Delirium in intensive care

Jennifer King MBChB FRCA
Andrew Gratrix MBChB FCARCSI

Key points

Delirium occurs in 60–80% of intensive care patients and is commonly overlooked.

The hypoactive form and mixed type are more common than the hyperactive type of delirium.

Prevention should consist of minimizing risk factors where possible.

Sedation scoring and sedation holds reduce the risk of delirium.

Assessment of delirium can be easily performed with the intensive care delirium screening checklist and confusion assessment method for the intensive care unit tools.

Delirium in intensive care

Delirium in critically ill patients is a common occurrence (between 60% and 80% of ventilated patients),[1] which has previously received little attention. Recent guidelines by the Intensive Care Society (ICS) and the Society of Critical Care Medicine (SCCM) recommend daily monitoring of sedation scores and delirium in all intensive care unit (ICU) patients. Recent studies have increased knowledge and interest in the treatment and prevention of delirium.

Delirium outside of the ICU has been studied in more detail, and is associated with a three-fold increase in mortality, increased incidence of infection, and increased hospital stay, along with long lasting and severe cognitive impairment. It would seem reasonable to expect that delirium in the ICU would cause the same problems.

Types of delirium

Delirium is defined as a disturbance of consciousness and a change in cognition that develops over a short period of time.[2] Although various terms have been used to describe delirium (e.g. ICU psychosis, ICU syndrome), any acute disturbance in cognitive function should now be described as delirium.

Delirium is a syndrome with a wide range of presentations. Most of us think of a delirious patient as one who is aggressive, agitated, pulling out lines, and possibly hallucinating. This is hyperactive delirium and occurs in only 5–22% of such patients. The majority of critically ill patients with delirium have either the hypoactive form or a mixed picture where they fluctuate between hyperactivity and hypoactivity. Patients with hypoactive delirium are most commonly missed. They often wake up from sedation peacefully, smile, nod, and say yes to all questions. Closer questioning will, however, reveal signs of inattention and decreased awareness of the environment.

Delirium is a psychiatric disorder and as such is classified in the diagnostic and statistical manual of mental disorders (DSM). The latest edition, DSM-IV, further subdivides it, according to aetiology:

(i) delirium due to a general medical condition;
(ii) substance induced delirium—including medication side-effects;
(iii) delirium due to multiple aetiologies;
(iv) delirium not otherwise specified.

The importance of diagnosing delirium to this degree in the critically ill is debatable and most of these patients will have multiple aetiologies which may be difficult to elicit.

Differential diagnosis

Several symptoms of delirium also occur in other psychiatric conditions and of course these psychiatric conditions may also coexist in the same patient, which can make the diagnosis problematic. The main differential diagnoses are dementia and depression, although other primary psychiatric disorders such as schizophrenia may be considered.

Cognitive impairment occurs in both delirium and dementia, although there are several other significant differences. Dementia has a prolonged onset and occurs over years. A good history of the patient's cognitive state in the months preceding their ICU admission is the most helpful in differentiating between the two. Patients often exhibit features of an acute confusional state before ICU admissions, as delirium can be the first sign of critical illness often occurring before hypotension or other systemic failures become apparent. It is therefore important to differentiate between long-standing cognitive impairment and acute onset. Patients with dementia do not show signs of inattention and will do their best to answer questions and maintain eye contact with the questioner, they are alert and do not have disturbances in consciousness. Their speech is usually coherent and they do not usually suffer delusions or hallucinations, which may occur in delirium. These differences usually allow a diagnosis of

Jennifer King MBChB FRCA
Specialist Registrar in Anaesthesia
Intensive Care Unit
Hull Royal Infirmary
Anlaby Road
Hull HU3 2JZ
UK

Andrew Gratrix MBChB FCARCSI
Consultant in Intensive Care and Anaesthesia
Intensive Care Unit
Hull Royal Infirmary
Anlaby Road
Hull HU3 2JZ
UK
Tel: +44 1482 675031
Fax: +44 1482 675238
E-mail: andrew.gratrix@hey.nhs.uk
(for correspondence)

doi:10.1093/bjaceaccp/mkp023 Advance Access publication 8 September, 2009
Continuing Education in Anaesthesia, Critical Care & Pain | Volume 9 Number 5 2009

either delirium or dementia to be made. However, pre-existing cognitive impairment is a significant risk factor for developing delirium, so they may co-exist.

Patients with hypoactive delirium are often misdiagnosed as depressed. The presence of cognitive impairment and disorientation, which do not occur in depression, helps in the diagnosis. The timing of onset of symptoms can also be helpful.

Hallucinations and delusions may cause the diagnosis of schizophrenia to be considered. Schizophrenic patients do not have altered levels of consciousness or cognitive impairment. They also tend to suffer from auditory hallucinations rather than visual hallucinations that characterize delirium.

Prevention

Most prevention strategies consist of minimizing risk factors (Table 1), although there are few studies looking at prevention in the ICU setting. A study of 53 critically ill patients showed that they were exposed to an average of 11 risk factors per patient.[3] Patients who have three or more risk factors have a 60% chance of developing delirium. Some risk factors cannot be altered such as old age, alcoholism, pre-existing cognitive impairment, depression, pre-existing hypertension, smoking, and visual/hearing impairment. Strategies used in the non-ICU setting include repeated reorientation of patients, addressing visual and hearing impairments, early mobilization, having the same nurse caring for the patient, reduction of noise/stimuli, non-pharmacological sleep protocols, and stimulating patient activities.

Iatrogenic factors can precipitate delirium and are common in the ICU: medication, sleep disturbance, and immobilization.

Sedation and analgesia medication

Almost all patients who are invasively ventilated receive continuous infusions of sedatives and analgesics, usually opioid-based; these are generally administered with the aim of reducing pain and stress and improving compliance with treatment. Multiple studies have shown an association between sedative drugs and delirium, with benzodiazepines being the most strongly associated. Daily wake-up tests and sedation scoring are recommended, as they allow dose titration on an individual patient basis, although a recent survey of ICUs in the UK revealed that they are rarely actually performed. New drugs such as dexmedetomidine, an α_2 agonist, may have a role in the future.

Table 1 Risk factors for delirium

Patient factors	Critical illness factors	Iatrogenic factors
Old age	Acidosis	Medication
Alcoholism	Anaemia	Sleep disturbance
Hypertension	Sepsis/fever	Immobilization
Depression	Hypotension	
Smoking	Metabolic disturbance	
Vision/hearing impairment		
Cognitive impairment		

The evidence for an association between opioids and delirium is less strong than that for benzodiazepines. Good pain control reduces the likelihood of delirium, but again these drugs should be used only as necessary. Protocols that use intermittent boluses of drugs rather than continuous infusions may improve a number of outcomes including delirium.

The short-acting opioid, remifentanil, has a context-sensitive half-life of 3–4 min and a terminal half-life of 10–20 min. Owing to its rapid offset, it may be useful in differentiating between oversedation and brain dysfunction. Currently, it is only licensed for use in the ICU for 3 days and further studies of its effects on delirium and other outcomes are required.

Sleep deprivation

Sleep deprivation is very common in critically ill patients, and may lead to impairment of cognition. On average, patients in the ICU sleep for only 2 h day^{-1}, and $<$6% of their sleep is rapid eye movement (REM), with polysomnography demonstrating severely disrupted sleep. Interestingly, excessive noise and patient care activities such as turning and tracheal suctioning account for only a minimal amount of sleep disturbance.[4] Metabolic derangements, invasive ventilation, and drugs are much more significant. Although it is difficult to improve sleep on ICU, certain measures can be taken such as attempting to have an appropriate day/night cycle, with lights on and off at the correct times, and encouraging sleeping at night time rather than during the day. Many of the drugs routinely administered in the ICU cause sleep disruption themselves, especially a decrease in REM sleep. These patients can be at risk of REM rebound when drugs are withdrawn, which can cause tachycardia, hypertension, and nightmares.

Immobilization

Immobilization is a common problem on ICU and is a risk factor for delirium. Fully ventilated patients may be unable to be mobilized, but movement should be encouraged wherever possible. Chemical and especially physical restraints should only be used when necessary and other causes of immobility should be identified and remedied where possible. Lines, monitoring, and catheters all prove a barrier to mobility along with more simple practical factors such as the need for extra staff to move patients and specialist equipment to get them out of bed. Encouraging those patients who are able to mobilize to do so is an important risk reduction step.

Assessment

In the non-ICU setting where there are fewer difficulties in communicating with patients, the diagnosis of delirium is based on the standard diagnostic criteria as defined in the DSM-IV. The criteria required are cognitive change, disturbance in consciousness, and

the disturbance must develop over a short period of time. These were previously considered to be difficult to measure in ICU patients due to the lack of communication and lack of psychiatric training of ICU staff. However, several studies have been published which use various screening tools for delirium in this group of patients. These include the cognitive test for delirium (1996) followed by the abbreviated cognitive test for delirium (1997). More recently, the intensive care delirium screening checklist (ICDSC)[5] and the confusion assessment method for the ICU (CAM-ICU)[6] have been validated for use. Both tests are designed to allow ICU staff to diagnose or screen for delirium in a quick and easy manner.

The ICDSC (Table 2) gives each patient a score from 0 to 8; a score of 4 or above has a sensitivity of 99% and a specificity of 64% for identifying delirium. The patients' level of consciousness should initially be assessed, which ranges from A (no response) to E (exaggerated response to normal stimulation). Any patient who is not comatose (A–B) is then assessed according to the rest of the checklist, and scored one point for the presence of any of the items in the previous 24 h. The advantages of this test are its simplicity and speed, and many of the observations are routinely assessed. However, the ICDSC does have a relatively high false-positive rate, and is recommended as a screening rather than a diagnostic tool.

The CAM-ICU test (Table 3) is derived from the confusion assessment method, and is designed to be used with patients receiving ventilator support. It has a high sensitivity (93–100%) and specificity (89–100%). The test is also simple and can be performed by all ICU staff. Level of consciousness/arousal is recorded using a standard sedation score such as the Richmond agitation sedation scale (RASS). This is a 10-point scale varying from −5 to +4 with a score of 0 being a calm and alert patient. Patients scoring −3 or greater can then be assessed for delirium (those with −4 or −5 being comatose by definition). The assessor asks the patient to squeeze their hand on the letter A and reads out 10 letters, four of which are A. Squeezing or not squeezing at the wrong time is inattention. Disorganized thinking is detected by asking the patient four simple yes/no questions and then issuing a simple command such as 'stick out your tongue' or 'hold up two fingers'. The test takes <2 min to perform and requires the patient to be able to open their eyes for about 10 s. The CAM-ICU does, however, require further evaluation in subsets of ICU patients, for example, those with previous psychosis or pre-existing neurological disease, to confirm its specificity and sensitivity.

While the DSM-IV criteria remain the gold standard, the patient must be unrestrained, either chemically or physically, and an experienced psychiatrist is required. In the ICU, the ICDSC is a useful screening tool and the CAM-ICU is currently the only validated delirium tool for patients requiring ventilator support.

Table 2 Intensive care delirium screening checklist

Level of consciousness	
A	No response
B	Response to intense and repeated stimulation
C	Response to moderate stimulation
D	Normal wakefulness
E	Exaggerated response to normal stimulation
Scoring for delirium checklist	**Description**
Inattentiveness	Difficulty following instructions or easily distracted
Disorientation	To time, place, or person
Hallucination–delusion–psychosis	Clinical manifestation or suggestive behaviour
Psychomotor agitation or retardation	Agitation requiring the use of drugs or restraints, or slowing
Inappropriate speech or mood	Related to events or situation or incoherent speech
Sleep/wake cycle disturbance	Sleeping <4 h day^{-1}, waking at night, sleeping all day
Symptom fluctuation	Above symptoms occurring intermittently
Total score	0–8

Table 3 Confusion assessment method for the ICU

Step 1: assess level of sedation (RASS)	
+4	Overtly combative, violent, danger to staff
+3	Pulls or removes tube/catheter(s); aggressive
+2	Frequent non-purposeful movement, fights ventilator
+1	Anxious but movements not aggressive or vigorous
0	Alert and calm
−1	Not fully alert, but has sustained awakening (eye-opening or eye-contact) in response to voice (>10 s)
−2	Briefly wakens with eye contact to voice (<10 s)
−3	Movement or eye opening to voice but no eye contact
−4	No response to voice, but movement or eye opening to physical stimulation
−5	No response to voice or physical stimulation
If RASS is above −4, then proceed to step 2	
Step 2: assess for delirium (CAM-ICU)	
1	Acute onset of mental status changes or a fluctuating course
	and
2	Inattention
	and
3	Disorganized thinking
	Or
4	Altered level of consciousness
	=Delirium

Treatment

Risk factors should be addressed and multi-system management should include sedation holds, sleep–wake cycle correction, orientation, and use of visual and hearing aids. Following this, pharmacological treatment may be required.

It is important to remember that drugs given to improve delirium may themselves cause delirium or increase sedation. There is very little evidence for the efficacy of such treatment, and because pharmacokinetics are very variable in critical illness, dosage should be minimized.

The SCCM and the American Psychiatric Association recommend haloperidol as the first-line drug of choice in the treatment of delirium. The optimal dosing regime is not well defined, but starting with a small i.v. dose, such as 2.5 mg, and doubling it as required every 20–30 min has been recommended. Once the patient is settled, they can be prescribed regular doses every 4–6 h, tapering off over a few days. It should be avoided in patients

with a prolonged QT interval, due to the risk of inducing torsade de pointes. If patients are unable to tolerate haloperidol due to extra pyramidal side-effects, olanzapine (5 mg orally) can be used, although there may be an increased risk of stroke in patients with dementia. I.M. olanzapine should be used as a last resort in those who cannot tolerate haloperidol and where the enteral route is not available.

Although benzodiazepines are of great use in alcohol withdrawal, they should be avoided in delirium as they may worsen symptoms and have been shown to be ineffective.[7]

The hypoactive form is more difficult to treat and the evidence in this area is limited. The role of antipsychotic agents is controversial; however, these drugs are often administered, especially when symptoms delay recovery.[8]

A small trial in cancer patients with hypoactive delirium showed that giving the stimulant methylphenidate improved cognitive scores, but more data from the ICU population are awaited.

Outcomes

While there are few studies examining the outcomes of ICU patients with delirium, there are many about other patients. These patients are three times more likely to die, have increased risk of infection, have longer hospital stays, and a much higher cost of care. They may also be left with permanent deficit such as cognitive impairment.

ICU patients with delirium spend more days on a ventilator, have more failed tracheal extubations, have a higher ICU mortality, a higher hospital and 6-month mortality, and have a longer ITU stay with its attendant increased costs.[9] There are also increased adverse outcomes such as self-extubation and removal of catheters and lines. Prolonged periods of delirium on ICU are associated with an increased risk of long-term cognitive impairment at 3 months post-discharge.[10] In addition to these numerous adverse outcomes, delirium is an unpleasant and frightening experience for patients, with many suffering from delusions and hallucinations after recovery, which in itself is a reason to treat.

Conclusion

Delirium is a common, underestimated, multi-factorial problem in ICU that requires a multidisciplinary approach for assessment, management, and treatment. Although more pharmacological trials are awaited, the mainstay of treatment remains minimizing and correction of risk factors along with regular screening of patients using simple checklist like the CAM-ICU or the ICDSC.

References

1. Ely EW, Inouye SK, Bernanrd GR *et al.* Delirium in mechanically ventilated patients: validity and reliability of the confusion assessment method for the intensive care unit (CAM-ICU). *J Am Med Assoc* 2001; **286**: 2703–10
2. American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders*, 4th Edn (DSM-IV). Washington, DC: APA, 1994
3. 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**: 1892–900
4. Gabor JY, Cooper AB, Crombach SA *et al.* Contribution of the intensive care unit environment to sleep disruption in mechanically ventilated patients and healthy subjects. *Am J Respir Crit Care Med* 2003; **167**: 708–15
5. Bergeron N, Dubois MJ, Dumont M *et al.* Intensive care delirium screening checklist: evaluation of a new screening tool. *Intensive Care Med* 2001; **27**: 859–64
6. Ely EW, Margolin R, Francis J *et al.* Validation of the confusion assessment method for the intensive care unit (CAM-ICU). *Crit Care Med* 2001; **29**: 1370–9. Available from www.icudelirium.org
7. Breitbart W, Marotta R, Platt MM *et al.* A double blind trial of haloperidol, chlorpromazine and lorazepam in the treatment of delirium in hospitalized AIDS patients. *Am J Psychiatr* 1996; **153**: 231–7
8. Ely W, Page V. Delirium. *Care Crit Ill* 2008; **24**: 31–2
9. Milbrandt EB, Deppen S, Harrison PL *et al.* Costs associated with delirium in mechanically ventilated patients. *Crit Care Med* 2004; **32**: 955–62
10. Jackson JC, Gordon SM, Girard TD *et al.* Delirium as a risk factor for long-term cognitive impairment in mechanically ventilated ICU survivors. *Am J Respir Crit Care Med* 2007; **175**: A22

Please see multiple choice questions 5–8