


LESS IS MORE IN INTENSIVE CARE

# Less pharmacotherapy is more in delirium



Shinn-Te Chou<sup>1</sup>, Melanie Pogach<sup>3,4</sup> and Laura K. Rock<sup>2,5,6\*</sup> 

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Treatments used in the practice of critical care medicine often lack evidence-based data supporting their use. Out of habit, anecdotal experience, frustration, hope, or an absence of gold standard alternatives, critical care physicians may continue to use ineffective treatments in challenging clinical scenarios, such as the management of delirium. Although no medications have consistently demonstrated therapeutic benefit [1], medications are too often utilized in an attempt to prevent delirium or to treat agitation associated with delirium, while failing to incorporate simple behavioral interventions that may be more effective.

Delirium is common in hospitalized and critically ill patients, with an incidence rate of 32% among patients admitted in an intensive care unit (ICU), increasing to 80% of mechanically ventilated patients [2, 3], 29–64% of elderly hospitalized patients [4] and 70% of elderly ICU patients [5]. Delirium is challenging to manage and costly, contributing to increased length of ICU and hospital stays and worse outcomes, including hospital-related falls, functional decline, cognitive impairment and a marked increase in mortality [2–5]. Delirium has been considered preventable in 30–40% of cases [4, 5]; however, a recent meta-analysis identified a 53% reduction in the incidence of delirium (odds ratio: 0.47) with intentional and meticulous implementation of nonpharmacological interventions, the Hospital Elder Life Program (HELP), when compared to a control group [6]. The SARS-CoV-2 pandemic and associated worldwide acute respiratory distress syndrome (ARDS) crisis resulted in the use of higher doses and more complex combinations of neuroactive medications than typically used. In that context, patients experiencing higher rates of associated post-extubation delirium are often treated with more

pharmacotherapy. Deliriogenic medications and isolation related to visitation restrictions have been identified as modifiable risk factors for coma and delirium among critically ill patients with coronavirus disease 2019 (COVID-19) [7]. The authors were inspired to write this piece after caring for a patient with persistent, severe, agitated delirium who responded poorly to medications, but dramatically improved with nonpharmacological interventions, notably enhancement of sleep through minimization of nocturnal disruptions and the use of earplugs and an eye mask, verbal redirection, and reorienting conversations.

Delirium is a form of brain dysfunction characterized by the acute onset of fluctuating mental status, inattention, disorganized thinking, and altered level of consciousness. These features are also seen in acute sleep deprivation. It is believed that the state of delirium contributes to disrupted sleep just as sleep deprivation is considered a modifiable risk factor for delirium [8]. Poor sleep quality is common in the ICU [9]. Small studies in hospitalized patients have shown that improving sleep—by minimizing nighttime disruption, noise and light exposure and/or using eye masks and earplugs—is associated with reduced episodes of delirium [10, 11]. Additionally, a meta-analysis concluded that multicomponent nonpharmacological interventions (as shown in Table 1) are highly effective in decreasing the occurrence of both delirium and falls during hospitalization of elderly individuals with a 53% and 62% odds reduction for the prevention of delirium and falls, respectively, with the understanding that delirium significantly increases the risk of falling [4].

Despite lacking evidence for their utility, medications are widely used for delirium management (86% in one retrospective study [12]). Various medications have been evaluated in the prevention of delirium, but none have been shown to have consistent benefit. Medications, such as typical and atypical antipsychotics, are often used to treat agitation associated with delirium. Although use of sedatives or antipsychotics may be warranted if patients

\*Correspondence: lrock@bidmc.harvard.edu

<sup>2</sup> Harvard Medical School, Boston, MA, USA

Full author information is available at the end of the article

**Table 1 Non-pharmacological interventions to prevent and treat ICU delirium**

Categories	Examples
Reorientation	Orient patient to time, place, and situation. Redirect, normalize fear, assure patient they are safe and being cared for and discuss their important people, places, pets to promote sense of self and connection. Involve family in their care.
Cognition	Engage in conversations. Books, puzzles, music.
Mobility	Sitting up. Early ambulation. Physical Therapy.
Sensorium	Glasses. Hearing aids. Interpreter assistance.
Sleep	Eye mask. Earplugs. Minimize unnecessary lab draws, procedures, or disruptions during the targeted sleep period, and optimize light and dark exposures to regulate sleep/wake patterns.
Agency and independence	Prompt removal of physical restraints. Review needs for foley, rectal tube, telemetry, and other tubes and catheters daily.
Nutrition and hydration	Provide assistance with drinking and eating, as appropriate.

are at risk of harm to themselves or others, no studies have demonstrated a definitive benefit over placebo in terms of delirium-free days, physical restraints use, or length of stay [1, 13]. Beyond lack of demonstrated efficacy in mitigating delirium, antipsychotics bring potential adverse effects, including arrhythmia and prolonged QTc, necessitating monitoring with electrocardiogram, and potential extrapyramidal reactions [1]. Recognizing an important limitation to the available data being that studies predominantly included patients with hypoactive delirium, there is no known effective pharmacological treatment for delirium.

Caring for critically ill patients is complex and their care often requires sedation, immobilization, isolation, uncomfortable interventions, and sleep deprivation, all of which contribute to delirium. Critical care clinicians should aim to prevent or diminish delirium by addressing the myriad suspected contributors to delirium, such as inadequately treated pain, acute illness, metabolic derangements, constipation, altered sensorium (due to lack of hearing aids or glasses), deliriogenic medications, immobility, restraints, isolation, disorientation, environmental noise, and disruption of sleep/wake cycles [14]. Important and inexpensive under-utilized strategies include: speaking to patients to reorient them, including using the names of their loved ones and pets if they are isolated; encouraging family presence; cognitive stimulation through conversations, activities and music; early mobilization; helping people feel more dignity and independence by providing their glasses and hearing aids and prompt removal of restraints, lines, tubes, and telemetry when safe; promoting sleep through minimizing nocturnal disruptions and offering an eye mask and earplugs to help facilitate sleep. Large prospective studies on implementation of protocols incorporating multiple nonpharmacological interventions demonstrated a decreased duration of delirium [15, 16].

Why is pharmacotherapy often used to target delirium when it is ineffective? Some of the barriers to

effective implementation of these nonpharmacological solutions include time and patient load, as it takes more time and/or additional dedicated team members [6] to sit with a patient, optimize early mobility, find out their interests that could be supported and provided in a hospital setting, etc. Our past training and culture may also explain the gap. It will take a cultural transformation, and support from hospital systems, to implement and study the effectiveness of these interventions. The paradigm is shifting to help patients feel less like a patient and more like themselves as we care for them. With less pharmacotherapy and a greater awareness of nonpharmacological interventions, we can try less medication and more personal care to promote patient dignity and minimize delirium.

#### Author details

<sup>1</sup> Lahey Hospital and Medical Center, Burlington, MA, USA. <sup>2</sup> Harvard Medical School, Boston, MA, USA. <sup>3</sup> St. Elizabeth's Medical Center, Brighton, MA, USA. <sup>4</sup> Tufts University School of Medicine, Boston, MA, USA. <sup>5</sup> Division of Pulmonary, Critical Care, and Sleep Medicine, Department of Medicine, Beth Israel Deaconess Medical Center, 330 Brookline Avenue, KSB23, Boston, MA 02118, USA. <sup>6</sup> 15 Borland Street, Brookline, MA 02446, USA.

#### Author contributions

S-TC and LKR wrote the manuscript and chose the selected references, LKR offered oversight and edits, S-TC prepared the table with input from LKR. MP provided expert guidance on the discussion section and reference selection related to sleep medicine. All authors commented on previous versions and read and approved the final manuscript.

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The participant has consented to the submission of the case report to the journal. The case is deidentified and has no individual details, images, or videos. Additionally, the patient whose case formed the basis of this brief report provided written and verbal permission to publish.

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