

What's New in the Patient Safety World

April 2016

Dexmedetomidine and Delirium

Pharmacologic interventions to prevent or treat delirium have been elusive. Antipsychotic drugs have sometimes been touted to be successful but the evidence has not been very convincing. A meta-analysis of antipsychotic treatment in patients with delirium ([Kishi 2015](#)) suggested that second generation antipsychotics have a benefit for the treatment of delirium with regard to efficacy and safety compared with haloperidol but emphasized that further study using larger samples is required. But another recent systematic review and meta-analysis found that current evidence does not support the use of antipsychotics for prevention or treatment of delirium ([Neufeld 2016](#)). Those authors found antipsychotic use was not associated with reduction in delirium incidence, change in delirium duration, severity, or hospital or ICU length of stay.

For several years now there has been interest in the use of dexmedetomidine, an α 2-adrenoreceptor agonist, as a sedation agent in the ICU because it might be associated with less delirium. In our February 10, 2009 Patient Safety Tip of the Week “[Sedation in the ICU: The Dexmedetomidine Study](#)” we discussed the SEDCOM (Safety and Efficacy of Dexmedetomidine Compared With Midazolam) Study, which concluded that dexmedetomidine was as effective as midazolam at keeping patients in the desired sedation range and was associated with a reduced prevalence of delirium and reduced time to extubation ([Riker 2009](#)). However, we urged caution in interpreting the conclusions of that study because of several methodological and other concerns outlined in our column. We again discussed dexmedetomidine in our June 16, 2015 Patient Safety Tip of the Week “[Updates on Delirium](#)”.

Now another study has addressed the use of dexmedetomidine in intubated ICU patients with delirium ([Reade 2016](#)). The Dexmedetomidine to Lessen ICU Agitation (DahLIA) study was a double-blind, placebo-controlled, parallel-group randomized clinical trial in 15 ICU's in Australia and New Zealand. Subjects were ICU patients who were deemed to be ready for extubation except that they had delirium. Dexmedetomidine increased ventilator-free hours at 7 days compared with placebo (median, 144.8 hours vs 127.5 hours, respectively). Among several secondary outcome measures they also found that dexmedetomidine reduced time to extubation (median, 21.9 hours vs 44.3 hours with placebo), and accelerated resolution of delirium (median, 23.3 hours vs 40.0 hours).

Again, this sounds encouraging, particularly since our pharmacologic armamentarium for managing delirium is so limited. Yet there are again some red flags that urge us to be

cautious in recommending widespread use of dexmedetomidine. First of all, this study applies only to a very select group of patients – those who were already well enough to be being considered for extubation except for their delirium. The authors note that they screened 21,500 patients to recruit just the 74 patients randomized in the study! That small sample size (actually only 71 patients after 3 withdrawals for various reasons). Even more importantly, the study was terminated before its planned recruitment of 96 patients. Studies with early termination typically show more exaggerated effect sizes. Early termination was apparently done because the funding source ceased funding beyond the originally defined period. The authors note that the funding source had no role in the design of the study and had no access to study data during the study, and the authors performed sensitivity analyses suggesting the abbreviated sample size was unlikely to alter the primary conclusion. Nevertheless, such occurrences always raise our “hype radar” or “spin radar” (see our February 16, 2010 Patient Safety Tip of the Week [“Spin/Hype...Knowing It When You See It”](#)).

So while we are somewhat encouraged by the results of the DahLIA study, we’re not yet ready to jump on the dexmedetomidine bandwagon for more widespread use. Remember, this was a very narrow patient population and it would be premature to extrapolate the results to patients with delirium earlier in their ICU course (i.e. before they were deemed otherwise ready for extubation). The good news, though, is that the dexmedetomidine seemed to be well tolerated in this study and adverse events were rare. We therefore look forward to further studies on the use of dexmedetomidine for either prevention or treatment of delirium.

Some of our prior columns on delirium assessment and management:

- October 21, 2008 [“Preventing Delirium”](#)
- October 14, 2008 [“Managing Delirium”](#)
- February 10, 2009 [“Sedation in the ICU: The Dexmedetomidine Study”](#)
- March 31, 2009 [“Screening Patients for Risk of Delirium”](#)
- June 23, 2009 [“More on Delirium in the ICU”](#)
- January 26, 2010 [“Preventing Postoperative Delirium”](#)
- August 31, 2010 [“Postoperative Delirium”](#)
- September 2011 [“Modified HELP Helps Outcomes in Elderly Undergoing Abdominal Surgery”](#)
- December 2010 [“The ABCDE Bundle”](#)
- February 28, 2012 [“AACN Practice Alert on Delirium in Critical Care”](#)
- April 3, 2012 [“New Risk for Postoperative Delirium: Obstructive Sleep Apnea”](#)
- August 7, 2012 [“Cognition, Post-Op Delirium, and Post-Op Outcomes”](#)
- September 2013 [“Disappointing Results in Delirium”](#)
- October 29, 2013 [“PAD: The Pain, Agitation, and Delirium Care Bundle”](#)
- February 2014 [“New Studies on Delirium”](#)
- March 25, 2014 [“Melatonin and Delirium”](#)

- May 2014 “[New Delirium Severity Score](#)”
- August 2014 “[A New Rapid Screen for Delirium in the Elderly](#)”
- August 2014 “[Delirium in Pediatrics](#)”
- November 2014 “[The 3D-CAM for Delirium](#)”
- December 2014 “[American Geriatrics Society Guideline on Postoperative Delirium in Older Adults](#)”
- June 16, 2015 “[Updates on Delirium](#)”
- October 2015 “[Predicting Delirium](#)”
- April 2016 “[Can Antibiotics Lead to Delirium?](#)”

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