Clinical Review

Delirium (acute toxic confusion) in the elderly

C Spice & M Bacon

Abstract

Delirium (also referred to as acute confusional state or toxic confusional state) is common in elderly patients admitted to hospital, and is usually secondary to an acute physical problem rather than being a primary abnormality. Physicians caring for acutely ill patients will frequently encounter those with delirium and need to be aware of the likely precipitants as well as the optimum management. We discuss the common precipitants, the clinical features, the differential diagnosis and the management of delirium.

Keywords

Delirium, Acute confusion, Toxic Confusion.

Introduction

Delirium is a frequent and important problem in elderly patients admitted to hospital. It is commonly a marker of an underlying disease process and patients with delirium have increased length of stay, mortality and institutionalisation. The recognition of the syndrome and the management of such patients is often poor, our understanding of its pathophysiological basis is patchy and there is relatively little evidence to guide those managing this common syndrome.

Terminology

The terms acute toxic confusion/acute confusional state have now been incorporated within the definition of delirium in the Tenth International Classification of Diseases.[1] Delirium is therefore synonymous with acute toxic confusion. Delirium tremens related to alcohol withdrawal will not be discussed.

How common is delirium?

14 – 30% of elderly patients admitted acutely will have delirium[2-6] although a proportion of these go unrecognised in routine clinical practice.[7,8] A further 10 – 30% may develop delirium during their hospital stay.[2,3]

What is delirium?

Delirium is a complex syndrome usually resulting from underlying physical problems and should not be accepted as a primary diagnosis in itself. The underlying cause or causes should be sought.[9] In clinical practice the full syndrome of delirium may not always be identified. In part this may reflect failure to identify or record non-cognitive features. The main features of delirium are ***global cognitive impairment, reduced awareness and attention, and perceptual disturbance.*** There may also be problems with psychomotor activity, sleep-wake cycle and emotional disturbance. The features typically come on over a relatively short period of hours/days.

Key Points

1. The main features of delirium are: global cognitive impairment, reduced awareness and attention and perceptual disturbance.
2. Infection, usually of urine or respiratory tract, is the most common precipating factor.
3. Delirium usually resolves with treatment of the underlying cause, but sedation may be necessary while awaiting a response.

Cognitive problems

All acutely ill elderly patients should have cognitive testing on admission. Most commonly used is the Abbreviated Mental Test score, which is quick to administer and easy to remember[10] (See Box 1). A score of seven or less has a 92% sensitivity for predicting delirium.[5] The Mini Mental State Examination[11] can also be used, with a score of 23 or less indicating disturbed cognition. The use of such tools increases the recognition of delirium on admission, as well as being a valuable guide to

Score one point for a fully correct answer to each of the following:

1. Age of patient
2. Time (to nearest hour)
3. Address for recall: 42 West Street (make the patient repeat this to ensure it has registered)
4. Year
5. Name of Hospital
6. Recognition of 2 persons (e.g. Doctor, Nurse)
7. Date of Birth (month and year sufficient)
8. Year of 1st World War
9. Name of present Monarch
10. Count backwards from 20 to 1

(Ask for recall address)

Box 1. Abbreviated Mental Test Score.[10]

Dr Claire Spice
BM MRCP
Locum Consultant in Elderly Medicine
Department of Medicine for Elderly People
Queen Alexandra Hospital
Portsmouth

Dr Michael Bacon
MRCP
Consultant Physician in Elderly Medicine
Department of Medicine for Elderly People
Queen Alexandra Hospital
Portsmouth

Correspondence:
Dr C Spice
Department of Medicine for Elderly People
Queen Alexandra Hospital
Southwick Hill
Cosham
Portsmouth PO6 3LY
Tel: 02392 286912
E-mail:
claire.spice@talk21.com

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monitoring resolution or change.[5] Cognitive testing is not specific for delirium and low scores can also be caused by language difficulties (e.g. dysphasia), dementia and depression. Immediate and short-term memory is affected primarily with relative preservation of long-term memory. Disorientation is nearly always present, particularly for time.

Attention

This is reduced and the patient may have difficulty focusing on questions and is easily distracted by their environment. Tests for attention include repeating the months of the year backwards and serially subtracting sevens from one hundred.

Perceptual disturbance

Visual *illusions*, involving misidentification by the patient of their surrounding, occur frequently.

Visual *hallucinations* (which have no basis in reality) are experienced by about a third of patients with delirium.[12] Patients and carers may not mention them and they should be asked about specifically. Auditory hallucinations are much less common but may be present. Delusions may occur but are usually transient and fragmented and have a paranoid theme. Perceptual disturbance can be particularly distressing for the patient and carers and may contribute to abnormal behaviour.

Psychomotor disturbance

The most commonly recognised disturbance is that of psychomotor agitation but patients may also have hypoactive behaviour or a combination of the two at different times during the illness.[13] A mixed picture is most commonly seen.[4,14] Patients with retarded delirium tend to be more severely ill and have a longer hospital stay,[14] perhaps because of failure to recognise the condition and provide appropriate treatment.

Differential Diagnosis

The main differential diagnoses are those of dementia, depression, mania and schizophrenia.

Dementia

Differentiation between dementia and delirium requires further information to be sought from those close to the patient regarding the pre-admission cognition, onset and fluctuation of the confusion. Anecdotally, this is often not done close to admission, which may lead to delay in diagnosis or incorrect attribution of the confusion to dementia. Of course, a patient with dementia may also suffer from delirium, in which case there will be a history of increasing confusion on a background of chronic stable cognitive impairment. There may be instances where the first presentation of dementia is as "acute confusion". Often in this scenario those close to the patient may not have recognised the mild cognitive decline over previous months and a careful history of memory and cognition may be required. (See Box 2)

	Delirium	Dementia
Onset	Acute over hours/days	Insidious over months/years
Course	Fluctuations throughout the day	Stable throughout the day
Orientation	Disorientation is a definite feature, particularly for time	Disorientation is a late feature
Consciousness	May be disturbed	Normal
Psychotic Features	Hallucinations often visual Delusions fleeting	Uncommon (unless Lewy Body Dementia)
Attention	Reduced	Reduced late in disease

Box 2. Delirium versus Dementia.

Lewy Body Dementia

This comprises progressive cognitive decline and one or more of: marked fluctuation in cognition and alertness, visual hallucinations or parkinsonism. If there is marked fluctuation then the patient may be thought to be acutely confused due to an underlying metabolic or infective cause that never really materialises. Patients with Lewy Body disease are highly sensitive to antipsychotic drugs which may provoke severe rigidity or excessive sedation, even in very small doses.

Depression / Schizophrenia

The onset of depression is often variable, but tends not to be acute. Consciousness and orientation are usually intact and the disturbance in cognition is mainly for attention rather than memory. The delusions and hallucinations of depression or schizophrenia are usually more complex in nature, and rarely visual.

Risk Factors

Pre-existing cognitive impairment, medical co-morbidity, severe physical illness, depression and visual or hearing impairment are independent risk factors for delirium in the elderly.[12,15-17] These baseline risk factors combine with precipitating factors (see below) to determine the degree of vulnerability of an individual patient. Physical restraints, malnutrition, addition of three or more medications, use of a bladder catheter and any iatrogenic event (e.g. cannula site infection) have been shown to be independent risk factors for the development of delirium in hospital inpatients.[18]

Precipitating Factors

A single precipitating factor is found in just over a third of patients and multiple potential causes are identified in 25% of patients (See Box 3).[16]

Infection, usually of the urinary or respiratory tract, is the most common precipitating factor.[6,14,16,19] Metabolic disturbances and cardiorespiratory diseases are also common precipitants. Occasionally acute confusion may be the only presenting feature in an elderly patient with myocardial infarction.

Infection	Cardiorespiratory
Chest	Myocardial infarction
Urine	Cardiac failure
Encephalitis	Thromboembolic disease
Meningitis	
Metabolic	Drugs (all have the potential)
Dehydration	Anticholinergic
Hyponatraemia	Antidepressant
Hypercalcaemia	Antiparkinsonian
Hypoglycaemia	Sedatives
Hyperglycaemia	Opiate analgesic
Renal failure	
Withdrawal phenomenon	Cerebral
Alcohol	Stroke
Antidepressant	Subdural haematoma
Sedative	Subarachnoid haemorrhage
	Tumour
Encephalopathy	Constipation
Hepatic	
Wernicke's	

Box 3. Precipitating Factors for delirium.

Chronic subdural haematoma can cause fluctuating cognitive problems and there is not always a history of falls or localising neurological signs. Non-convulsive epilepsy has been reported as a cause of acute confusion.[20] Delirium may sometimes be the presenting feature of a stroke, although expressive and / or receptive dysphasia due to a stroke may also be misinterpreted as confusion.

Virtually any drug can cause delirium in a vulnerable patient; the major groups are listed in Box 3. Alcohol withdrawal should be considered, as should withdrawal from drugs such as benzodiazepines and antidepressants. The serotonin reuptake inhibitor and monoamine oxidase inhibitor antidepressants are particularly associated with discontinuation reactions when stopped abruptly, leading to a delirium. In a small number of patients an aetiological cause is never found.[21]

Pathophysiology

Neurotransmitter disturbance is the most likely cause and it may be that there is dysfunction of multiple interacting neurotransmitter systems.[22] Acetylcholine is the neurotransmitter most studied, but virtually all pathways have been implicated.[12] Thiamine deficiency might contribute to the development of delirium, possibly through reduction in cerebral glucose metabolism and cholinergic neurotransmission.[19] It is most likely that delirium is a result of a global dysfunction but some discrete anatomical areas have been linked to an increased risk, such as the thalamus and right parietal cortex.[23,24]

Clinical Assessment

It may not be possible to do this in one session with the patient, and the clinician may need to return at an interval as the patient allows.

History

A full medical history is required. In reality this is sometimes difficult and in nearly all cases the doctor will need to acquire corroborative history from those close to the patient, residential and nursing home staff and/or the patient's General Practitioner. The history should enable confirmation of the diagnosis of delirium and recognition of the aetiological factors listed in Box 3.

Examination

Full examination is required within the limits of what the patient will allow. An Abbreviated Mental Test Score (Box 1) should be calculated. An assessment of hearing and vision should be attempted although co-operation may be difficult.[16] Nutritional and hydration status should be assessed and a rectal examination for faecal impaction/loading should be done if possible. Clinical signs of infection should be sought, although in reality, even quite severe physical illness can be difficult to detect in frail, confused elderly patients.

Investigation

Simple haematology and biochemistry will point to the possible presence of anaemia, infection and dehydration. Deranged liver function may indicate biliary sepsis. Hypercalcaemia is difficult to detect clinically but may present as acute or subacute confusion in the elderly. An ECG will sometimes show otherwise silent myocardial infarction and a chest x-ray may indicate infection or pulmonary congestion. In most patients with delirium these simple investigations will be sufficient for diagnosis and management.

CT brain scanning should be considered if there is focal neurology, a history of head injury or falls preceding the onset of confusion or signs of raised intracranial pressure. Electroencephalography (EEG) is occasionally useful, showing non-specific generalised slowing of background activity. It may also identify focal brain lesions or non-convulsive epilepsy. Lumbar puncture should be considered if there is any possibility of meningitis, encephalitis or subarachnoid haemorrhage and a CT brain scan is normal. Other investigations may occasionally need to be considered. (See Box 4)

Initial (all patients)
Bloods: Full blood count, urea & electrolytes, glucose, calcium, liver function tests, thyroid function tests, blood cultures
Urinalysis (MSU if abnormal)
ECG
Chest X-ray
Second Line (as indicated by relevant history/examination features)
Arterial Blood Gases
Cardiac Enzymes
CT brain scan
EEG
Lumbar puncture
B12 and folate
Urinary toxicology screen
Syphillis serology
HIV antibodies

Box 4. Investigation of delirium

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Management

The evidence base for the management of delirious patients is small, both for non-pharmacological and pharmacological management. The mainstay of treatment is based mainly on clinical experience and case reports with very few randomised research trials.

Treatment of Underlying Causes

Offending drugs should be withdrawn and dehydration should be treated. If sepsis is strongly suspected then empirical treatment with broad-spectrum antibiotics is usually justified after appropriate cultures have been taken. Drugs and fluids will often have to be given parenterally because of the difficulty in getting confused elderly patients to take oral preparations.

Environmental Factors

Simple environmental strategies are frequently overlooked in the management of delirious patients.[25] Nursing and other staff should be encouraged to consider environmental factors including bed position. If the patient is wandering then they should be nursed as far away as possible from the entrance/exit to the ward. Patients may be more settled in single rooms. Restraints should generally be avoided as they may contribute to injurious complications and rarely calm the patient.[26] Occasionally a patient may be most safely nursed with a mattress on the floor. Darkness often exacerbates delirium and the levels of lighting should be adequate, even at night. Orientation should be maintained with accurate clocks and calendars and gentle verbal reminders. There should be consideration of sensory needs to aid orientation, such as a functional hearing aid and clean glasses.

Whenever possible, transfer of delirious patients between wards should be avoided to reduce exacerbation of disorientation. Those close to the patient may be able to provide reassurance.

Behavioural problems

These may include wandering, aggression, shouting out, paranoia and hallucinations. Diversion tactics may be employed with wandering patients e.g. television, talking with staff or relatives. Possible precipitants for shouting out or changes in behaviour should be considered, such as pain, constipation and urinary retention.

Aggression may occasionally require rapid sedation but environmental considerations, diversion tactics and non-confrontational communication should be attempted before this. If the patient is a danger to themselves or others then restraint may be necessary, in their best interests, under Common Law followed by rapid sedation.

Pharmacological

Sedation should be avoided whenever possible but sometimes its use is necessary to reduce risk and distress to the patient. There is virtually no good randomised data for the drug management of delirium in the elderly although there has been a study in younger AIDS patients.[27] In general, if sedation is needed it is best given in small regular doses in order to reduce over sedation and the need for repeated rapid sedation. There are a number of options for the pharmacological management if required but the type and route of sedation need to be carefully considered for each patient (see Box 5). It is suggested that clinicians become familiar with the use of a small number of drug agents. The major groups used are antipsychotics (e.g. Haloperidol), atypical antipsychotics (e.g. Risperidone, Olanzapine, Quetiapine) and benzodiazepines (e.g. Lorazepam, Midazolam). We discuss here the ones we most commonly use.

Risperidone, Olanzapine and Quetiapine are all newer atypical antipsychotic agents. They have fewer extrapyramidal effects than other neuroleptic agents. Risperidone is the most commonly used in the acute setting and is licensed for acute psychoses. Olanzapine and Quetiapine are licensed for schizophrenia but have been used in delirium.[28]

Drug	Type	Cautions	Routes	Doses
Risperidone	Atypical antipsychotic		Oral	0.5mg od/bd initially. Increase by 0.5mg increments to a max of 2mg bd
Quetiapine	Atypical antipsychotic		Oral	25mg od/bd initially. Increase by 25mg increments
Olanzapine	Atypical antipsychotic		Oral Buccal	2.5mg initially increased by 2.5mg increments to max of 10mg daily
Lorazepam	Benzodiazepine	Respiratory failure	Oral Intramuscular Intravenous	0.5mg – 1mg qds PO IM – 0.5mg – 2mg stat (repeat after 2 hours if necessary) IV – see box 6
Midazolam	Benzodiazepine	Respiratory failure	Intravenous	IV – see box 6
Haloperidol	Butyrophene antipsychotic	Parkinsonism Lewy Body Dementia Liver failure	Oral Intramuscular	0.5mg – 1mg PO initially. Increase by 0.5mg increments to max of 5mg tds 1-5 mg IM initially. Repeated 4-8 hourly to a total of 10mg in 24 hours

Box 5. Drugs used in the management of delirium.

Haloperidol is a butyrophene antipsychotic with a peak effect at 4-6 hours when given orally and 20-40 minutes intramuscularly. Because of its extrapyramidal effects and the need to avoid in those with parkinsonism and Lewy Body disease its use is declining. It is no longer considered a first line agent and is being superseded by the benzodiazepines.

Benzodiazepines are often used in those with contraindications to antipsychotics and in those with drug and alcohol withdrawal syndromes. They should be avoided in respiratory failure.

Rapid sedation is occasionally required for patient safety as an emergency procedure when other measures have failed. Frail elderly delirious patients are particularly vulnerable to the effects of over sedation and its consequences, and lower doses are generally needed. We have local guidelines for this established by collaboration between Elderly Medicine Physicians, Elderly Mental Health doctors and Pharmacists. (See Box 6)

Possible reasons for rapid sedation
1. Severe agitation
2. Physical aggression to patients or staff
3. Significant risk of harm to self
4. Prolonged overactivity with risk of exhaustion
5. Determined attempts to abscond that have not been contained by other measures (in an incompetent patient)

Drug Administration
Intravenous Lorazepam: 25-30mcg/Kg by slow injection into a large vein
OR
Intravenous Midazolam: 1.5mg over 30 seconds with further doses of 0.5mg – 1mg at two minute intervals until sedation achieved

Monitoring and Management
1. Baseline pulse, respiratory rate, blood pressure, oxygen saturation
2. Observations immediately after administration and then every 15 minutes for the first hour and then hourly for twelve hours
3. Cardiopulmonary resuscitation facilities should be immediately available
4. Flumazenil should be instantly available for over-sedation
5. Inform doctor if: Pulse <50 or >110/min, respiratory rate <10 or >20/min, systolic BP <100mmHg, diastolic BP >110mmHg, oxygen saturation <90%, temperature > 38°C, sedation prolonged greater than expected
6. One to one nursing
7. Adequate pressure relief
8. Hydration (IV or SC)
9. Prescription of regular oral medication e.g. 0.5mg qds of Lorazepam once patient has woken

Box 6. Rapid intravenous sedation with Lorazepam.
(Adapted from Portsmouth Healthcare NHS Trust Guidelines on the Management of Acute Confusion).

The need for sedative agents should be reviewed regularly and reduced accordingly. Most patients will not need long term drug treatment once the delirium has resolved. Investigators are beginning to consider whether cholinesterase inhibitor drugs may have a place in the management of delirium in dementia.[29]

Systematic detection and intervention for delirium has been shown to reduce the incidence and severity of delirium and reduce length of stay, although most studies have been in young patients or surgical patients.[30]

Legal and Ethical Considerations

Under Common Law, if patients are not mentally competent to be involved in decisions about their own treatment (which would be the case with many delirious patients) then their doctors are authorised to administer treatment to them that they consider "in the patient's best interest". Most clinicians would use sedation in delirious patients on this basis; it is required in order to administer treatment which could not otherwise be given for the underlying condition and is therefore in the patient's best interest. In most cases it is possible to treat patients under Common Law in this way although rarely Section 5(2) of the Mental Health Act may be required. This allows the doctor in charge of the patient to initiate the detainment of the patient in hospital. The patient must be suffering from a mental disorder and the detainment must be for the health and safety of the patient, or to protect others. Section 5(2) should be used if it is anticipated that the patient will need to be detained under sections 2 or 3 of the Mental Health Act. The form for this must be filled in by the doctor and should be passed to the nursing staff and then on to the relevant manager. This allows the patient to be detained for up to 72 hours in hospital. Within this period the patient must receive a full psychiatric assessment by an approved senior psychiatrist. Where possible, we would recommend discussion with mental health specialists before invoking Section5(2).

If a patient is treated under Common Law or a Section 5(2) is invoked, the next of kin should be informed as a matter of good practice. Communication with those close to the patient is particularly important for delirious frail elderly patients who have a high mortality and morbidity.

Complications

Patients with delirium are at risk of falls, pressure sores, functional impairment and the inherent risks of over sedation and constipation. Assessment for such complications should occur daily and be actively managed. Antipsychotic medications may precipitate the neuroleptic malignant syndrome and increase extrapyramidal problems in those with parkinsonism or Lewy Body Disease.

Prevention

It is clear that some patients are at increased risk of delirium and there has been interest in the prevention of delirium in recent years. There have been two small trials of enhanced nursing care in delirious older patients with ambiguous results. A large prospective matched study of an intervention targeting six risk factors for delirium (cognitive impairment, sleep deprivation, immobility, visual impairment, hearing impairment and dehydration) in hospitalised elderly patients showed a significant reduction in the number and duration of episodes of delirium.[31]

Prognosis and Outcome

It has been found that those with delirium are consistently more likely to have higher mortality, longer length of stay and increased institutionalisation than those without.[16,32,33] A UK prospective study showed that those with delirium were twice as likely to die, four times more likely to be placed in institutional care and twice as likely to be readmitted within 12 months than non-delirious controls.[16] This may reflect factors such as severity of illness.[2]

It is not fully clear whether those without prior cognitive impairment who develop delirium are more likely to go on and develop dementia. It has been suggested that although there is generally improvement in cognition following delirium it may be a marker of underlying mild unrecognised cognitive impairment.[16] In general, studies of cognitive outcome following delirium have shown that 45-80% of patients have improved mental status at one month after the onset of delirium.[2]

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Discharge

All patients should have a record at discharge of their functional status (e.g. Barthel index) and cognitive function. Delirium should be recorded on the discharge information so that those subsequently managing the patient are aware of the vulnerability of the patient, particularly for future drug prescribing.

Summary

Delirium is a common problem in older patients admitted to hospital and its presence marks a particularly vulnerable group of patients. Recognition of those with delirium and a comprehensive common sense management approach is likely to reduce complications and may improve outcome.

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