


Agitated Patients in the Intensive Care Unit: Guidelines for Causal Rather Than Symptomatic Treatment are Warranted

Omid Azimaraghi, MD¹, Vance Smith, MD², William J. Sauer, MD¹, Jonathan E. Alpert, MD, PhD³, and Matthias Eikermann, MD, PhD^{1,4} 

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An agitated, intubated and mechanically ventilated patient in the intensive care unit (ICU) represents a stress test to the multidisciplinary care team because immediate treatment is required to prevent self-harm and provider injuries. In this issue of the *Journal of Intensive Care Medicine*, Prendergast et al,¹ provide important new data which suggest that ICU physicians do not consistently have the knowledge and skillset needed to treat agitation in the ICU appropriately.

Agitation is a psychomotor disturbance characterised by a marked increase in both motor and psychological activities, often accompanied by a loss of control of action and disorganisation of thought.² It may be isolated, or accompanied by other mental disorders, such as anxiety or delirium. Agitation was described as a clinical symptom about 70 years ago,^{3,4} when antipsychotic medications (neuroleptics) were introduced in clinical practice.⁵⁻⁷ Thus, the administration of antipsychotics or other sedatives, primarily the benzodiazepines or IV haloperidol, often represents our stereotypical approach to agitation treatment.

Agitation is an International Classification of Diseases (ICD)-10 diagnosis which can be found under symptoms and signs involving emotional state (R45.1). In the *Diagnostic and Statistical Manual of Mental Disorders (DSM-5)*, agitation is defined as “excessive motor activity associated with a feeling of inner tension. The activity is described as non-productive and repetitious and consists of behaviours such as pacing, fidgeting, wringing of the hands, pulling of clothes, and inability to sit still”.⁸

For a long time, agitation in ICU patients was ignored, probably because our patients often were deeply sedated. While the Ramsay scale was developed in 1974 for measuring the level of sedation in the ICU - agitation, the other side of the consciousness coin was ignored.⁹ In 1989, the Agitated Behaviour Scale was developed as the first instrument to quantify agitation in patients.¹⁰ ABS is a 14-item scale to quantify agitation in patients with traumatic brain injury. The authors categorised different types of predictive behaviour such as attention span, ability to concentrate, impulsiveness versus patience, tolerance for frustration and mood changes.¹⁰ The Richmond Agitation-Sedation Scale was introduced 20 years ago as the first ICU specific instrument which allowed for quantification of the continuous spectrum between unresponsiveness and agitation in the ICU.¹¹ However, the instrument does not help the clinicians identify the cause of their patients’ agitation.

Agitation can be the consequence of a neurological disease, or an expression of discomfort such as pain, full bladder or severe dyspnea (See Figure 1).

Prendergast et al,¹ used a survey including a quantitative clinical vignette to determine how agitation (indicated by a Riker Sedation Agitation Scale SAS score of 4)¹² influenced clinical decision making. Almost all clinicians believe that agitation is a common symptom in mechanically ventilated critically ill patients. The majority of respondents considered it as a barrier to extubation. Not surprisingly, their results also indicate that treatment of agitation varies across clinicians with differing training backgrounds. These results support the view that guidelines for treatment of agitation in critically ill patients are warranted. Such guidelines should not just focus on the question which antipsychotic, sedative, or nonpharmacologic intervention should be used to eliminate the combative behaviour as rapidly and safely as possible. They should rather describe a framework for differential diagnosis and treatment of patients presenting with agitation in the intensive care unit.

The symptom of agitation in the ICU is an indication of imminent harm that needs to be immediately addressed,¹³ in order to improve patient comfort and long-term outcomes. Prior to treating the symptom agitation with a sedative or an antipsychotic medication, clinicians should evaluate the main reasons for agitation: hemodynamic instability leading to inadequate oxygen delivery to the brain, hypercarbia, hypoxia (pneumonia, pulmonary emboli), acute brain dysfunction (delirium), pain, a full bladder, severe anxiety, drug withdrawal or infectious sources that can present as agitation and confusion. We have developed a checklist which may be considered by

¹Department of Anesthesiology, Montefiore Medical Center and Albert Einstein College of Medicine, Bronx, NY, USA

²Department of Surgery, Montefiore Medical Center, The Bronx, 111 E 210th St, Bronx, NY, USA

³Department of Psychiatry, Montefiore Medical Center and Albert Einstein College of Medicine, The Bronx, 111 E 210th St, Bronx, NY, USA

⁴Klinik für Anästhesiologie und Intensivmedizin, Universität Duisburg-Essen, Essen, Germany

Corresponding Author:

Matthias Eikermann, MD, PhD, Department of Anaesthesiology, Montefiore Medical Center, 111 East 210th Street, Bronx, NY 10467, USA.
Email: meikermann@montefiore.org

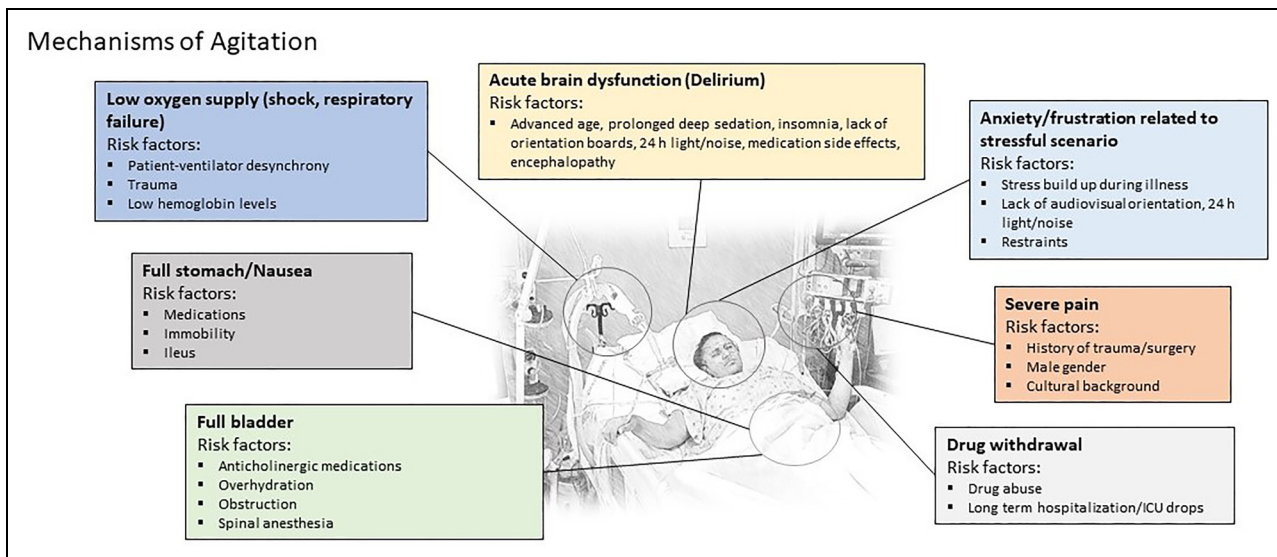


Figure 1. Risk factors of agitation. Agitation is a psychomotor disturbance characterized by a marked increase in both motor and psychological activities, often accompanied by a loss of control of action and disorganization of thought. Prior to treating the symptom agitation with a sedative or an antipsychotic medication, clinicians should evaluate the main reasons for agitation: hemodynamic instability leading to inadequate oxygen delivery to the brain, hypercarbia, hypoxia (pneumonia, pulmonary emboli), acute brain dysfunction (delirium), pain, a full bladder, severe anxiety, drug withdrawal or infectious sources that can present as agitation and confusion.

Agitation Checklist

		Yes	No	Tips
1	Is the patient in severe pain ?	<input type="radio"/>	<input type="radio"/>	Administer regional blocks, Administer analgesics (opioids or IV Acetaminophen or NSAIDs)
2	Does the patient have hypercarbia ?	<input type="radio"/>	<input type="radio"/>	Optimize ventilator support, Consider changing the mode of ventilation
3	Does the patient have high anxiety levels ?	<input type="radio"/>	<input type="radio"/>	Consider low dose IV benzodiazepines, alpha 2 agonists or non pharmacological interventions
4	Is there a decrease in arterial oxygen levels (hypoxia)?	<input type="radio"/>	<input type="radio"/>	Optimize oxygen therapy or ventilator support
5	Has the cardiac output decreased significantly?	<input type="radio"/>	<input type="radio"/>	Consider vasoactive drugs or fluid resuscitation
6	Is the patient in an uncomfortable position ?	<input type="radio"/>	<input type="radio"/>	Consider turning or sitting up the patient,/ Mobilize the patient if possible
7	Does the patient have nausea or a full stomach ?	<input type="radio"/>	<input type="radio"/>	Suction nasogastric-tube/ give antiemetic medications
8	Does the patient have a full bladder ?	<input type="radio"/>	<input type="radio"/>	Check if the foley catheter is working/clamped? Is it needed
9	Are there any sign or symptoms of drug withdrawal ?	<input type="radio"/>	<input type="radio"/>	Consider opioids or benzodiazepines if tapered recently
10	Is the patient confused and disoriented (delirious) ?	<input type="radio"/>	<input type="radio"/>	Reorient patient, establish sleep/wake cycle

Figure 2. Agitation checklist. We have developed a checklist which may be considered by the clinicians prior to the administration of intravenous sedatives or antipsychotics. This checklist may be used by critical care physicians to screen for underlying mechanisms of agitation. NSAIDs; Nonsteroidal anti-inflammatory drug.

the clinicians prior to the administration of intravenous sedatives or antipsychotics (Figure 2).

Both non-pharmacological and pharmacological strategies should be used to prevent and treat agitation. Non-pharmacological strategies require effective communication with the patient. This is challenging in intubated patients who wake up from sedation and needs to be trained – and

essentially needed to identify the optimal causal therapy of agitation (See Figure 2).

Drugs that reduce dopaminergic or noradrenergic tone or increase serotonergic or GABAergic tone attenuate agitation.¹⁴ However, a non-causative, symptomatic treatment of agitation with antipsychotics or sedatives has negative effects. While sedatives can immediately relieve anxiety, reduce the stress,

and prevent agitation-related harm, their prolonged use prolongs the duration of mechanical ventilation, immobility, and increases mortality.^{15,16}


Additional studies are needed. It is not known if causal therapy of agitation improves patients' outcomes.^{17,18} The severity of patients' agitation often may be a function of the injury severity rather than an independent disease or symptom that can be causally treated.¹⁹

We propose that before treating agitation in the ICU symptomatically, the clinician should evaluate primary mechanisms of agitation. A better understanding of available pharmacological and non-pharmacological interventions for differential and causal treatment of agitation will help clinicians break down the barrier of agitation to recovery in the ICU.

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ORCID iD

Matthias Eikermann  <https://orcid.org/0000-0002-7893-0596>

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