The Comprehensive Review of the Condition and Management of ICU Delirium in the Intensive Care Unit

Zohreh Ostadi[1], Ata Mahmoodpoor[1], Kamran Shadvar[1], Sarvin Sanaie[2], Seied Hadi Saghaleini[1*]
[1]Department of Anesthesiology, Tabriz University of Medical Sciences, Tabriz, Iran
[2]Department of Nutrition, Tabriz University of Medical Sciences, Tabriz, Iran

ABSTRACT

ICU delirium is a common medical problem occurring in patients admitted to the Intensive Care Units (ICUs). The occurrence of ICU delirium increases mortality, length of hospital stay and mechanical ventilation, treatment costs and incidences of cognitive disturbances. Critically ill patients are subject to numerous risk factors for delirium. Some of these, such as exposure to sedative and analgesic medications, may be modified to reduce risk. Surveys conducted in several countries indicated that delirium in ICU was inadequately monitored, underdiagnosed and lacked standardized treatment. Thus, this article seeks to provide a succinct but comprehensive review of the condition, aiming to help physicians in the ICU to have a better understanding of delirium in the ICU and act as efficiently as possible to decrease upcoming untoward consequences associated with it.

KEYWORDS
Delirium, Monitoring, Critical care, ICU

*Corresponding Author:
Seied Hadi Saghaleini,
Department of Anesthesiology, Tabriz University of Medical Sciences,
Tabriz, Iran;
E-mail: hsaghaleini@gmail.com

How to Cite This Article:

Ostadi Z, Mahmoodpoor A, Shadvar K, et al. The Comprehensive Review of the Condition and Management of ICU Delirium in the Intensive Care Unit. J Evid Based Med Healthc 2022; 9(9):27.

*Received: 03-Mar-2022,
Manuscript No: JEBMH-22-53789;
Editor assigned: 07-Mar-2022,
PreQC No. JEBMH-22-53789 (PQ);
Reviewed: 21-Mar-2022,
QC No. JEBMH-22-53789;
Revised: 02-May-2022,
Manuscript No. JEBMH-22-53789 (R);
Published: 17-May-2022,
DOI: 10.18410/jebmh/2022/09/9/27.*

INTRODUCTION

Delirium in the Intensive Care Unit (ICU) is a common and clinically problematic condition that may increase the pressure of the burden on the shoulders of the health system, and at the same time cause the process of healing to derail from its natural course. This rapidly developing and daily fluctuating disturbance of cognition and consciousness has four key elements according to the American Psychiatric Association's (APA) Diagnostic and Statistical Manual of Mental Disorders (DSM) - IV:

- Impairment of consciousness and altered attention.
- Compromised perception and cognition, not because of an underlying cause such as dementia.
- Development of abnormalities in a short period, tending to fluctuate during the day.
- Evidence of an etiologic cause.

According to previous studies, delirium increases the risk of estuation and catheter removal by the patient, longer periods of mechanical ventilation, and the requirement for physical restraints, need for a longer hospital stay, mortality rate, and the need for care after discharge.[1-5] Longer duration of delirium may cause longstanding cognitive problems such as compromised executive function, immediate and delayed memory, and verbal abilities that in turn result in a decreased life quality and increased costs.[6] Therefore, to increase the quality of caregiving and enhance the outcome of patients, it is necessary to accurately predict and adequately treat delirium in ICU cases. Achieving this goal requires a good understanding of the condition *i.e.* its definition, precipitating / risk factors, pathophysiology, and preventive / therapeutic approaches. Although delirium in the ICU may develop in any given patient, it is seen more frequently in vulnerable subjects, for example, who have multiple predisposing factors that encounter a huge insult (s).

LITERATURE REVIEW

Definition and Classification

Originally derived from the Latin word de lira meaning "off the path", delirium is an acute but fluctuating mental change over the course of a day that brings about unconsciousness, inattention and disorganized thinking.[7-8] Indeed, delirium is a syndrome rather than a disease a spectrum with the overt disease on one extreme end and normal mentation on the other extreme end.[9,10] This condition in ICU patients is also known as ICU delirium, acute confessional state, sun downing, acute brain dysfunction, ICU psychosis, ICU encephalopathy, and ICU syndrome. Despite a notable prevalence and the clinical importance of ICU delirium.[11-15] It has only received enough attention within the last decade. Geriatrics and critically ill patients have an increased risk of developing delirium during their hospital stay. This condition is thought to be multifactorial and generally classified into three type's hypoactive, hyperactive, and a mixed form of both hypoactive and hyperactive delirium (Table 1). There is also a subtype of the disease that is known as subsyndromal delirium, in which patients exhibit some typical signs of delirium only.[16]

Hyperactive	Hypoactive
Restlessness	Apathy
Agitation	Flat affect
Attempts to remove attached equipment / devices	Compromised motor skills and decreased responsiveness

Table 1. Clinical Characteristics of Hyperactive and Hypoactive Intensive Care Unit Delirium.

Epidemiology

According to some epidemiological studies delirium develops in 20 % - 50 % of patients with conditions of lower severity and those who receive no mechanical ventilation, and 60 % - 80 % of ICU patients who need mechanical ventilation.[17] This high variability partly stems from using various assessment tools in different settings.[18] It seems that the incidence of ICU delirium is more than the previously reported figures, because sometimes it develops unobtrusively in ICU patients and is reported as dementia, depression, or even a normal reaction in critically ill patients.[19] This is particularly true in patients present with hypoactive delirium. According to a report by the incidence of purely hyperactive delirium, purely hypoactive delirium and a mixed subtype was 1.6 %, 43.5 % and 54.1 %, respectively. This high rate of hypoactive ICU delirium is assumed to be the main reason for the under - recognition of the syndrome.[21]

Pathophysiology and Risk Factors

Delirium, as a manifestation of acute illness may develop because of problems in recovery from sedation.[22] Although the exact physiopathology of ICU delirium is not fully understood, it seems that the brain inflammatory reactions play a pivotal role in this regard. Neuroinflammation possibly exerts this effect *via* increasing oxidative damage and apoptosis. Briefly, the brain produces and releases various cytokines in response to harmful stimuli such as hypoxia, hypo perfusion and ischemia which in turn cause cell infiltration and tissue damage.[23] indeed these alterations cause imbalances of neurotransmitters, leading to changes in activities of local neurons. The altered neurotransmitters are major modulators of cognitive function, mood and behavior including dopamine, acetylcholine and γ - amino butyric acid (GABA).[24,25] The main alterations in association with delirium are reported to be an excess of dopamine and depletion of acetylcholine. However, abnormal changes in production and release of other neurotransmitters such as serotonin, endorphin and noradrenalin have been also suggested in the pathogenesis of delirium in ICU patients.[26] Besides alteration in chemical components of the brain regulatory system, structural changes in the vascular and structural components and abnormal coagulation have been also evident in delirious ICU cases.[27] Delirium has been also found in association with anatomical changes in the brain such as cerebral atrophy and white matter disruption. Abnormal levels of tryptophan and serotonin may also associated with the pathophysiology of delirium in ICU.[28,29] Finally, it has been proposed that the underlying illness itself and administered medications, especially sedatives such as benzodiazepines may have untoward effects on circadian rhythm, sleep patterns and immunity, contributing to delirium.[30] Risk factors for delirium, in general, could be classified in three categories, including acute illness, host factors, and environmental / iatrogenic causes.[31] It has been suggested that for developing delirium in a given ICU patient, he or she has to have in average 11 known risk factors.[32] When the risk factors are more frequent or among the major ones, the patient is considered vulnerable to delirium and may develop the condition with only a minor insult. For example, an elderly patient may

become delirious during ICU stay after a simple urinary tract infection. In contrast, a less vulnerable patient may need a higher number of risk factors to develop ICU delirium. For example, a young ICU patient usually does not affected with delirium unless a series of major risk factors such as septic shock, ARDS and the need for mechanical ventilation are present concomitantly. The most important and prevalent risk factors for ICU delirium are age, comorbidities and chronic health problems, current medical / neurocognitive conditions, sepsis, hypoxia, metabolic abnormalities and medications.

DISCUSSION

Among the most important medications in this regard are narcotics (opioids such as fentanyl and morphine), psychoactive agents (benzodiazepines such as clonazepam, midazolam), antihistamines (such as diphenhydramine), metoclopramide, promethazine, H_2 antagonists (such as famotidine and ranitidine) and corticosteroids.[33] The environmental / iatrogenic category comprises sleep deprivation, immobilization and social isolation.[34-35] Sleep deprivation can be caused by surrounding noise, lack of natural light, patient care, mechanical ventilation, medications, anxiety, pain and stress.[36] Immobilization is more prominent in mechanically ventilated subjects, as well as in those under heavy sedation. Early physical and occupational therapy has been found useful in the latter group. The sense of social isolation is usually develops after patients wake in unfamiliar ICU environment and need to stay there for a while. Education and orientation programs have been found effective in reducing the burden of this problem and associated delirium.[37] Another method of risk stratification in ICU delirium is based on dividing potential contributors as predisposing and precipitating (Table 2 and 3).[38]

Risk Factors	
Predisposing	Precipitating
Advanced age	Medications
Depression	Dehydration
Underlying dementia	Seizure
Severity of underlying condition	Hyperthermia
Chronic illness	Withdrawal syndromes
Smoking / Alcohol use	Metabolic derangement
Visual / hearing impairment	Head trauma
Apo E 4 polymorphism	Infection / sepsis

Table 2. Predisposing and Precipitating Risk Factors of Intensive Care Unit Delirium.

Tool and Description	Score
Ramsy scale	
Presence of anxiety / agitation, restless or both	1
Presence of cooperation, orientation and tranquility	2
Response to commands only	3
Fast response to loud auditory stimulus or light glabellar tap	4
Slow response to loud auditory stimulus or light glabellar tap	5
No response	6
Richmond agitation sedation scale	
Highly combative / violent, dangerous for staff (Combative)	4
Aggressive behavior, tries to manipulate tube(s) / catheter(s) (Highly agitated)	3
Patient – ventilator dyssynchrony or multiple nonpurposeful movements (Agitated)	2
Anxious / apprehensive without abnormal movements (Restless)	1
Attentive (Alert and calm)	0
Semi - alert (Drowsy)	-1
Less than semi - alert (light sedation)	-2
Responsive to voice with no eye contact (Moderate sedation)	-3
Response by movement to physical stimulation (Deep sedation)	-4
No response (Unarousable)	-5
Riker sedation agitation scale	
Manipulating catheter(s) / tube(s), (Dangerous agitation), struggling movement, trying to harm staff	7
Biting, requiring restraint (very agitated)	6
Agitated but calms to verbal orders	5
Calm and cooperative but still easily arousable	4
Sedated (responsive to verbal stimuli)	3
Very sedated (responsive to physical stimuli only)	2
Unarousable	1

Table 3. Ramsy Scale, Richmond Agitation Sedation Scale and Sedation Agitation Scale for Assessment of the Level of Sedation and Consciousness of Patients in the Intensive Care Unit.

This classification is important in terms of devising preventive strategies, because predisposing risk factors are often present at ICU admission and are less modifiable. In contrast, precipitating risk factors could be modified with significant impacts on prognosis. Finally, a third method for risk stratification, which is more useful in defining preventive programs, is categorizing them as modifiable / unpreventable and potentially modifiable / preventable risk factors. In such a scenario, baseline risk factors such as age, Apo lipoprotein E (APOE) 4 genotype, previous illness such as hypertension and cognitive disorders, and a history of tobacco / alcohol use the factors in association with the existing illness such as severe underlying condition, respiratory problems, medical surgical) illness, need for mechanical ventilation, presence of an inflammatory condition and high Large Neutral Amino Acids (LNAA) metabolites levels and hospital - related factors such as lack of day and isolation are counted as modifiable / unpreventable risk factors. Dynamic light therapy could be effective only when the patient's eyes are open to let it reach the specific retinal cell.[39] In comparison, sensory deprivation such as in hearing / vision impairment, pathologic conditions such as anemia, acidosis, hypotension, infection / sepsis, metabolic disturbances (such as serum electrolyte abnormalities like hypernatremia, hypokalemia, azotemia, transaminases, hyperamylasemia, hyperbilirubinemia) and fever and hospital - related conditions such as lack of vision, immobility, vascular catheters, gastric tubes, bladder catheters, sleep deprivation, and receiving sedatives / analgesics. Nevertheless, it should be noted that the physiopathology of delirium in ICU patients is complex and any suggested etiology is only speculative. [40]

Prognosis

Unlike in the past, it is now clear that ICU delirium is a neither benign nor self - limited condition. Numerous adverse consequences have been reported in association with ICU

delirium, such as an increased risk of intubation, prolonged duration of mechanical ventilation, prolonged ICU and hospital stay, higher medical expenditures and long - term cognitive disorders. A significant increase in the likelihood of in - hospital and long - term mortality has been also reported in patients with ICU delirium.

Monitoring

It has been suggested that the level of sedation and consciousness of ICU patients should be assessed by health care staff using specific tools such as Ramsay scale, Richmond agitation sedation scale and Riker sedation agitation scale. This is important not only in preventing over - sedation and earlier liberation of patients from mechanical ventilators, but also in alerting the clinicians that which patients should be screened for delirium, because the cardinal feature of delirium is inattention.[41] In fact, using monitoring instruments enable us to quantify untoward consequences of delirium in ICU and better evaluate the risk factors such as sedative medications. Accordingly, all patients who respond to verbal stimulation should be considered for delirium screening. When screening for ICU delirium by a validated tool is neglected, it is estimated that up to 70 % of delirium cases can go unnoticed. Although the standard of reference for diagnosis of delirium is the DSM - IV criteria applied by a trained psychiatrist, the routine application is often not possible as psychiatric services are not reachable around the clock. Thus, various surrogate tools have been developed and validated against DSM - IV criteria for employment in the ICU. Currently, two major tools for assessment of delirium in ICU are available, including the Intensive Care Delirium Screening Checklist (ICDSC) and the confusion assessment method for the ICU (CAM - ICU). The latter is more preferred by ICU staffs because it is both more convenient to use and more accurate for routine bedside screening purposes. The cardinal feature of delirium, inattention, is included in both CAM - ICU and ICDSC tools. Delirium screening and awareness of the associated risk factors are mutually dependent for the successful management of delirium. Van den Boogaard recently developed a delirium - predicting model for intensive care patients based on ten risk factors including age, Apache II score, admission group, coma, infection, metabolic acidosis, use of sedatives and morphine, urea concentration and urgent admission. Many of these risk factors are irreversible, but others, such as the use of sedatives and morphine, could potentially be modified. Nowadays, using cutting - edge technologies has significantly facilitated screening and preventive actions in patients at higher risk of ICU delirium.[44]

Prevention

According to several surveys conducted in the western countries, delirium still is not an extensively focused problem in the ICU settings.[45] So, an appropriate ICU staff education is one of the mainstays in developing an efficient preventive and therapeutic plan against ICU delirium.[46] For this purpose, ICU nurses and clinicians should have a complete comprehension of delirium and be aware of its importance as a significant comorbidity that should be immediately intervened. Generally, the risk factors for delirium affecting individual ICU patients are different from patient to patient and therefore an individualized delirium preventive strategy is an ideal approach. Nevertheless, three risk factors in particular, including sedatives, immobility and sleep disruption, are widespread in the ICU, and it has been supposed that these three factors constitute the most important parameters in association with ICU delirium. Thus, in the next step all potential risk factors of delirium, particularly the three mentioned ones should be eliminated or minimized. For example, sepsis and hypoxia should be identified and treated in time and new protocols should be implemented to minimize the use of narcotic and psychoactive medications. Some studies have shown that α_2 - agonists (such as dexmedetomidine) lower the risk of delirium in ICU patients under mechanical ventilation by 20 % more than benzodiazepines.[47] The advantages of dexmedetomidine over benzodiazepines are its analgesic effect, less respiratory depression and enabling patients to better communicate. Comparing to clonazepam dexmedetomidine has been found in association with longer sedation and survival, and less agitation / anxiety compared to protocol. As compared to haloperidol, this medication was along with a shorter time to estuation and ICU stay. In comparison with midazolam although dexmedetomidine has not significantly decreased the rate of delirium the resolution from delirium was more rapid with dexmedetomidine. Statins may also decrease the risk of delirium in ICU, especially when it develops early in ICU stay. A recent study, however, has report no such a significant improvement by using rosuvastatin. It should be noted that various statins might differ from each other in terms of their lipophilic properties and hence their effect on the CNS. The effect of statins seems to be through reducing systemic inflammation and enhancing endothelial function.[48] Strategies to prevent sleep deprivation and maintain patient's circadian rhythm are necessary. Prevention is vital in high - risk patients. The initial attempts include using non - pharmacological approaches, such as prescribing eyeglasses and hearing aids, sleep promotion strategies, enhancing communication, facilitating early mobilization through encouraging exercise or range of motion, introducing cognitively stimulating activities, ensuring adequate fluid intake, withdrawal of ventilators, if possible, and removal of unnecessary tubes / catheters.[49] It has been suggested that the daily cessation of sedatives (infusion / bolus) combined with daily spontaneous breathing trials in the Awakening and Breathing Controlled (ABC) Trial may significantly decrease the number of days of acute brain dysfunction and coma in ICU patients.[50] Accordingly, this approach increases the possibility of daily assessment of patients in the ICU for early indicators of delirium, and so can be considered an indirect preventive approach. Besides the method of sedative administration, the type of sedatives is also important in preventing delirium in ICU patients. There are several reports indicating that benzodiazepines are associated with an increased risk of delirium in ICU. For examples, reported that lorazepam independently increases the risk of delirium the next day in a dose - dependent manner. For example, patients who received 20 mg or more of this medication on a given day were almost all delirious the following day. In another study, Pandharipande showed that the receipt of midazolam was along with a 2.75 - fold increase in the odds of developing delirium in ICU patients after adjusting other possible confounders. So, avoiding benzodiazepines for routing sedation in ICU patients seems a reasonable way to decrease the risk of delirium.[51] Although many studies have reported faster awakening times from sedation and shorter duration of mechanical ventilation in ICU patients who received alternative sedatives (such as propofol and dexamethasone) rather than benzodiazepines, scarce studies are present that have examined the effect of this substitution on the daily occurrence of delirium in ICU patients. The Maximizing the Efficacy of Targeted Sedation and Reducing Neurologic Dysfunction (MENDS) trial compared the effect of lorazepam and dexamethasone and

found that the status of delirium was better in dexamethasone receivers.[51] In another similar study by the Safety and Efficacy or Dexmedetomidine Compared With Midazolam (SEDCOM) trial, patients sedated with midazolam had 23 % higher delirium prevalence than those receiving dexmedetomidine. Two other similar trials, however, did not find a significant difference between dexamethasone and midazolam / propofol receivers for the occurrence of delirium in ICU.[52] So, it seems that due to this heterogeneity in reports, further studies are still needed to draw a solid conclusion.

Treatment

If all these preventive strategies failed, prompt interventions to correct the condition and treat delirium should be initiated. In such cases, pharmacological treatments are often necessary. Haloperidol, a typical antipsychotic, is the most commonly used empiric agent in this regard, but the staff need to be very vigilant upon potential, significant side - effects of this medication, including extrapyramidal symptoms, torsade's de points, prolongation of the Q - T interval, and neuroleptic malignant syndrome. Although the exact mechanism of action of this medication in treating delirium is unknown, it is thought that haloperidol acts through antagonizing brain dopamine - 2 receptor and reducing dopaminergic activity at the cerebral synapses and basal ganglia.[53] initially, 2 mg of the medication is administered intravenously. It could be repeated every 15 - 20 min, doubling the dose each time until agitation is resolved. After stabilizing the patient, the least effective dose should be used every 4 – 6 h as the maintenance. Olanzapine (2.5 - 5 mg orally per day) and other atypical antipsychotics such as ziprasidone (40 mg orally every 6 – 12 h) and quetiapine (50 mg orally every 12 h) have also been used in treating ICU delirium.

CONCLUSION

However, there is still controversy in this regard, because these drugs may increase death risk.[54] The mechanism of action of atypical antipsychotics in treating delirium is unknown, but it is suggested that they act by affecting neurotransmitter balance. Although, compared to haloperidol, they are along with less dangerous side - effects, atypical antipsychotics may also be accompanied by drowsiness, QT interval changes, extrapyramidal symptoms and metabolic changes. Other types of medications that have been found effective in treating ICU delirium are risperidone, low dose of ketamine during the induction phase of anesthesia, quetiapine, benzodiazepines, propofol and dexmedetomidine. Dexmedetomidine (0.2 μg - 1.5 μg / kg / h, intravenously) is a centrally acting alpha – 2 a agonist with rapid sedative effects and anxiolytic / analgesic properties. This medication has gained popularity among ICU physicians, because it has minimal impact on respiratory drive, proposes predictability and has an aminobutyric acid – sparing mechanism of action. No pharmacological agent has been found for treating hypoactive delirium.[55]

REFERENCES

1. Brummel NE, Girard TD. Preventing delirium in the intensive care unit. Crit Care Clin 2013;29(1):51-65.
2. Ely EW, Shintani A, Truman B, et al. Delirium as a predictor of mortality in mechanically ventilated patients in the intensive care unit. JAMA 2004;291(14):1753-1762.
3. Ouimet S, Kavanagh BP, Gottfried SB, et al. Incidence, risk factors and consequences of ICU delirium. Intensive Care Med 2007;33(1):66-73.
4. Thomason JW, Shintani A, Peterson JF, et al. Intensive care unit delirium is an independent predictor of longer hospital stay: a prospective analysis of 261 non-ventilated patients. Crit Care 2005;9(4):375-381.
5. Milbrandt EB, Deppen S, Harrison PL, et al. Costs associated with delirium in mechanically ventilated patients. Crit Care Med 2004;32(4):955-962.
6. Needham DM, Colantuoni E, Dinglas VD, et al. Rosuvastatin versus placebo for delirium in intensive care and subsequent cognitive impairment in patients with sepsis-associated acute respiratory distress syndrome: an ancillary study to a randomised controlled trial. Lancet Respir Med 2016;4(3):203-212.
8. Krupp A, Balas MC. Application of Clinical Practice Guidelines for Pain Agitation, and Delirium. Crit Care Nurs Clin North Am 2016;28(2):241-52.
9. Kress JP. The complex interplay between delirium, sepsis and sedation. Critical care 2010;14(3):164.
10. Allen J, Alexander E. Prevention recognition and management of delirium in the intensive care unit. AACN advanced critical care 2012;23(1):5-11.
11. Xie GH, Fang XM. Importance of recognizing and managing delirium in intensive care unit. Chin J Traumatol 2009;12(6):370-374.
12. Ely EW, Stephens RK, Jackson JC, et al. Current opinions regarding the importance, diagnosis, and management of delirium in the intensive care unit: a survey of 912 healthcare professionals. Crit Care Med 2004;32(1):106-112.
13. Lin SM, Liu CY, Wang CH, et al. The impact of delirium on the survival of mechanically ventilated patients. Crit Care Med 2004;32(11):2254-2259.
14. Pandharipande P, Cotton BA, Shintani A, et al. Prevalence and risk factors for development of delirium in surgical and trauma intensive care unit patients. J Trauma 2008;65(1):34-41.
15. Jackson JC, Gordon SM, Hart RP, et al. The association between delirium and cognitive decline: a review of the empirical literature. Neuropsychol Rev 2004;14(2):87-98.
16. Ouimet S, Riker R, Bergeron N, et al. Subsyndromal delirium in the ICU: evidence for a disease spectrum. Intensive Care Med 2007;33(6):1007-1013.
17. Mehta S, Cook D, Devlin JW, et al. Prevalence, Risk Factors, and Outcomes of Delirium in Mechanically Ventilated Adults. Crit Care Med 2015;43(3):557-566.
18. McPherson JA, Wagner CE, Boehm LM, et al. Delirium in the cardiovascular ICU: exploring modifiable risk factors. Crit Care Med 2013;41(2):405-413.
19. Francis J, Martin D, Kapoor WN. A prospective study of delirium in hospitalized elderly. Jama 1990;263(8):1097-1101.
20. Peterson JF, Pun BT, Dittus RS, et al. Delirium and its motoric subtypes: a study of 614 critically ill patients. J Am Geriatr Soc 2006;54(3):479-484.
21. Spronk PE, Riekerk B, Hofhuis J, et al. Occurrence of delirium is severely underestimated in the ICU during daily care. Intensive Care Med 2009;35(7):1276-80.
22. Reade MC, Finfer S. Sedation and delirium in the intensive care unit. N Engl J Med 2014;370(5):444-454.
23. Perry VH, Andersson PB, Gordon S. Macrophages and inflammation in the central nervous system. Trends in neurosciences 1993;16(7):268-273.
24. Hill NS, Levy MM. Ventilator management strategies for critical care. Marcel Dekker 2001;833.
25. Webb JM, Carlton EF, Geehan DM. Delirium in the intensive care unit: are we helping the patient? Crit Care Nurs

Q 2000;22(4):47-60.
26. Meagher DJ, Trzepacz PT. Motoric subtypes of delirium. Seminars in clinical neuropsychiatry 2000;5(2):75-85.
27. Hopkins RO, Jackson JC. Long-term neurocognitive function after critical illness. Chest 2006;130(3):869-878.
28. Simons KS, Laheij RJ, van den Boogaard M, et al. Dynamic light application therapy to reduce the incidence and duration of delirium in intensive-care patients: a randomised controlled trial. Lancet Respir Med 2016;4(3):194-202.
29. Pandharipande P, Banerjee A, McGrane S, et al. Liberation and animation for ventilated ICU patients: the ABCDE bundle for the back-end of critical care. Crit Care 2010;14(3):157.
30. Pandharipande PP, Sanders RD, Girard TD, et al. Effect of dexmedetomidine versus lorazepam on outcome in patients with sepsis: an a priori-designed analysis of the MENDS randomized controlled trial. Crit Care 2010;14(2):38.
31. Ely EW, Siegel MD, Inouye MDSK. Delirium in the Intensive Care Unit: An Under-Recognized Syndrome of Organ Dysfunction. Semin Respir Crit Care Med 2001;22(02):115-126.
32. Ely EW, Gautam S, Margolin R, et al. The impact of delirium in the intensive care unit on hospital length of stay. Intensive Care Med 2001;27(12):1892-1900.
33. Inouye SK, Schlesinger MJ, Lydon TJ. Delirium: a symptom of how hospital care is failing older persons and a window to improve quality of hospital care. Am J Med 1999;106(5):565-573.
34. Schweickert WD, Pohlman MC, Pohlman AS, et al. Early physical and occupational therapy in mechanically ventilated, critically ill patients: a randomised controlled trial. The Lancet 2009;373(9678):1874-1882.
35. Pisani MA, Kong SYJ, Kasl SV, et al. Days of Delirium Are Associated with 1-Year Mortality in an Older Intensive Care Unit Population. Am J Respir Crit Care Med 2009;180(11):1092-1097.
36. Van Rompaey B, Elseviers MM, Schuurmans MJ, et al. Risk factors for delirium in intensive care patients: a prospective cohort study. Crit Care 2009;13(3):77.
37. Colombo R, Corona A, Praga F, et al. A reorientation strategy for reducing delirium in the critically ill. Results of an interventional study. Minerva anestesiologica 2012;78(9): 1026-1033.
38. Pandharipande P, Shintani A, Peterson J, et al. Lorazepam is an independent risk factor for transitioning to delirium in intensive care unit patients. Anesthesiology 2006;104(1):21-26.
39. Annane D. Light therapy and chronobiology in critical illness. The Lancet Respiratory medicine 2016;4(3):167-168.
40. Mashour GA, Avidan MS. Postoperative delirium: disconnecting the network? Anesthesiology 2014;121(2):214-216.
41. van den Boogaard M, Pickkers P, Slooter AJ, et al. Development and validation of PRE-DELIRIC (PREdiction of DELIRium in ICu patients) delirium prediction model for intensive care patients: observational multicentre study. Bmj 2012;344:420.
42. Guo Y, Fan Y. A Preoperative, Nurse-Led Intervention Program Reduces Acute Postoperative Delirium. J Neurosci Nurs 2016;48(4):229-235.
43. Bergeron N, Dubois MJ, Dumont M, et al. Intensive Care Delirium Screening Checklist: evaluation of a new screening tool. Intensive care med 2001;27(5):859-864.
44. Yang F, Ji M, Ding S, et al. The Development and Evaluation of Delirium Assessment and Nursing Care Decision-Making Assistant Mobile Application for Intensive Care Unit. Studies in health technology and informatics 2016;225:668-672.
45. Van Eijk MM, Kesecioglu J, Slooter AJ. Intensive care delirium monitoring and standardised treatment: a complete survey of Dutch Intensive Care Units. Intensive and critical care nursing 2008;24(4):218-221.
46. Piao J, Jin Y, Lee SM. Triggers and nursing influences on delirium in intensive care units. Nurs Crit Care 2016;23(1):8-15.
47. Riker RR, Shehabi Y, Bokesch PM, et al. Dexmedetomidine vs midazolam for sedation of critically ill patients: a randomized trial. JAMA 2009;301(5):489-499.
48. Furlow B. Might statins prevent delirium in intensive care units? Lancet Respir Med 2(3):180.
49. Pun BT, Ely EW. The importance of diagnosing and managing ICU delirium. Chest 2007;132(2):624-636.
50. Girard TD, Kress JP, Fuchs BD, et al. Efficacy and safety of a paired sedation and ventilator weaning protocol for mechanically ventilated patients in intensive care (Awakening and Breathing Controlled trial): a randomized controlled trial. Lancet 2008;371(9607):126-134.
51. Pandharipande PP, Pun BT, Herr DL, et al. Effect of sedation with dexmedetomidine vs lorazepam on acute brain dysfunction in mechanically ventilated patients: the MENDS randomized controlled trial. JAMA 2007;298(22):2644-2653.
52. Maldonado JR, Wysong A, van der Starre PJ, et al. Dexmedetomidine and the reduction of postoperative delirium after cardiac surgery. Psychosomatics 2009;50(3):206-217.
53. Lawrence KR, Nasraway SA. Conduction disturbances associated with administration of butyrophenone antipsychotics in the critically ill: a review of the literature. Pharmacotherapy 1997;17(3):531-537.
54. Schneider LS, Dagerman KS, Insel P. Risk of death with atypical antipsychotic drug treatment for dementia: meta-analysis of randomized placebo-controlled trials. Jama 2005;294(15):1934-1943.
55. Haenggi M, Blum S, Brechbuehl R, et al. Effect of sedation level on the prevalence of delirium when assessed with CAM-ICU and ICDSC. Intensive Care Med 2013;39(12):2171-2179.