2013: Updates in Delirium

Eduard E. Vasilevskis, MD, MPH^{1,2,3}, and E. Wesley Ely, MD, MPH^{2,3,4}

The Neurohospitalist
2014, Vol. 4(2) 58-60
© The Author(s) 2014
Reprints and permission:
sagepub.com/journalsPermissions.nav
DOI: 10.1177/1941874414524796
nhos.sagepub.com

Keywords

delirium, ICU delirium, cognitive impairment

Introduction

Delirium is a frequent condition in the acute care setting and poses ongoing patient and societal burdens. We performed a review of the literature to inform practicing hospitalists, neurologists, and neurohospitalists about advances in delirium research in the prior year. We reviewed internal medicine, neurology, critical care, geriatric, and psychiatric literature from 2013 and selected manuscripts that were assessed to advance our understanding of measurement, epidemiology, outcomes, and treatment of delirium. Within this brief report, we highlight the pain, agitation, and delirium guidelines and stress their importance in light of recent research that links delirium with long-term impairments in cognitions and function. We conclude with research updates in the pharmacologic and nonpharmacologic treatment of delirium.

Measurement

Early in 2013, the much anticipated guidelines for the management of pain, agitation, and delirium (PAD) were published.¹ The 20-person panel reviewed over 19 000 publications and used Grades of Recommendation Assessment, Development and Evaluation methodology and extensive psychometric analyses to assess the strength of evidence² of 5 delirium monitoring tools. Two tools, the Confusion Assessment Method for the ICU^{3,4} and the Intensive Care Delirium Screening Checklist (ICDSC),⁵ were judged to have A-level evidence and it was formally recommended for the first time that all patients in the ICU be routinely monitored using one of these instruments. Brummel et al published a follow-up manuscript that provided “secrets to success” for implementing such monitoring.⁶ Yu et al further strengthened this evidence base in their evaluation of feasibility and reliability of delirium monitoring in neurologically critically ill patients.⁷ In over 400 individual assessments, performed by neurologists, intensivists, neurosurgeons, and nurses, the ICDSC was found to have excellent agreement (κ coefficient between 0.58 and 0.91) across each of the 8 items that make up the ICDSC and showed excellent predictive validity. Along with pain and sedation, this study further demonstrates that delirium measures endorsed in the

PAD guidelines can be used for systematic delirium screening among neurologically critically ill patients.⁷

Epidemiology and Outcomes

Per the recently published data from the Bringing To Light The Risk Factors And Incidence Of Neuropsychological Dysfunction in ICU Survivors (BRAIN-ICU) cohort study, delirium continues to occur in as many as 75% of critically ill mechanically ventilated patients⁸ and in 27% of patients with acute stroke (per 2 recent reports^{9,10}), including those with intracerebral hemorrhage (ICH). The majority of patients, regardless of setting, exhibit features of hypoactive delirium with inattention as the cardinal feature of this form of organ dysfunction.

The high prevalence of delirium is especially disturbing in light of its relationship to long-term cognitive impairment. Pandharipande et al described 3- and 12-month outcomes in the BRAIN-ICU cohort (N = 821) of medical/surgical ICU survivors.⁸ Although only 6% of these patients had baseline cognitive impairment, at 12 months about 1 in 3 had cognitive dysfunction on par with mild to moderate dementia or traumatic brain injury. Longer duration of delirium was independently associated with worse global cognition ($P = .04$) and executive function at 1 year ($P = .007$).

In addition to long-term cognition, delirium may affect functional outcomes in hospitalized populations. Among

¹ Department of Medicine, Division of General Internal Medicine and Public Health, Vanderbilt University School of Medicine, Nashville, TN, USA

² Center for Health Services Research, Vanderbilt University School of Medicine, Nashville, TN, USA

³ Department of Veterans Affairs Medical Center, Geriatric Research, Education and Clinical Center (GRECC), Tennessee Valley Healthcare System, Nashville, TN, USA

⁴ Department of Medicine, Division of Allergy, Pulmonary, and Critical Care Medicine, Vanderbilt University School of Medicine, Nashville, TN, USA

Corresponding Author:

Eduard E. Vasilevskis, Department of Medicine, Division of General Internal Medicine and Public Health, Vanderbilt University School of Medicine, 1215 21st Ave S., 6006 MCE, Nashville, TN 37232, USA.

Email: eduard.vasilevskis@vanderbilt.edu

ICH survivors, Naidech et al showed that ever having delirium was associated with over 8 times higher odds of poor functional outcome at 28 days ($P = .018$), even after adjustment for National Institute of Health stroke scale.¹⁰ This independent effect of delirium, however, no longer existed at 3 and 12 months. Two additional studies, in postoperative and medical/surgical ICU populations, found independent relationships between delirium and increased dependence in activities of daily living at 6 months ($P < .001$) and 12 months ($P = .002$), respectively.^{11,12} Collectively, these data highlight that as more patients survive their acute care hospital stay, the hospital provider community must bolster efforts to prevent and treat delirium and improve long-term outcomes.

Treatment

Advances in treatment include both pharmacologic and non-pharmacologic considerations. Although antipsychotic medications have been the mainstay of pharmacologic treatment of delirium, data from randomized trials are sparse with regard to their benefits and harms. Page et al recently published one of the largest ($N = 142$) randomized controlled, double-blinded trials of haloperidol versus placebo.¹³ This trial showed no difference in duration of delirium or coma among mixed medical/surgical ICU patients. Additional trials with differing doses, agents, and populations need to be performed to further solidify this evidence base.

Among nonpharmacologic interventions, multicomponent strategies continue to be mainstay of prevention. A systematic review by Reston and Schoelles of in-facility delirium prevention programs concluded that evidence is moderately strong in support of multicomponent strategies for delirium prevention.¹⁴ Most programs include interdisciplinary teams with standardized protocols for early mobilization, volume repletion, medication management, and vision/hearing protocols. Multicomponent strategies were further advocated in Society of Critical Care Medicine's PAD guidelines, including daily sedation interruption or light-targeted sedation, spontaneous breathing trials, avoidance of benzodiazepines, early mobilization, and sleep hygiene.^{1,15} Further testing of these approaches, as shown by Balas et al, is required to understand the barriers/facilitators to implementation and to refine further strategies to maximize effectiveness.¹⁶

Declaration of Conflicting Interests

The authors declared the following potential conflicts of interest with respect to the research, authorship, and/or publication of this article: The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health or the Department of Veterans' Affairs. Dr Ely reports grant support from NIA/NIH and VA GRECC; personal fees from Hospira, Abbott, and Orion; and other support from the Institute for Healthcare Improvement outside the submitted work. Dr Vasilevskis reports grant support from NIA/NIH and VA GRECC.

Funding

The authors disclosed receipt of the following financial support for the research, authorship and/or publication of this article: Supported by grants from the National Institutes of Health (AG027472; HL111111 to Dr Ely; AG040157 to Dr Vasilevskis); the Veterans Affairs (VA) Clinical Science Research and Development Service (to Dr Ely); and the VA Tennessee Valley Geriatric Research Education and Clinical Center (to Drs Vasilevskis and Ely).

References

1. Barr J, Fraser GL, Puntillo K, et al. Clinical practice guidelines for the management of pain, agitation, and delirium in adult patients in the intensive care unit. *Crit Care Med*. 2013;41(1):278-280.
2. Barr J, Kishman CP, Jaeschke R. The methodological approach used to develop the 2013 pain, agitation, and delirium clinical practice guidelines for adult ICU patients. *Crit Care Med*. 2013;41(9 suppl 1):S1-S15.
3. Ely EW, Margolin R, Francis J, et al. Evaluation of delirium in critically ill patients: validation of the confusion assessment method for the intensive care unit (CAM-ICU). *Crit Care Med*. 2001;29(7):1370-1379.
4. Ely EW, Inouye SK, Bernard GR, et al. Delirium in mechanically ventilated patients: validity and reliability of the confusion assessment method for the intensive care unit (CAM-ICU). *JAMA*. 2001;286(21):2703-2710.
5. Bergeron N, Dubois MJ, Dumont M, Dial S, Skrobik Y. Intensive care delirium screening checklist: evaluation of a new screening tool. *Intensive Care Med*. 2001;27(5):859-864.
6. Brummel NE, Vasilevskis EE, Han JH, Boehm L, Pun BT, Ely EW. Implementing delirium screening in the ICU: secrets to success. *Crit Care Med*. 2013;41(9):2196-2208.
7. Yu A, Teitelbaum J, Scott J, et al. Evaluating pain, sedation, and delirium in the neurologically critically ill—feasibility and reliability of standardized tools. *Crit Care Med*. 2013;41(8):2002-2007.
8. Pandharipande PP, Girard TD, Jackson JC, et al. Long-term cognitive impairment after critical illness. *N Engl J Med*. 2013;369(14):1306-1316.
9. Carin-Levy G, Mead GE, Nicol K, Rush R, van Wijck F. Delirium in acute stroke: screening tools, incidence rates and predictors: a systematic review. *J Neurol*. 2012;259(8):1590-1599.
10. Naidech AM, Beaumont JL, Rosenberg NF, et al. Intracerebral hemorrhage and delirium symptoms. length of stay, function, and quality of life in a 114-patient cohort. *Am J Respir Crit Care Med*. 2013;188(11):1331-1337.
11. Abelha FJ, Luís C, Veiga D, et al. Outcome and quality of life in patients with postoperative delirium during an ICU stay following major surgery. *Crit Care*. 2013;17(5):R257. doi:10.1186/cc13084.
12. Brummel NE, Jackson JCP, Pandharipande PP, et al. Delirium in the ICU and subsequent long-term disability among survivors of mechanical ventilation. *Crit Care Med*. 2014;42(2):369-377.

13. Page VJ, Ely EW, Gates S, et al. Effect of intravenous haloperidol on the duration of delirium and coma in critically ill patients (Hope-ICU): a randomised, double-blind, placebo-controlled trial. *Lancet Respir Med*. 2013;1(7):515-523.
14. Reston JT, Schoelles KM. In-facility delirium prevention programs as a patient safety strategy: a systematic review. *Ann Intern Med*. 2013;158(5 pt 2):375-380.
15. Barr J, Pandharipande PP. The pain, agitation, and delirium care bundle: synergistic benefits of implementing the 2013 pain, agitation, and delirium guidelines in an integrated and interdisciplinary fashion. *Crit Care Med*. 2013;41(9):S99-S115.
16. Balas MC, Burke WJ, Gannon D, et al. Implementing the awakening and breathing coordination, delirium monitoring/management, and early exercise/mobility bundle into everyday care: opportunities, challenges, and lessons learned for implementing the ICU pain, agitation, and delirium guidelines. *Crit Care Med*. 2013;41(9 suppl 1):S116-S127.