7 articles discussing EM in intensive care units were included, and conflicting and inconclusive results were found on the effects of EM in relation to the duration and incidence of delirium and functional outcomes. A single strategy for performing EM was also not defined, the ABCDEF bundle obtained the most favorable results in relation to functional outcomes, incidence and duration of delirium. Conclusion: EM is both viable and safe, being an important tool in the multidisciplinary care of critically ill patients, however its use for delirium has demonstrated conflicting results. The available studies present large methodological differences, a small population studied, and, in general, few studies addressing the subject. We emphasize the need for further studies to be able to define both the effectiveness of the EM and a protocol for its implementation.

Keywords: Rehabilitation; Delirium; Intensive Care Units.

INTRODUCTION

Delirium is understood as an acute alteration of mental status, characterized by a wide range of neuropsychiatric signs and symptoms, with a fluctuating course and explained by disorders in cerebral homeostasis. Some authors refer to it as Acute Brain Insufficiency Syndrome. [1,2]

This condition is extremely common in hospitalized elderly patients. One-third of general medicine patients aged 70 years or older experience delirium; the condition is present in half of these patients at admission and develops during hospitalization in the other half. The prevalence in patients admitted to intensive care units (ICUs) who have undergone mechanical ventilation and in patients receiving palliative care can exceed 75% and 85%, respectively. [1]

In the study by Park and Kim, [3] the in-hospital mortality rates at 3, 6, and 12 months were significantly higher in patients with delirium. The delirium group also showed higher rates of adverse events, increased hospital costs, and higher rates of hospital readmission.

Delirium can be classified into three types. Hyperactive delirium is characterized by restlessness, agitation, and emotional lability. Hypoactive delirium is defined by the presence of apathy and reduced response capacity. Mixed delirium features alternating between hypoactive and hyperactive types. [4]

Delirium has a multifactorial etiology. Among non-modifiable risk factors, those stemming from preexisting patient conditions include advanced age and prior cognitive impairment; abstinence, smoking, and alcohol consumption. Modifiable risk factors relate to acute conditions or iatrogenic and environmental events that are amenable to intervention, such as emergency admission, hypoxia, pain, infections, physical restraints, sleep disturbances, invasive devices, surgical procedures, sedatives, opioid analgesics, and environmental factors like artificial lighting, noise, and family isolation.[5]

To prevent and treat delirium, non-pharmacological treatments such as Early Mobilization (EM) are recommended. EM is defined as any activity that expends energy, aimed at maintaining or supporting patient mobility through passive or active movement exercises. [6]

In a randomized controlled trial involving 104 patients, those in the EM intervention group demonstrated better functional outcomes (measured by the Barthel Index) at hospital discharge, a significant reduction in mechanical ventilation duration, and a notable decrease in the number of days with delirium during hospitalization. [7]

The aim of this work is to review the current knowledge regarding the effects of EM on in-hospital delirium in critically ill patients.

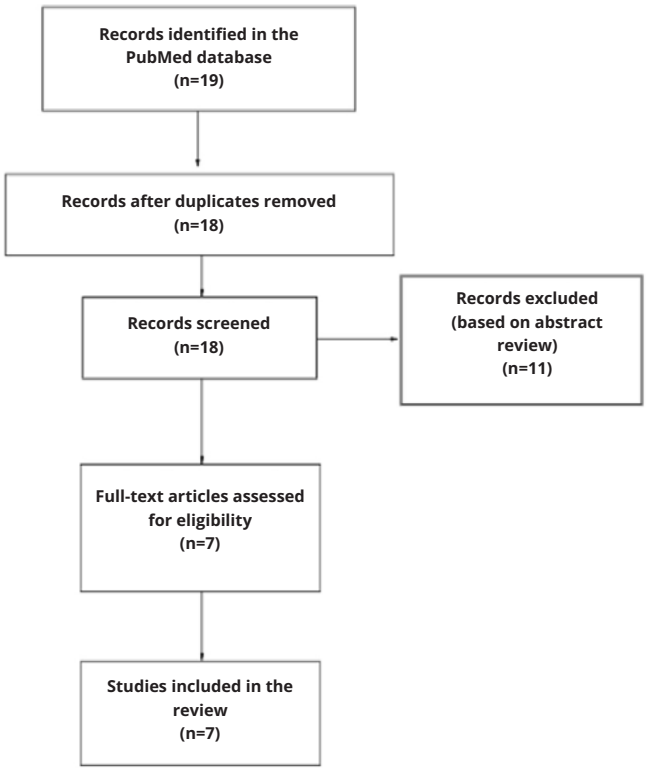
METHOD

A literature review was conducted in the PubMed database. The keywords used for the search were “delirium,” “intensive care units,” and “rehabilitation.” These keywords were combined using the Boolean operator AND (for different terms).

Articles were selected based on the following inclusion criteria: publication between January 2014 and May 2024, in Portuguese, English, or Spanish; and methodological design including meta-analyses with human samples.

Studies that did not address the effects of rehabilitation or Early Mobilization (EM) in patients with delirium and those for which full-text access was not available were excluded.

Figure 1 – Flowchart Demonstrating the Selection of Articles



RESULTS

Initially, 19 articles were found. After removing one duplicate and reviewing the abstracts, 12 articles were excluded for not meeting the inclusion criteria. The remaining 7 articles (totaling 42,003 patients) were assessed for eligibility and subsequently included in the review.

Data regarding the included articles can be viewed in Table 1.

Table 1. Summary of Included Articles, Their Objectives, and Main Conclusions
ABCDEF (Assess, prevent, and manage pain; Both spontaneous awakening and spontaneous breathing trials; Choice of analgesia and sedation; Delirium: assess, prevent, and manage; Early mobility and exercise; and Family engagement and empowerment); PICS (Post-Intensive Care Syndrome); MRC (Medical Research Council); ICU-AW (Intensive Care Unit-Acquired Weakness); ECR (Randomized Controlled Trial); RV (Virtual Reality); UTI (Intensive Care Unit); Early Mobilization (EM)

Table 1. Summary of Included Articles, Their Objectives, and Main Conclusions

Author/Yer	Number of participants	Objective	Conclusion
Sosnowski[8], et al / 2022	29.576	Identify the effectiveness of the ABCDEF bundle in delirium prevention, functional prognosis, and quality of life in adult ICU patients, and identify barriers and facilitators for the adoption of the ABCDEF bundle in practice.	Positive results for patients, including a reduction in the incidence and duration of delirium, have been demonstrated in the available research. Although limited and of variable quality, an increasing body of research supports the implementation of the ABCDEF bundle in its entirety for both ventilated and non-ventilated ICU patients. High-quality randomized controlled trials are needed to formally determine the relationship between the ABCDEF bundle and delirium outcomes in ICU settings worldwide.

Fuke[9], et al. / 2018	590	This meta-analysis aimed to evaluate the effectiveness of early mobilization (EM) for the prevention of post-intensive care syndrome (PICS) in ICU patients.	Early mobilization (EM) has a limited effect on the prevention of post-intensive care syndrome (PICS), although it has led to significant improvements in short-term physical outcomes, including MRC scores and the incidence of ICU-acquired weakness (ICU-AW). However, EM did not have a significant effect on cognitive function ('delirium') or mental health outcomes, nor on mortality in critically ill patients. Furthermore, rigorous randomized controlled trials are needed to confirm these results.
Xu[10], et al. / 2022	1.291	Search and collect randomized clinical trials on delirium in ICU patients following cognitive-functional exercise therapy interventions for systematic review and meta-analysis, in order to provide evidence for the prevention and treatment of delirium.	The results of the meta-analysis confirmed that cognitive-functional exercises can reduce the incidence and duration of delirium in ICU patients, as well as shorten patients' hospital stay. In conclusion, this study provides an evidence-based reference for the application of cognitive exercises in patients admitted to the ICU.
Herling[11], et al. / 2018	3.885	Evaluate the existing evidence on the effect of preventive interventions on delirium in the ICU, in-hospital mortality, number of delirium cases, days without coma, days without ventilator, length of ICU stay, and cognitive impairment.	There is insufficient evidence to determine the effects of physical and cognitive interventions on delirium. The effects of other pharmacological interventions, sedation, environmental interventions, and preventive nursing are unclear and warrant further investigation in large multicentric studies. Five studies are awaiting classification, and we identified fifteen ongoing studies evaluating pharmacological interventions, sedation regimens, physical therapy, occupational therapy, either combined or separately, and environmental interventions, which may alter the conclusions of the review in the future.
Hill[12], et al. / 2021	660	Identify the range of uses of Virtual Reality (VR) in intensive care unit (ICU) patients and assess its current stage of development, effectiveness, acceptability, and tolerability.	VR for intensive care is a new research domain, with most applications (including delirium) still in the early stages of development. There is significant potential for the use of VR in this clinical environment. A more robust evaluation of its effectiveness is needed before any clinical recommendations can be made.
Wang[13], et al / 2020	3.837	Evaluate the effects of early mobilization (MP) in critically ill patients.	The evidence from this review indicates that early mobilization (MP) can improve muscle strength in critically ill patients, reduce the incidence of complications in the ICU, and shorten the duration of mechanical ventilation, ICU stay, and hospital length of stay. The effect on delirium rates still needs to be determined through large-scale studies.
Nydahl[6], et al/2022	2.164	Determine whether early mobilization (MP) in adult ICU patients, either alone or as part of an intervention package, compared to standard practice, is effective in preventing delirium or reducing its duration.	Early mobilization (MP) in ICU patients may be effective in preventing delirium and potentially reducing its duration. However, due to the heterogeneity of the sample, specific methods, frequency, duration, or intensity of mobilization cannot be defined at this time. The key point is to reduce the time spent in bed.

DISCUSSION

This study aimed to verify the evidence regarding the practice of Early Mobility (EM) in patients diagnosed with delirium in a critical hospital environment. To this end, the ABCDEF bundle has supposedly proven to be a great ally when it comes to reducing the incidence and duration of delirium[8]. Sosnowski's study[8] investigated the efficacy of this bundle on delirium, functional outcomes, and quality of life through a meta-analysis of 18 articles that applied it entirely to adult patients admitted to an ICU. The ABCDEF bundle emerged as an evidence-based, multicomponent guide to coordinate and facilitate interdisciplinary care described in the 2013 guidelines on the management of Pain, Agitation, and Delirium in adult patients in critical care units[14]. Its components are: Assess, prevent, and manage pain; spontaneous awakening trials and spontaneous breathing trials; choice of analgesia and sedation; delirium: assess, prevent, and manage; early mobilization and exercise; and family engagement and empowerment[8]. EM is an integral part of the ABCDEF bundle and is considered one of the only interventions that resulted in a decrease in the days of delirium[14].

Although Sosnowski's study[8] indicates that the implementation of the ABCDEF bundle is associated with a decrease in the incidence and duration of delirium, several points must be considered, such as the considerable heterogeneity among the analyzed studies, which introduces variability in the potential benefit of the intervention and a lower level of certainty of evidence. Additionally, the application of the ABCDEF bundle can be hindered by several barriers: hemodynamic or respiratory instability; patient fatigue or refusal; deep sedation; lack of glasses and/or hearing aids; lack of knowledge and communication issues among the multidisciplinary team; and limited treatment time8 due to light and noise conditions. Therefore, it can be inferred that the implementation of this bundle cannot guarantee the specified results with precision, and high-quality clinical trials are needed to formally determine these benefits.

Corroborating the uncertainty of these benefits, Fuke[9] conducted a meta-analysis to evaluate the effectiveness of Early Mobility (EM) in preventing Post-Intensive Care Syndrome (PICS). PICS is defined as a syndrome encompassing new or worsening impairments in physical, cognitive, or mental health that arise after critical illness and persist after acute care hospitalization9. The complications experienced by ICU survivors include deterioration in physical capabilities (decreased muscle strength), psychological health (anxiety and depression), and cognitive function (delirium). The persistence of symptoms such as reduced ability to perform activities of daily living, depression, post-traumatic stress disorder, anxiety, and delirium contributes to adverse effects on the quality of life of individuals who have survived a critical illness[15].

As inferred by Fuke[9], Early Mobility (EM) significantly improved short-term physical performance (increased scores on the Medical Research Council and lower incidence of ICU-acquired muscle weakness) in the groups that performed EM compared to those that did not or only followed standard treatment. On the other hand, there were no differences between the two groups in terms of delirium-free days. However, the authors noted that the sample size studied for evaluating delirium was small; this, combined with the fact that the study analyzed EM individually without the interference of multiple components and the multidisciplinary team (as advocated by the ABCDEF bundle), strengthens the argument and the results found by Sosnowski[8].

In Herling's meta-analysis[11], which included randomized controlled trials, no evidence was found of preventive effects of Early Mobility (EM) and cognitive exercises for delirium. Additionally, Herling[11] concluded that while EM may reduce the duration of ventilation and hospital stay, the effect of abstaining from sedation for delirium prevention is uncertain.

However, as the authors themselves mentioned, the quality of the included study on delirium is low due to the small sample size of only 87 participants.The study in question, conducted by Brummel[16], implemented early intervention in surgical and medical ICU patients. The control group only received mobilization when requested by the medical team, about 1 to 2 times per week. There were two intervention groups: one performing only EM once a day and the other undergoing physical therapy combined with cognitive exercises (such as puzzles, recalling phrases, and sequences of numbers, among others). The primary objective of this study was to determine the feasibility of combined EM and cognitive exercises in ICUs. Therefore, the authors discussed that the ability to assess the effectiveness of the interventions on patient outcomes is limited.

In Xu's study[10], seven articles were included in the meta-analysis and evaluated functional cognitive exercises (active or passive exercises in bed, sitting at the bedside, standing, sitting in a chair, and ambulation with assistance) for the treatment of delirium in the ICU. Comparing the cognitive interventions between Xu's[10] meta-analysis and Herling's[11], it was observed that Xu's intervention[10] focused on motor activities, while Herling's aimed at exercises that stimulate memory and logical reasoning. Thus, motor activities presented better evidence in reducing the length of stay in patients with delirium, also reducing the incidence of delirium in ICU patients and improving quality of life compared to patients who did not undergo the intervention. Functional cognitive exercises combined with medication treatment for delirium yielded better results than cognitive exercises alone, provided that sedatives are managed correctly to ensure cognitive stimulation is effectively performed.

In the Nydahl meta-analysis[6], an analysis of 13 studies with 2,164 patients was performed, and it was shown that EM can reduce the risk of developing delirium in the ICU in 47% of cases, and reduce the duration of existing delirium by almost two days, as long as the dosage is adapted to the patients' conditions in relation to duration, frequency and intensity (favoring more frequent and shorter sessions) and centering on the patient and their family. Given all this, adherence to the ABCDEF package should be a priority, as it has a multidisciplinary approach focused on the patient in a biopsychosocial way. However, there are specific cases in which EM did not show benefits, such as in those patients with acute and severe cases of stroke, as it can generate a reduction in cerebral perfusion and an increase in its dysfunction.

The study by Hill[12] aimed to develop the use of virtual reality (VR) in ICU patients to prevent post-traumatic stress disorder (PTSD). Twenty-one studies were included in the review. The most common approach using VR for relaxation was to develop relaxing environments with corresponding ambient sounds. A similar approach was used regarding delirium, utilizing VR to help relax patients; other studies employed natural environments with guided meditation through VR software. For neurocognitive stimulation and sleep, similar approaches to those used for relaxation and delirium were implemented. The study indicated that there was no effect on delirium itself, but it significantly reduced anxiety and depression in these patients. There are substantial limitations to the evidence base used in the review. There was widespread methodological fragility in the studies themselves, which were also small and employed a wide range of varied outcomes to assess efficacy and acceptability. Based on this, limited confidence should be placed in the estimates of effects identified in the studies.

The systematic review and meta-analysis by Wang[13] investigated the effects of early mobilization on the prognosis of critically ill patients, including thirty-nine studies in the current meta-analysis. The main findings of this article identified that early mobilization improved some physical functional indices (MRC score, Barthel index, lower occurrence of acquired weakness, decreased complication rates, and shorter length of stay). However, early mobilization did not show any results regarding handgrip strength, delirium rates, mortality,

or health-related quality of life concerning the physical and mental functions of these patients. Overall, the results indicated that early mobilization improved the progression of these critically ill patients. Although many studies reported that early mobilization reduced the incidence of delirium or increased delirium-free days, this was not supported by the current meta-analysis, consistent with the findings of other studies where no observable relationship was found between physical rehabilitation and the incidence of delirium. However, this discrepancy may be explained by the late initiation of mobilization exercises and differences in the diagnosis and assessment of delirium.

CONCLUSION

The EM is both viable and safe, serving as an important tool in the multidisciplinary care of critically ill patients; however, its use for delirium has shown conflicting results. The available studies exhibit significant methodological differences, small study populations, and overall few studies addressing the subject. We emphasize the need for larger studies to define both the effectiveness of EM and a protocol for its implementation.

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