

An Overview of Delirium in the Critical Care Setting

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Delirium is a morbid and common complication in the critically ill patient. Its recognition is made more difficult by the inability to interview the intubated patient, and by the presence of drugs and confounding comorbidities. Delirium screening (described with the ICDSC and the CAM-ICU) with tools specifically designed for the acute care setting can help the nurse or clinician identify its presence. Risk factors for delirium in the critical care setting differ from those described in other populations. Treatment is currently empiric.

Key words: delirium, critical care, outcomes, intensive care, screening.

Introduction

Delirium in hospitalized patients is well recognized as morbid,^{1,2,3} costly and disturbing to patients, caregivers and family.⁴ Delirium in the intensive care unit (ICU) is associated with adverse outcomes such as self-extubation, removal of indwelling catheters,⁵ prolonged ventilator dependence⁶ and lengthened ICU and hospital stay.⁷⁻⁹ Although delirium has not been associated clearly with increased ICU mortality,^{5,6} it seems to be an independent marker for increased one-year mortality.¹⁰ Identification of delirium in a critical care patient, in whom sedation and analgesia affect level of consciousness, is challenging.^{11,12} Agitation and anxiety in the critical care setting may be due to delirium, pain or emotional distress—all are common and may mimic one another. It is not in the scope of this review to address pain and anxiety evaluation, neither of which has been well described in the critical care context as publications focus primarily on sedation.¹³ Delirium screening tools to facilitate identification or recognition of delirium in the ICU setting, and what is known of the disorder in the ICU, are described herein, with the goal of providing the practitioner with perspective on this important clinical syndrome.

Screening for Delirium in the ICU

Delirium, a transient neuropsychiatric syndrome, is associated with decline in

cognitive function and change in behaviour. The essential diagnostic features are defined by the Diagnostic and Statistical Manual of Mental Disorders, version IV (DSM-IV), as follows:¹⁴

- Disturbance of consciousness with reduced ability to focus, sustain or shift attention.
- A change in cognition or the development of a perceptual disturbance that is not better accounted for by a pre-existing dementia.
- The disturbance develops over a short period of time and tends to fluctuate.
- There is evidence from history, physical examination or laboratory findings that the disturbance is caused by the physiological consequences of a general medical condition.

The critical care setting, which includes intubated and often sedated patients, makes it difficult to apply the DSM-IV criteria using the standard interview methods described in other populations. Recent studies have assessed evaluation methods applicable to the critical care setting. The patient's critical care context usually implies a life-threatening medical condition. The tools that have been developed recently to screen for¹⁵ and facilitate identification of delirium¹⁶ in the ICU thus base their criteria primarily on the first three elements of the DSM-IV definition.

The intensive care delirium screening checklist (ICDSC; Table 1) was described in serially admitted medical-surgical critical care patients and compared to a psychiatrist's clinical diagnosis in a recent evaluation.¹⁵ Every eight-hour shift, 93 patients were evaluated with the screening tool. The mean age of patients was 62 years, the mean APACHE score was 14 and the incidence of delirium was 22%. The checklist was found to screen with great sensitivity (99%) and good specificity (64%). All patients with a false-positive screening score (of 4/8 points or more) had a structural neurologic abnormality or active neurologic disease.

The confusion assessment method for the intensive care unit (CAM-ICU; Table 2) was evaluated in 111 intensive care patients.¹⁶ Psychotic, neurologically ill, deaf and comatose patients were excluded from the screening process. The screening tool was administered by one of two research nurses and compared to a delirium expert's opinion (psychiatrist, geriatrician or neuropsychologist). The mean age of the patients was 55.3 years, the mean APACHE score was 22.9 and the incidence of delirium was 83.3%.

Both screening tools were described as user-friendly, had good inter-rater reliability, and were usable by nurses and other staff after minimal training. Both have now been integrated in the daily functioning of intensive care units because of the conviction of medical and nursing staff that screening for delirium is an important component of ensuring quality care and adequate assessment of patients.

Incidence of Delirium in the ICU

How can the important differences between the reported incidences of delirium (22% versus 83%) be explained? There are obvious differences in screened populations (e.g., diagnoses, ages, severity scores, sources and times for evalua-

Table 1

The Intensive Care Delirium Screening Checklist (ICDSC)

Patient Evaluation	Day 1	Day 2	Day 3	Day 4	Day 5
Altered level of consciousness (A–E)*					
Inattention					
Disorientation					
Hallucination, delusion, psychosis					
Psychomotor agitation or retardation					
Inappropriate speech or mood					
Sleep/wake cycle disturbance					
Symptom fluctuation					
Total Score (0–8)					
*Level of Consciousness	Score				
A: no response	–				
B: response to intense and repeated stimulation (loud voice and pain)	–				
C: response to mild or moderate stimulation	1				
D: normal wakefulness	0				
E: exaggerated response to normal stimulation	1				
If A or B, do not complete patient evaluation for the period.					
Scoring System					
The scale is completed based on information collected from each eight-hour shift or from the previous 24 hours. Obvious manifestation of an item = 1 point. No manifestation of an item or no assessment possible = 0 points. The score of each item is entered in the corresponding space and is 0 or 1. A total score of ≥ 4 on any given day has a 99% sensitivity for correlation with a psychiatric diagnosis of delirium.					
1. Altered level of consciousness					
A) No response or B) the need for vigorous stimulation in order to obtain any response signified a severe alteration in the level of consciousness precluding evaluation. If there is coma (A) or stupor (B) most of the time period, then a dash (—) is entered and there is no further evaluation for that period.					
C) Drowsiness or response to a mild to moderate stimulation implies an altered level of consciousness and scores 1 point.					
D) Wakefulness or sleeping state that could easily be aroused is considered normal and scores zero points.					
E) Hypervigilance is rated as an abnormal level of consciousness and scores 1 point.					
2. Inattention					
Difficulty in following a conversation or instructions, easily distracted by external stimuli, or difficulty in shifting focus all score 1 point.					
3. Disorientation					
Any obvious mistake in time, place or person scores 1 point.					
4. Hallucination, delusion or psychosis					
The unequivocal clinical manifestation of hallucination or of behaviour probably due to hallucination (e.g., trying to catch a non-existent object) or delusion, or gross impairment in reality testing all score 1 point.					
5. Psychomotor agitation or retardation					
Hyperactivity requiring the use of additional sedative drugs or restraints in order to control potential danger (e.g., pulling out i.v. lines, hitting staff), hypoactivity or clinically noticeable psychomotor slowing all score 1 point.					
6. Inappropriate speech or mood					
Inappropriate, disorganized or incoherent speech, inappropriate mood related to events or situation all score 1 point.					
7. Sleep/wake cycle disturbance					
Sleeping less than four hours or waking frequently at night (do not consider wakefulness initiated by medical staff or loud environment), or sleeping during most of the day all score 1 point.					
8. Symptom fluctuation					
Fluctuation of the manifestation of any item or symptom over 24 hours (e.g., from one shift to another) scores 1 point.					

Source: 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):859-64. Copyright notice of Springer-Verlag.

tion), and the scales themselves may favour different aspects of the clinical manifestations of delirium. The ICDSC screens for fluctuations in thought content, whereas the emphasis of the CAM-ICU is on arousal which conceivably could lead to positive scores with fluctuations in level of consciousness. Patients

with worsening or improving encephalopathy, or in whom sedative drug dosages are altered, may thus account for the high incidence of positive scoring with the CAM-ICU.

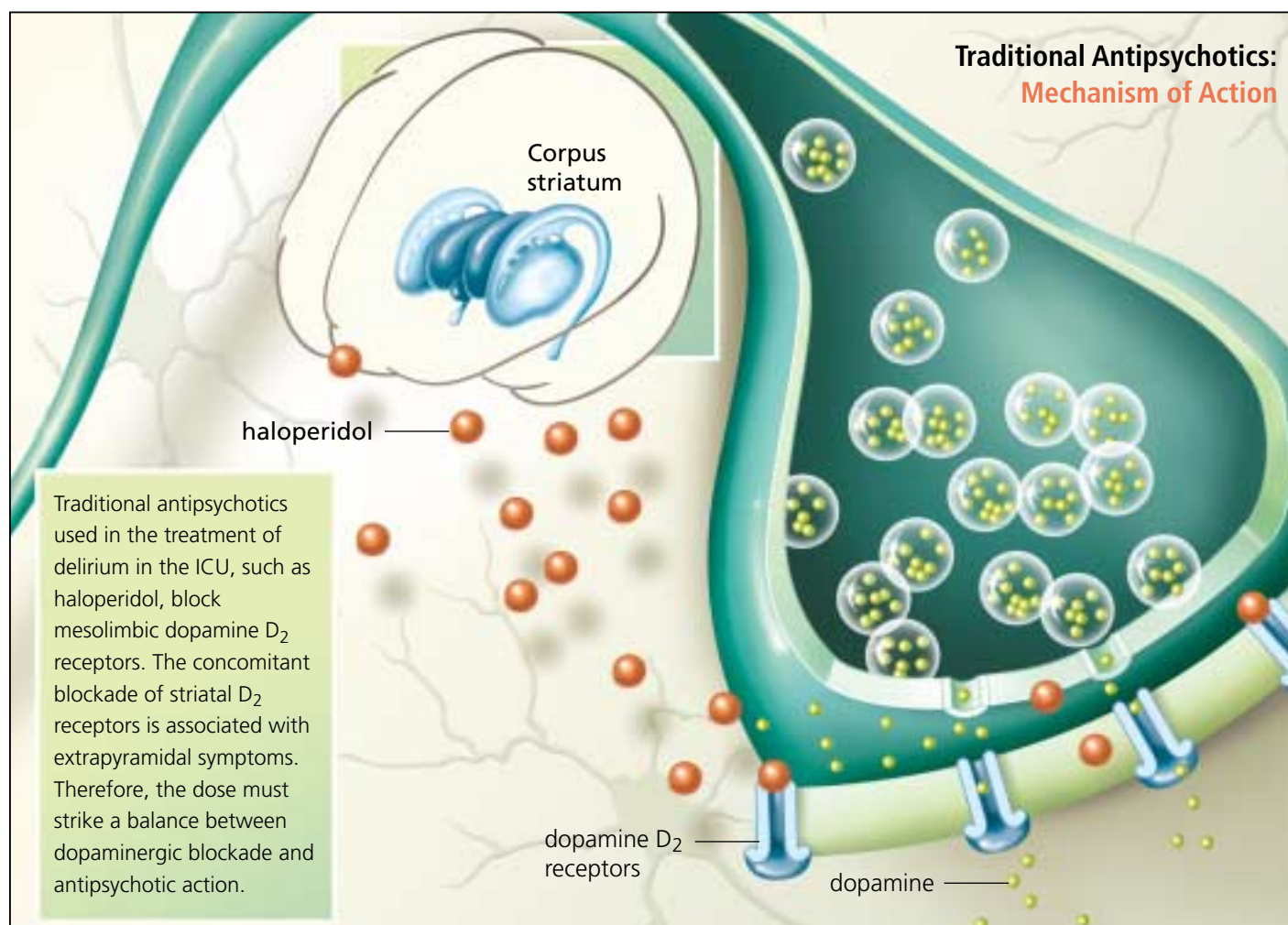
The question that ultimately needs resolving is what one calls delirium. Establishing a common definition is dif-

ficult, as psychiatric diagnoses differ notoriously among psychiatrists and between psychiatrists and other evaluators.^{11,12} In addition, the phenomenologic approach to delirium espoused by the consultation liaison psychiatrist—for whom hepatic encephalopathy, alcohol withdrawal and the delirium without

Table 2

The Confusion Assessment Method for the Intensive Care Unit (CAM-ICU)

Features and Descriptions	Absent	Present
I. Acute onset or fluctuating course A. Is there evidence of an acute change in mental status from the baseline? B. Or, did the (abnormal) behaviour fluctuate during the past 24 hours, that is, tend to come and go or increase and decrease in severity as evidenced by fluctuations on the Richmond Agitation Sedation Scale (RASS) or the Glasgow Coma Scale?	☐	☐
II. Inattention Did the patient have difficulty focusing attention as evidenced by a score of less than 8 correct answers on either the visual or auditory components of the Attention Screening Examination (ASE)?	☐	☐
III. Disorganized thinking Is there evidence of disorganized or incoherent thinking as evidenced by incorrect answers to 3 or more of the 4 questions and inability to follow the commands? Questions: 1. Will a stone float on water? 2. Are there fish in the sea? 3. Does 1 pound weigh more than 2 pounds? 4. Can you use a hammer to pound a nail? Commands: 1. Are you having unclear thinking? 2. Hold up this many fingers. (Examiner holds 2 fingers in front of the patient). 3. Now do the same thing with the other hand (without holding the 2 fingers in front of the patient). If the patient is already extubated from the ventilator, determine whether the patient's thinking is disorganized or incoherent, such as rambling or irrelevant conversation, unclear or illogical flow of ideas, or unpredictable switching from subject to subject.	☐	☐
IV. Altered level of consciousness Is the patient's level of consciousness anything other than alert, such as being vigilant or lethargic or in a stupor or coma? Alert: Spontaneously fully aware of environment and interacts appropriately. Vigilant: Hyperalert. Lethargic: Drowsy but easily aroused, unaware of some elements in the environment or not spontaneously interacting with the interviewer; becomes fully aware and appropriately interactive when prodded minimally. Stupor: Difficult to arouse, unaware of some or all elements in the environment or not spontaneously interacting with the interviewer; becomes incompletely aware when prodded strongly; can be aroused only by vigorous and repeated stimuli and as soon as the stimulus ceases, stuporous subject lapses back into unresponsive state. Coma: Unarousable, unaware of all elements in the environment with no spontaneous interaction or awareness of the interviewer so that the interview is impossible even with maximal prodding.	☐	☐
Overall CAM-ICU Assessment (Features I and II and either Feature III or IV):	Yes ____	No ____
Source: Ely, <i>et al.</i> JAMA 2001;286:2707-10.		



clear causal etiology are all called “delirium” and are associated with different diseases—may differ from what the intensive care clinician labels delirium, which is more likely to be of uncertain, and possibly multiple factor causality. Consensus expert groups and inter-institutional comparisons are required before recommending one screening or identification tool. Both bedside evaluation instruments are useful to teach and raise awareness of the diagnosis of delirium in the ICU among nursing and medical staff. Regrettably, a minority of institutions in the U.S.¹⁷ and in Canada¹⁸ perform this screening systematically.

Delirium Subtypes

The importance of systematic screening for delirium in the critical care setting becomes clear when one considers the various clinical manifestations of delirium.^{19,20} Every clinician is able to recog-

nize the thrashing, agitated and floridly paranoid patient with hyperactive delirium. However, investigators point out a significant incidence of “quiet”, or hypoactive, delirium, whereby the patient hallucinates or is paranoid but is not agitated.¹⁵ These patients are seldom clinically identified unless one seeks the diagnosis and inquires about thought content. Quietly delirious patients have a worse prognosis than non-delirious patients,¹⁵ supporting the theory that delirium is a reflection of organ dysfunction or psychological reserve.

Risk Factors

Very little data exist on factors associated with the development of delirium in the ICU. The only study directly assessing this issue suggested a marked difference in predictors of developing delirium in the ICU versus hospitalized surgical or medical patients.⁵ In ICU delirium, risk

factors related to medical history included hypertension and a recent smoking history, the latter raising the possibility of nicotine withdrawal as a potential triggering mechanism. During ICU stay, the factor most strongly associated with the development of delirium was opiate use, an association that was dose-dependent.⁵ In another study, agitation without systematic diagnostic screening for delirium was evaluated in a large medical and surgical critical care population.⁶ Associations between delirium and age, severity of illness and benzodiazepine use were suggested.

The association of opiates and benzodiazepines with delirium or agitation in the critical care setting may reflect the use of these drugs in incremental amounts by the nursing personnel, perhaps because of early manifestations of psychiatric symptoms. A cause and effect association between benzodiazepine or

opiate use and delirium cannot be established based on the data currently available. The importance of titrating doses of either sedatives or analgesics to the needs of the patient deserves emphasis, however, as long as the possibility of a causal association remains. In addition, a number of studies have now established the high morbidity and cost associated with the administration of sedatives without careful adjustment of doses to match the patient's sedation level with established therapeutic goals.^{20,21}

Older Adults in the ICU

Our aging population and the fact that we are living longer with diseases likely to require intensive care, combined with the latter's rising costs, have motivated evaluations of the populations likely to benefit from critical care interventions.²² Currently published data are conflicting with regard to the association between geriatric admission to an ICU and the tendency to develop delirium.^{5,23} Patients with cognitive impairment before admission to an ICU do no worse in terms of number of ICU interventions required, ICU or hospital mortality or length of stay.²⁴ Those with prior cognitive impairment, however, are much more likely to be discharged to a nursing home.

Treatment

The clinical management and pharmacologic treatment of delirium remain unexplored. Many of the published recommendations for treatment of delirium in the ICU are empiric and extrapolated from case studies in other populations. Antipsychotic administration is broadly accepted, especially for agitated delirium.²⁵ Haloperidol, a potent dopaminergic antagonist, is the medication most commonly used in critical care practice. Intravenous haloperidol use presumes the parenteral route is more effective in emergency situations. Intravenous administration of the drug, with rapid dose escalation, is specifically recommended in textbooks and recently published guidelines.²⁶

Traditional antipsychotics, including haloperidol, act by blocking

mesolimbic dopamine D2 receptors (Figure). Concomitant blockade of striatal D2 receptors is associated with extrapyramidal effects. There is no consensus on the ideal dosage to balance the relationship between dopaminergic blockade and antipsychotic action. However, a threshold of 60% of D2 receptor blockade has been suggested, with higher levels conveying a higher risk for the development of neurological side effects with no further clinical improvement.²⁷ This threshold corresponds to doses of 2–20mg/day. Much higher doses are suggested in the recent recommendations²⁶ and textbooks. Extrapyramidal symptoms can be quite morbid, particularly in older patients in whom Parkinsonian symptoms are more likely;²⁸ some symptoms, such as acute laryngeal dystonia, can complicate upper airway management.²⁹ Torsades de pointes, particularly in cardiac patients, have been described with and occasionally without³⁰ a prolonged QT interval. Although many patients improve with intravenous haloperidol, "resistant" patients do occur.³¹ They may be exposed to potentially risky doses of a drug not scientifically investigated for this indication in the ICU setting. Haloperidol should thus be used sparingly, with close clinical evaluation.

New second-generation antipsychotics with more favourable pharmacologic profiles have been introduced for the treatment of schizophrenia. Their potential benefit in the treatment of delirium has recently been explored.³² Unfortunately, most of these drugs (with the exception of olanzapine) have active metabolites, and metabolism in older patients is unpredictably prolonged. The majority also require a normal gastrointestinal motility and are contraindicated in the presence of renal or hepatic dysfunction.

Benzodiazepines have long been used in the critical care setting to help manage anxiety and agitation. Many European centres choose benzodiazepines as first-line treatment for identified delirium. A recent North American survey polled primarily physicians

(567/726) about their drug of choice in the management of delirium;¹⁷ 73% of respondents used haloperidol, 14% used lorazepam and the remainder cited propofol—which has never been evaluated in delirium—and other drugs. No study has addressed the role of non-pharmacologic intervention (e.g., reassurance, day/night re-orientation) in the critical care setting, despite the usefulness of this type of intervention in the non-critical care context.³³ In some intensive care units, reassurance and other non-pharmacologic interventions are used as first-line approaches. In addition to being inherently sensible, their value lies in their low cost and low risk.

Conclusion

Screening for delirium in the critical care setting is paramount, as manifestations of the disorder are markers for prolonged ICU stay and may predict worse prognosis. Titrating sedatives and opiates to minimize their overall administration may help differentiate delirium from other disorders; the patient will be more awake and thought content will be easier to assess. An association exists between opiates, and perhaps benzodiazepines, and the occurrence of delirium. This supports the rationale of nonopiate co-analgesia as well as reassurance rather than pharmacologic intervention as a first-line approach to delirious patients. As treatment recommendations are strictly empirical at this time, a cautious approach with careful titration of drug dosage, and an emphasis on "doing no harm", is warranted. Regardless of therapeutic choice in the pharmacologic management of delirium, careful monitoring of response is important. ♦

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