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Delirium in the elderly: a clinical review

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ABSTRACT

Delirium is a common condition in the elderly, affecting up to 30% of all older patients admitted to hospital. There is a particularly high risk of delirium in surgical inpatients, especially following operations for hip fracture or vascular surgery, but also for patients in the intensive care unit. Patients with delirium have higher morbidity and mortality rates, higher re-admission rates, and a greater risk of long term institutionalisation care, thereby having a significant impact on both health and social care expenditure. Delirium frequently goes unrecognised by clinicians and is often inadequately managed. Recent evidence suggests that a better understanding and knowledge of delirium among health care professionals can lead to early detection, the reduction of modifiable risk factors, and better management of the condition in the acute phase. Many cases of delirium are potentially preventable, and primary and secondary care services should be taking active steps in order to do prevent this condition.

The word delirium comes from the Latin *delirare*. In its Latin form, the word means to become “crazy or to rave”. Delirium has many synonyms, which include acute brain failure, acute organic brain syndrome, acute confusional state, and postoperative psychosis. However, delirium is now the preferred term.¹

Delirium is reported to be present in 11–24%² of older adults on admission to hospital (prevalent cases) and will develop in another 5–35% of patients (incident cases).³ It occurs with higher frequency in those with pre-existing cognitive impairment. Among hospitalised patients, those particularly at high risk are surgical inpatients, especially patients undergoing cardiothoracic, emergency orthopaedic procedures, vascular surgery or cataract removal. Following operations for hip fracture in the elderly, delirium is common, with the incidence varying between 16–62%.⁴ In the intensive care unit it occurs in 70–87% of elderly persons and is often a symptom that heralds the presence of life threatening conditions.⁵ Fewer studies have been done in the community, and these suggest a prevalence of about 0.4–1.1% among the elderly⁶ in the community, residential and nursing home setting.

Delirium has adverse consequences. Patients diagnosed with delirium in the general hospital have an overall high morbidity due to a high risk of dehydration, malnutrition, falls, continence problems, and pressure sores. They also have higher 1 year mortality rates (35–40%), higher readmission rates, and a higher risk of institutionalisation (47% vs 18%).^{7–8} Delirium contributes to excess health expenditure due to an increased length of stay (21 vs 9 days)^{9–10} and an estimated additional US\$2500 (£1500, €1800) per patient (a \$6.9 billion annual expenditure for Medicare in 2004).¹¹ In one

third of patients, the symptoms of delirium persist¹² and the prognosis is worse in this group.¹³

Despite all of the above, delirium is frequently under detected, poorly understood, and is often mismanaged by clinicians. This review aims to highlight the issues, evidence base and clinical guidelines regarding the detection, features, diagnosis, pathophysiology, aetiology, prevention, and management of delirium in order to enhance understanding of a condition that often falls between the stools of primary care, secondary hospital care and psychiatry.

CLINICAL FEATURES

Several clinical subtypes of delirium have been described on the basis of the level of psychomotor activity such as hypoactive, hyperactive, mixed and unclassified^{13–14} (table 1).

The hyperactive (increased psychomotor activity) variant of delirium is most commonly recognised and tends to be readily apparent even to the casual observer. It is often associated with the adverse effects of anticholinergic drugs, drug intoxication, and withdrawal states. Characteristically, patients may exhibit agitation, psychosis, and mood lability, and may refuse to cooperate with medical care, may demonstrate disruptive behaviours (such as shouting or resisting), and may sustain injuries from falling, combativeness, or pulling out catheters and intravascular lines.

The hypoactive (decreased psychomotor activity) variant of delirium is more common than hyperactive delirium in elderly patients. It is less frequently recognised or is often dismissed as a transient, insignificant problem due to absence of disruptive, bizarre, and injurious behaviours. Patients with hypoactive delirium may appear sluggish and lethargic, or apparently low in mood, as well as confused, the confusion not being apparent on superficial conversation.

Certain types of delirium may frequently occur in patients with particular disease states; however, they are neither exclusive to nor diagnostic of specific underlying medical conditions. Similarly, the manifestation of delirium cannot be fully predicted by the presence of a particular aetiological toxin or illness.

Because of the multiple aetiological factors, the fluctuating course, and the individual medical comorbidities, many patients who experience delirium have a mixture of both hypoactive and hyperactive variants. Some studies suggest that such patients present the greatest risk of substantial morbidity and mortality.¹⁵

Onset of symptoms

Typically, the onset of delirium is rapid—over a few hours or days—and the symptoms can be

Review

Table 1 Clinical subtypes of delirium in the elderly and their presentation¹⁴

| | |
|----------------------------|--|
| Hyperactive delirium (21%) | Agitation, confusion, mood lability, psychotic symptoms, disruptive behaviours (see box 1) |
| Hypoactive delirium (29%) | Lethargy, apathy, confusion (see box 2) |
| Mixed (43%) | Features of both increased and decreased psychomotor activity |
| Unclassified (7%) | Psychomotor activity is normal |

highly variable and intermittent. Variability in attention, arousal or both can occur unpredictably and irregularly, often worsening at night. This may be witnessed as different behaviours occurring within a relatively short time, due to the fluctuation. For example, drowsiness, hypervigilance, normal wakefulness, and agitation, may occur within minutes to hours of each other. As a result, the diagnosis may be overlooked. The carers might recognise that the elderly patient is confused but fail to appreciate the significance of this change in condition and, consequently, the problem may not be addressed until further deterioration ensues.

Attentional deficits

A disturbance of attention is a cardinal symptom with patients presenting as distractible with an impaired ability to focus, concentrate, process information, and think clearly. Patients may be distractible, being sensitive to irrelevant stimuli in their surroundings. Due to fatigue and reduced sensory input these disturbances in attention often increase towards the evening—a phenomenon referred to as “sun downing”.

Disorganised thinking

Patients may present as confused, being unable to maintain the clarity, coherence and speed of thought. This is often mirrored in speech that can be rambling, tangential and circumlocutory, sometimes with an altered rate of speech with a reduced relevance with regards to the content.

Altered levels of consciousness

Patients may be lethargic with a reduced arousal or may be hyperalert with increased arousal. The level of consciousness may fluctuate between extremes in the same patient, or alternatively may present with more subtle signs, such as mild drowsiness, or an impaired level of attention.

Disturbance of perception

Hallucinations, misperceptions, illusions, and delusions are reported to occur in at least 40% of cases of delirium¹⁶ and can accompany both hypoactive and hyperactive subtypes. These result from abnormal sensory discrimination. Hallucinations are usually visual, ranging from dreamlike experiences to terrifying visions (for example, seeing dangerous animals, bizarre images, etc). Less frequently auditory hallucinations or those involving taste and smell may occur. Delusions are often paranoid or persecutory in nature (for example, suspicion of being poisoned or fear of intended harm by nursing staff).

Disturbed sleep–wake cycle

Typically there is disruption of the day–night cycle leading to excessive drowsiness by day and increased alertness on a night. There is disturbance of the circadian sleep cycle. A not unusual

Box 1**Case example 1**

Mr A is a 91-year-old man who was admitted from his home after falling in the garden. He had cataracts, diabetes and osteoarthritis but was not on any regular medication. He underwent successful surgery for a fractured neck of femur. A few days later, he becomes confused, disorientated and agitated. He tried to pull his intravenous cannula out and was found wandering outside the ward. He became paranoid, anxious and believed that the hospital staff wanted to harvest his organs.

Features

This is a hyperactive delirium in which the patient frequently has a deficit in attention and orientation, a heightened level of arousal, a variable mood, an increased sensitivity to his or her immediate surroundings, with restlessness, possible wandering and the risk of possible aggression. Patients frequently have psychotic symptoms, with fleeting and fragmented hallucinations and delusional ideas.

scenario is for a delirious patient to be found wandering outside on the streets at night in an inadequately dressed state.

Other features

There is often an altered psychomotor activity that forms the basis of the clinical subtypes of delirium (table 1).

Emotional disturbances can be prominent; intermittent and labile symptoms of anxiety, fear, irritability, anger, depression, or euphoria may also be noted. It is not unusual for suicidal thoughts, or grandiose ideas to be expressed.

Disturbance of orientation is common and poor memory usually represents an inability to register recent information because of inattentiveness, but retrieval of stored information can also be disturbed. Higher integrative functions are similarly affected; the result is a reduced ability to plan, solve problems or disrupted sequencing or praxis of actions (for example, rising from a bed or walking which can lead to injury or falls). Disturbances can also occur in visuospatial abilities and in writing.

It is important to note that the sensory features tend to be less common in elderly than in younger patients. Somatic

Box 2**Case example 2**

The manager of a nursing home referred Mrs B, an 80-year-old woman with a moderate degree of dementia, who suffered a sudden change in her level of confusion and orientation. Although responsive, she appeared lethargic, apathetic and was incoherent. She refused medication and food, and had disturbed sleep, being awake and alert during the night, but drowsy at times during the day. She was subsequently admitted to a general hospital, and was found to have suffered a stroke.

Features

The clinical features of delirium are harder to detect in patients with a pre-existing dementia, though any alteration in the level of orientation and behaviour of a patient with dementia should be seen as possible delirium until proven otherwise. This patient had a hypoactive delirium, which is the more common presentation in older people, and is frequently undetected, or misdiagnosed as possible depression.

features such as urinary incontinence, gait impairment, tremor, and language disorders (including receptive and expressive dysphasias) tend to be more common in older people with delirium.¹⁷

DIAGNOSIS OF DELIRIUM

Nurses and physicians consistently under diagnose delirium in clinical practice.¹¹ Studies suggest that between a third and two-thirds of delirium goes unrecognised.¹² Delirium is a bedside, clinical diagnosis and understanding of its clinical features is crucial to its diagnosis. Non-identification in the elderly is frequent due to the prevalence of the more common “hypoactive” form of delirium, which can be easily missed on bedside evaluation, and also in patients on surgical wards and intensive care units.¹⁸ Other possible reasons for non-detection of delirium are due to its fluctuating nature, its overlap with dementia, the lack of formal cognitive assessment as a routine within general hospitals, and failure to consider either the possibility of the condition or its consequences. The lack of obtaining an adequate informant history regarding the patient’s premorbid level of cognition and function, ageist attitudes towards older people with an “expectation” of confusion, and systems and communication problems due to multiple ward transfers, shift patterns of working and understaffing can all contribute to missed diagnoses.

A study by Zhou *et al* that compared use of the Confusion Assessment Method (CAM) with a clinical evaluation of delirium by psychiatrists showed a lower sensitivity and specificity for the latter.¹⁹ It is therefore advisable to use validated assessment scales to support and enhance the clinical evaluation of delirium. CAM is the most widely studied research tool in delirium (box 3)²⁰ and is perhaps the best tool for screening delirium.^{21 22} In addition, the Delirium Rating Scale can be used to rate symptom severity.²³ A formal diagnosis can be confirmed by using the Diagnostic and Statistical Manual of Mental Disorders, 4th revision (DSM-IV) criteria presented in box 4.²⁴

The main differential diagnoses to consider are dementia, depression and functional psychosis (such as schizophrenia and manic depression) (table 2).

The disturbance of thought and perception seen in delirium is often fragmentary, fluctuating and less complex than that seen in schizophrenia, in which delusions and hallucinations tend to be much more persistent and consistent. First rank symptoms of schizophrenia, such as thought insertion or auditory hallucinations which provide a running commentary on the patient’s actions, are uncommon in delirium, and the hallucinations tend

Box 3 Confusion Assessment Method (CAM)²⁰

The diagnosis of delirium by CAM requires the presence of features a and b and either c or d.

- (a) **Acute onset and fluctuating course:** evidence of an acute change in mental status from the patient’s baseline that changes in severity during the day.
- (b) **Inattention:** patient has difficulty focusing attention—for example, is easily distractible or has difficulty keeping track of conversation.
- (c) **Disorganised thinking:** patient’s thinking is disorganised or incoherent, as evidenced by rambling or irrelevant conversation and unclear or illogical flow of ideas.
- (d) **Altered consciousness:** a rating of a patient’s level of consciousness as other than alert (normal)—that is, vigilant or hyperalert, lethargic or drowsy, stuporous or comatose.

Box 4 Diagnostic and Statistical Manual of Mental Disorders (DSM-IV)²⁴: diagnostic criteria for delirium

In order to make a diagnosis of delirium, a patient must show each of features 1–4 listed below:

- (1) Disturbance of consciousness (that is, reduced clarity of awareness of the environment) with reduced ability to focus, sustain or shift attention.
- (2) A change in cognition (such as memory deficit, disorientation, language disturbance) or the development of a perceptual disturbance that is not better accounted for by a pre-existing or evolving dementia.
- (3) The disturbance develops over a short period of time (usually hours to days) and tends to fluctuate during the course of the day.
- (4) There is evidence from the history, physical examination, or laboratory findings that the disturbance is caused by the direct physiological consequences of a general medical condition, substance intoxication or substance withdrawal.

to be visual rather than auditory, in contrast to schizophrenia or other functional psychotic disorders. Dementia and depression may present as impairment of orientation, memory and communication; however, the level of consciousness and attention remains unaffected in these disorders (table 3). Hypoactive delirium can mimic a subcortical dementia or apathetic depression (psychomotor slowing, sleep disturbance, irritability). However, the presentation in delirium tends to be more acute and mood symptoms predominate, and are pervasive and persistent in depressive illness. In dementia with Lewy bodies (DLB), although, like delirium, there may be a fluctuating level of consciousness and visual hallucinations may be prominent, the history is likely to be much longer (months or years), and parkinsonian symptoms may be present.

It is important to note that in about 13% of elderly patients, delirium is superimposed on a pre-existing dementia.²⁵

PATHOPHYSIOLOGY OF DELIRIUM

The pathophysiology of delirium is poorly understood. O’Keeffe states that delirium represents the clinical manifestation of diffuse, non-specific neuropsychiatric manifestation of a generalised disorder of cerebral oxidative metabolism and neurotransmission.²⁶ This final common pathway most likely involves a variety of neurotransmitters, such as acetylcholine, dopamine, and traversing cortical and subcortical central nervous system pathways. Therefore, any process interfering with neurotransmitter function or with the supply or use of substrates can cause delirium. There is evidence that cholinergic deficiency can induce delirium, which has led to the hypothesis that cholinesterase inhibitors may have some benefit in the treatment of delirium.²⁷ Dopaminergic excess can also contribute to

Table 2 Differential diagnosis of delirium

| | |
|------------------------|--|
| Common conditions | Dementia Depression |
| Less common conditions | Dementia with Lewy bodies Functional psychosis—for example, schizophrenia, or mania |
| Rare | Hysterical states Post-ictal confusion Dysphasia |

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Box 5 Predisposing factors of delirium

- ▶ Demographic characteristics
 - age \geq 65 years
 - male sex
- ▶ Cognitive status
 - dementia
 - other causes of cognitive impairment
 - previous history of delirium
 - depression
- ▶ Visual and hearing impairment
- ▶ Decreased oral intake
 - dehydration
 - malnutrition
- ▶ Drugs
 - treatment with multiple drugs
 - treatment with psychoactive drugs
 - alcohol abuse
- ▶ Coexisting medical condition
 - severe illness
 - multiple coexisting conditions
 - chronic renal or hepatic disease
 - history of stroke
 - neurologic disease
 - metabolic derangements
 - fracture or trauma
 - terminal illness
 - infection with HIV illness
- ▶ Functional status
 - dependence, immobility
 - frailty, history of falls,
 - pain
 - constipation
- ▶ Prolonged sleep deprivation

or precipitate delirium, and indeed this can be a side effect of the dopaminergic drugs used to treat Parkinson's disease, whereas dopamine antagonists, such as antipsychotic drugs, can be used to treat it.²⁸ Other neurotransmitters such as γ -aminobutyric acid (GABA), serotonin, norepinephrine, and glutamate may have a role through interactions with cholinergic and dopaminergic pathways.²⁹ However, some types of delirium can be caused by drugs or toxins that act on specific brain neurochemical systems, rather than creating a global disturbance in cerebral function. Chronic hypercortisolism has also been implicated in the development of delirium.

AETIOLOGY AND RISK FACTORS

Various studies have indicated the multifactorial nature of delirium and have found that between two and six factors may be present in any single case.^{30–31} Next to increasing age, pre-existing cognitive decline is the most confirmed risk factor.³² Delirium may be the first indicator of dementia in elderly, and may “unmask” an insidiously developing cognitive decline.^{32–33} Inouye *et al* identified four independent baseline risk factors for delirium using proportional hazards analysis. These included impairment of vision, severe illness, cognitive impairment and a high blood urea nitrogen/creatinine ratio.³⁴

A study of delirium in elderly people admitted to hospital³⁵ showed that the most common precipitating factors were infections (43%) and cerebrovascular disease (25%). Inouye has

Box 6 Precipitating factors of delirium

- ▶ Intercurrent illnesses
 - infections—for example, chest infection, urinary tract infections, septicaemia, etc
 - hypoxia, hypercapnia
 - severe acute illnesses—for example, myocardial infarction, heart failure, etc
 - renal or hepatic failure
 - urinary retention
 - anaemia
 - constipation, faecal impaction
 - fever or hypothermia
 - shock
- ▶ Iatrogenic complications
- ▶ Metabolic
 - metabolic derangements (electrolyte disturbances, glucose, acid–base balance)
 - dehydration
 - endocrine: hypo- or hyperthyroidism, Addisonian crisis, hypopituitarism, hypo- and hyperparathyroidism
 - vitamin deficiencies: thiamine, nicotinic acid, B12
 - poor nutritional status
 - low serum albumin
- ▶ Neurological conditions
 - meningitis or encephalitis
 - cerebrovascular accident, subarachnoid haemorrhage, hypertensive encephalopathy
 - head trauma
 - epilepsy: complex partial seizures, post-ictal states, petit mal
- ▶ Surgery
 - orthopaedic, cardiac surgery
 - prolonged cardiopulmonary bypass
- ▶ Drugs
 - toxicity or overdose
 - sedatives, narcotics, anticholinergic drugs, anticonvulsants
 - treatment with multiple drugs
 - withdrawal syndromes: alcohol, hypnotics, barbiturates
 - carbon monoxide poisoning
- ▶ Environmental issues
 - admission to intensive care unit
 - use of physical restraints
 - bladder catheterisation
 - multiple procedures
 - prolonged sleep deprivation
 - emotional stress
- ▶ Pain

proposed a model that takes account of the many factors that play a role in the development of delirium.³⁶ This suggests that a combination of five precipitating factors—consisting of the use of physical restraints, bladder catheterisation, malnutrition, the addition of four or more medications on the previous day, and any iatrogenic event—is a valid model to predict the development of delirium in the hospitalised elderly. This study suggests that patients who have a greater number of, or more severe, predisposing factors may develop delirium in the presence of relatively benign precipitating factors, while patients with a low vulnerability due to few predisposing factors require multiple noxious insults. Therefore, in a typical case, the development of

Table 3 Comparison of the features of delirium, dementia and depression

| Feature | Delirium | Dementia | Psychotic depression |
|-----------------------------------|--|--|---|
| Onset | Acute (hours to days) | Insidious (weeks to months) | Acute (days to weeks) |
| Course | Fluctuating, lucid periods in a day | Relatively stable | Relatively stable |
| Duration | Days to weeks | Months to years | Weeks to months |
| Consciousness | Reduced | Clear | Clear |
| Attention | Impaired | Normal, except severe cases | May be disordered |
| Hallucinations | Usually visual or visual and auditory | Often absent | Predominantly auditory |
| Delusions | Fleeting, poorly systematised | Often absent | Sustained, systematised |
| Orientation | Usually impaired, at least for a time | Often impaired | May be impaired |
| Memory | Immediate and recent memory impaired, remote memory intact | Immediate memory intact, recent memory more impaired than remote | May be selectively impaired |
| Psychomotor | Increased, reduced or shifting unpredictably | Often normal | Varies from retardation to hyperactivity (in agitated depression) |
| Speech | Often incoherent slow or rapid | May have word finding difficulties, perseveration | Normal, slow or rapid |
| Thinking | Disorganised or incoherent | Impoverished and vague | Impoverished, retarded |
| Physical illness or drug toxicity | One or both present | Often absent in Alzheimer's disease | Usually absent, but debatable |

Adapted from: Evans JG, Williams TF, eds. *Oxford textbook of geriatric medicine*. Oxford Textbooks, p494.

Box 7 Clinical guidelines to prevent and treat delirium in hospital (British Geriatric Society)³⁹

Step 1:

Identify all older patients (> 65 years) with cognitive impairment using the Abbreviated Mental Test or Mini-Mental State Examination on admission.

Step 2:

Consider delirium in all patients with cognitive impairment and at high risk (severe illness, dementia, fracture neck of femur, visual and hearing impairment). Use the Confusion Assessment Method screening instrument.

Step 3:

Identify the cause of delirium if present from the history, examination and investigations, and treat underlying cause or causes—commonly drugs or drug withdrawal, infection, electrolyte disturbance, dehydration or constipation.

Step 4:

In patients with delirium and patients at high risk of delirium:

- Do**
- ▶ provide environmental and personal orientation
 - ▶ ensure continuity of care
 - ▶ encourage mobility
 - ▶ reduce medication but ensure adequate analgesia
 - ▶ ensure hearing aids and spectacles are available and in good working order
 - ▶ avoid constipation
 - ▶ maintain a good sleep pattern
 - ▶ maintain good fluid intake
 - ▶ involve relatives and carers (carers leaflet)
 - ▶ avoid complications (immobility, malnutrition, pressure sores, over sedation, falls, incontinence)
 - ▶ liaise with old age psychiatry service

Do not

- ▶ catheterise (if possible)
- ▶ use restraint
- ▶ sedate routinely
- ▶ argue with the patient

Step 5:

Ensure a safe discharge and consider follow-up with old age psychiatry team. Provide family/carer education and support.

delirium would involve a complex interaction between a vulnerable patient (those with predisposing factors) and an exposure to precipitating factors (boxes 5 and 6). Most prescribed drugs can precipitate delirium, with benzodiazepines, narcotics, and drugs with anticholinergic activity having a particular propensity.³⁷ In older people with cognitive impairment, it is not unusual for delirium to be triggered by a hospital admission in which prescribed medication is reinitiated or increased, following a period of unsuspected or undetected poor compliance in the community. Pain and constipation are also common conditions, which can predispose to and precipitate delirium, particularly in older people.

MANAGEMENT

The Royal College of Physicians³⁸ and British Geriatric Society³⁹ have provided excellent guidelines with regards to the prevention, diagnosis and management of delirium in older people some of the principles of which are described below. The main aspects of the management of delirium are listed in box 7.

Identifying and treating the underlying causes

Any alteration or change in the mental state of hospital patients should lead to the consideration of delirium as a possible diagnosis, particularly in those with predisposing/risk factors, such as a pre-existing dementia. Initial signs may be subtle, such as evidence of an altered level of attention through a reduced ability to think clearly and focus in conversation, without obvious evidence of the patient being unwell. This is particularly true in older patients, who are more likely to present atypically, with delirium sometimes being the only symptom of an underlying physical illness. It is therefore important to be vigilant and proactive in approach. All elderly patients should be screened for risk factors and cognitive impairment (for example, via the routine use of CAM and Mini Mental State Examination (MMSE))^{40–41} at admission to hospital and at regular intervals thereafter.

Initial evaluation of patients with suspected delirium should include a thorough history taking, with an informant account from the family, carer and general practitioner being a vital part of the process, in order to clarify and elucidate the onset and course of the symptoms. Any history of alcohol or benzodiazepine use should be sought, as well as ascertaining the medication that patients have been prescribed and compliant within the community, including over the counter or herbal remedies. Such medication should be reviewed, and only essential medication

Table 4 Antipsychotics in delirium

| Drug | Dosage | Adverse effects | Comments |
|--------------------------------------|--|---|--|
| Haloperidol (antipsychotic) | 0.5–1 mg twice daily oral; additional doses every 4 h as needed (peak effect 4–6 h) 0.5–1 mg intramuscular; observe effects and repeat after 30–60 min if needed (peak effect in 20–40 min) | Extra pyramidal symptoms especially at doses more than 3 mg, though may take 14 days+ to develop Prolongs QTc interval | Most commonly used drug; few anticholinergic effects; less sedating Effectiveness demonstrated in randomised control trial. Avoid in withdrawal states, hepatic insufficiency, Lewy body dementia, Parkinson's disease, neuroleptic malignant syndrome |
| Olanzapine (atypical antipsychotic) | 2.5–5.0 mg once daily | Prolong QTc interval | Tests in uncontrolled trials have been done; less frequent extrapyramidal side effects noted in some studies; some studies have suggested increased mortality in elderly with dementia or cardiovascular/cerebrovascular risk factors. Olanzapine not licensed for "acute psychosis" |
| Risperidone (atypical antipsychotic) | 0.5 mg twice daily | | |
| Quetiapine (atypical antipsychotic) | 25 mg twice daily | | |
| Lorazepam (benzodiazepine) | 0.5–1.0 mg oral every 4 h, as needed (up to 3–4 mg in 24 h) (peak effect 120 min) Can be given 0.5–1.0 mg im or iv (peak effect 10 min after iv) | Can cause paradoxical excitation, over sedation, respiratory depression | Second line agent—can be given as adjuvant to antipsychotic when ineffective. Reported to worsen delirium in clinical trials; useful in alcohol or sedative withdrawal, Lewy body dementia, parkinsonism, neuroleptic malignant syndrome |

im, intramuscularly; iv, intravenously.

continued at as low a dose as is possible to be effective. A full physical and neurological examination should be performed, with initial investigations to screen for the more common precipitants of delirium, and with blood tests including full blood count, urea and electrolytes, blood glucose, liver function and thyroid function tests performed routinely. An electrocardiogram (ECG) may also be appropriate in the majority of patients. An elevated C reactive protein (CRP)/erythrocyte sedimentation rate (ESR) may indicate the presence of delirium when the diagnosis is in doubt. As infection is implicated in around a third of hospital patients with delirium, a mid-stream urine sample (MSU), blood cultures, and chest x ray (CXR) are also usually appropriate. Other laboratory investigations that may be considered in some cases include assessment of blood vitamin B12, folate, and cortisol values, arterial blood gases, and a toxicology screen. An electroencephalogram (EEG) may be useful in helping to differentiate delirium from functional psychiatric disorders. Neuroimaging, such as computed tomography (CT) scan or magnetic resonance imaging (MRI), has a limited utility and should be considered in those in whom the cause of delirium is not apparent with routine investigations, as well as those with focal neurological signs or a history of head injury or falls. Lumbar puncture should not be performed routinely, but should be reserved for those in whom there is reason to suspect a cause such as meningitis.

Once any potential contributing factors have been identified, they should be treated appropriately. It is important to remember that there may be a lag between the resolution of an underlying physical health problem, and the symptoms of delirium, which may be several days, weeks or even months.

Providing environmental and supportive measures⁴²

Nursing supportive measures include maintaining the patient's airway, volume status through the correction and prevention of dehydration, ensuring adequate nutrition, providing skin care to prevent sores, and mobilisation to prevent deep vein thrombosis and pulmonary embolism. The use of restraints, bladder catheterisation or regular sedation should be avoided, if at all possible.

The aims of providing general environmental support are: firstly, to create an environment that places minimum demands on a patient's impaired cognitive function; and, secondly, to limit the risk of harm to the patient and others that may result from any disturbed behaviour. It is essential to involve familiar

family, friends and carers to provide reassurance and assist with orientation. Conflict with the patient should be avoided, if at all possible, with gentle reorientation approaches taken. Other orientation measures include providing patients with hearing aids, glasses, clocks, calendars, etc, and by providing as consistent care as is possible, keeping moves within the hospital to as few as possible. Steps should be taken to allow patients uninterrupted sleep by adjusting the noise and lighting levels, assisting patients to be able to distinguish between day and night more readily, and coordinating schedules for drug dosing and performing investigations or other procedures.

Prescribing drugs aimed at managing symptoms^{43 44}

Whereas the primary purpose of drug treatment for delirium is to treat the underlying cause, it may also sometimes be necessary to prescribe medication to treat distressing or dangerous behavioural disturbances (for example, agitation and hallucinations) or to provide sedation (for example, when patients are a danger to themselves or are in a highly distressed state or at risk of disrupting their essential medical care (for example, intubation)).³⁹

Haloperidol has traditionally been the drug of first choice in treating behavioural disturbances associated with delirium (table 4). A Cochrane database systemic review⁴⁵ has shown that low dose haloperidol (<3 mg/day) may be effective in reducing the degree and duration of delirium in postoperative patients, and therefore has a direct effect on the course of the delirium rather than merely being helpful in treating the behavioural symptoms. Low dose haloperidol has a similar efficacy to atypical antipsychotics (olanzapine and risperidone) and there is no evidence of greater adverse effects than these drugs. However, the review indicates that haloperidol in higher doses is associated with more adverse effects.

A recent review study⁴⁶ has compared the efficacy of risperidone and olanzapine in the management of behavioural symptoms of delirium. This showed that risperidone was 80–85% effective at the dosage of 0.5–4 mg daily in treating behavioural disturbances of delirium, while olanzapine was 70–76% effective at a dosage of 2.5–11 mg daily. There were a limited number of trials that compared the efficacy of the atypical antipsychotics to haloperidol and these showed a higher frequency of adverse effects with haloperidol. The majority of

studies so far suggest some evidence to support the efficacy of antipsychotics in treating the behavioural symptoms of delirium, although no double blind, placebo controlled trials have been undertaken.

Haloperidol is the most commonly used drug in the management of delirium. Although a “typical” antipsychotic, it has few anticholinergic side effects, minimal cardiovascular side effects, is less sedating and therefore less likely to exacerbate delirium. However, it may cause excessive falls, particularly in higher doses. An oral dose of 0.5 mg of haloperidol given up to 2 hourly with a maximum dosage of 5 mg (orally or intramuscularly) in 24 h is a general guide, but may occasionally need to be exceeded depending on the severity of distress, severity of the psychotic symptoms, weight and sex. Haloperidol can be given intramuscularly at a dose of 1–2 mg. Committee on Safety of Medicines (CSM) guidance suggests that, as olanzapine and risperidone have been linked to an increased risk of stroke in elderly patients with dementia, the use of risperidone in such patients with acute psychosis (of which delirium may be one example) should be limited to short term use under specialist advice; olanzapine is not licensed for acute psychoses. However, it is important to consider the risk of stroke in all patients, particularly in those with cardiovascular and cerebrovascular risk factors, as there is some evidence that all antipsychotic drugs may share this adverse risk.⁴⁷

Benzodiazepines are usually preferred when delirium is associated with withdrawal from alcohol or sedatives, or when DLB is a possibility. They may also be used as an alternative or adjuvant to antipsychotics when these are ineffective or cause unacceptable side effects. Short acting benzodiazepines, such as lorazepam, 0.5 mg–1 mg every 2 h (up to 3 mg in 24 h), may be seen as a suitable first line agent by clinicians, particularly as the effects can be rapidly reversed using flumazenil. Lorazepam has several other potential advantages such as those owing to its sedative properties, rapid onset, and short duration of action. If necessary, lorazepam can be given at a dose of 0.5–1.0 mg intravenously or intramuscularly.

It is possible for the prescription of antipsychotic drugs or benzodiazepines to make delirium worse or exacerbate any

underlying causes (for example, benzodiazepines may worsen respiratory failure). Therefore, it is preferable to use one drug only, starting at the lowest possible dose, and using small increments, if necessary, after an interval of 2 h. Patients should be closely monitored for response and possible side effects. It is important to recognise that the benefits of the antipsychotic drugs, which occur over hours and days, appear to be independent of any antipsychotic action, which would take days and weeks to take effect. As patients with DLB can be particularly sensitive to the effects of antipsychotics, it is important to exclude this before considering the use of an antipsychotic. In a large randomised, double blind placebo controlled trial, rivastigmine was more effective than a placebo in patients with DLB in controlling the symptoms of delirium.⁴⁸

The pharmacological treatment should be continued until symptoms fully resolve.⁴⁹ There is a consensus that medication should be discontinued once the patient has been free of symptoms for 1 week,⁵⁰ though it is sensible to titrate the dose downwards, monitoring for the re-emergence of symptoms, re-increasing or restarting the medication if necessary.

Regular clinical review

One of the most consistent failings in the management of delirium is the lack of regular review. During a hospital stay, it is not only essential to review prescribed medication regularly, but also to manage any ongoing risk factors for delirium.⁵¹ Any management plan put into place, including the prescription of medication to treat behavioural complications of delirium, needs regular review and modification, at least every 24 h,³⁹ in order to reduce the risk of further complications, such as pressure sores, incontinence, malnutrition and functional impairment.

Discharge planning and follow-up

Delirium can be a psychologically traumatic experience not only for the patient but also their family, and a careful explanation of the diagnosis is essential. The provision of written information can help in this process. It is not uncommon for patients to harbour unpleasant and vivid memories of their period of delirium, which can continue to frighten them, and lead to withdrawal and dysfunction following discharge. The potential outcomes of delirium should be discussed realistically with the patient and their family; the symptoms may take a long time to resolve, with a lag between the resolution of the underlying physical health difficulties and an improvement in mental state, which can be days, weeks or even months in duration. A study conducted by Levkoff *et al* 1994³ revealed that a quarter or more elderly people may continue to have symptoms—inattention, reduced awareness of environment and disorientation—for up to 6 months after hospital discharge. Complete resolution can take from 6 months to years. Furthermore, delirium may herald the onset of dementia and may also reflect a severe underlying illness and comorbidity. It is therefore good practice to plan the patient’s discharge from hospital carefully, using the vehicle of a multidisciplinary team meeting to involve the patient, carers or family, and other involved professionals. It may also be appropriate to refer the patient to a geriatrician, old age psychiatrist, community psychiatric nurse (CPN), occupational therapist or social services for further assessment, follow-up and/or social support. Follow-up of patients after discharge from the hospital can help to identify residual cognitive, social or functional problems, modify risk factors, and help to reduce the risk of recurrence of delirium.

Key learning points

- ▶ Delirium is an acute confusional state, more commonly seen in the elderly, with a multifactorial aetiology including physical and environmental factors.
- ▶ Delirium leads to an increased mortality, morbidity, loss of independence, and rate of institutionalisation, and places a huge burden on the health and social care system from a financial perspective.
- ▶ Evidence suggests that a third of cases of delirium are potentially preventable, through the introduction of strategies aimed at identifying patients at risk and modifying underlying predisposing factors, with the use of systematic screening and regular monitoring of cognition essential to this process.
- ▶ The early identification of delirium, with prompt and optimal management of the underlying medical and environmental factors contributing to it, reduces the severity of delirium and can lead to improved outcomes for the patient.
- ▶ It is important that staff working within hospital and community settings receive regular training and education, in order to enhance the prevention of delirium, its early detection, and management.

Review

Research questions

- ▶ *The pathogenesis of delirium*—Further clarity is needed on the pathogenesis of delirium, particularly investigating the condition in special groups, such as postoperative patients, patients with sepsis, dementia, the terminally ill, etc. Such knowledge is likely to lead to the development of specifically targeted prevention techniques and drug treatments.⁵⁸
- ▶ *Prevention measures*—Further work needs to take place to refine preventative techniques, particularly exploring the possible use of drug prophylaxis in high risk groups (for example, using pro-cholinergic drugs, or antipsychotics). Specific questions such as cost effectiveness, adverse effects, which patients are most likely to benefit, timing of administration, dose and duration of treatment, etc²⁷ need to be addressed.
- ▶ *Treatment*—There is need for randomised, double blind, placebo controlled trials of drugs, such as antipsychotics, used to speed or enhance the resolution of delirium, and to look at longer term outcome of patients with delirium (for example, in terms of quality of life, cost of intervention, activities of daily living, rates of psychological morbidity, duration of treatment, mortality, etc).

PREVENTION OF DELIRIUM

The prevention of delirium is essential in trying to reduce the morbidity, complications, and adverse outcomes caused by the condition. As delirium is most frequently multifactorial, successful preventative strategies are multi-component and aimed at reducing risk factors. In a trial conducted by Inouye *et al* in 1999, a multi-component targeted intervention strategy^{34–51} was found to be effective in preventing delirium in hospitalised elderly patients who were at high risk of developing delirium. The prevention strategies involved were simple, and included ensuring the early involvement of family members in care, optimising effective communication through the use of visual and hearing aids, involvement in therapeutic activities, early mobilisation and walking, non-pharmacological approaches to sleep and anxiety, adequate nutrition and hydration, and careful and effective prescribing of medication for pain relief. Once delirium had developed, the intervention was found to be less effective and less efficient.

In a randomised study of patients who underwent gastric or colonic resection, a “delirium free protocol” of intravenous pethidine and diazepam infusion over 8 h for the first 3 postoperative days significantly reduced the incidence of delirium when compared to the “care as usual group”.⁵² Cole⁵³ reviewed trials of preventative interventions and concluded that a broad spectrum of interventions may be modestly effective in preventing delirium among surgical patients. These included education, support, reorientation, anxiety reduction and pre-operative medical assessment.

In another study, Lundstrom *et al*⁵⁴ concluded that a multifactorial intervention reduced the duration of delirium, length of hospital stay and the mortality of elderly patients on medical wards with delirium, when they were assigned to an intervention group, in contrast to a control group. The intervention consisted of staff education focusing on the assessment, prevention and treatment of delirium and on caregiver–patient interactions on an individualised basis. A single, blind, case–control study conducted by Tabet *et al* examined the effects of an inexpensive educational programme

Key references

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- ▶ British Geriatric Society. Clinical guidelines for the prevention, diagnosis and management of delirium in older people in hospital. Published January 2006. http://www.bgs.org.uk/Publications/Clinical%20Guidelines/clinical_1-2_fulldelirium.htm
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aimed at nursing and medical staff, and found that it reduced the prevalence of delirium in the elderly on acute medical admission wards.⁵⁵ A recent Cochrane review⁵⁶ investigating interventions for preventing delirium concluded that proactive consultation with a geriatrician, and use of haloperidol, can reduce the incidence and duration of delirium, and length of hospital stay, in patients with a hip fracture. The review suggests that there is a need for more trials to study the prevention of delirium, particularly looking at relevant long term outcomes, such as the use of psychotropic medication, activities of daily living, psychological morbidity, quality of life, cost of intervention and health care services, and mortality.

However, sufficient evidence has now been accrued to indicate that up to a third of delirium is preventable, and it is therefore essential that a systematic and organisational approach is taken in order to prevent this condition.³⁸

CONCLUSIONS

Delirium is a serious public health issue with a high incidence and prevalence across community and hospital settings, particularly in older people. Despite this, it is frequently under recognised, badly managed, and poorly understood. However, what is now clearly understood is the need to focus resources on preventing delirium and identifying and treating the underlying causes as early as possible. An organisational approach is necessary to ensure the success of this process on a consistent basis, with education of staff an essential component. Using this approach is likely to not only lead to better patient outcomes, but it also has implications regarding the efficient use of hospital and social care resources, the performance of acute hospitals, and the cost of health and social care. Delirium meets Williamson’s criteria for an indicator of the quality of health care provision,⁵⁷ and it may be appropriate to adopt the use of incident delirium as a performance measure of the quality of acute service care for older people, on a national basis.

Symptoms of delirium can often persist beyond the acute phase of treatment, for several days, weeks or months, and may herald the onset of dementia. It is therefore good clinical practice to ensure that there is good communication and partnership working across the interfaces of primary care, geriatric medicine, old age psychiatry, and social services in the management of such patients.

MULTIPLE CHOICE QUESTIONS (TRUE (T)/FALSE (F); ANSWERS AFTER THE REFERENCES)

1. Delirium is often missed by clinicians.
2. The Confusion Assessment Method is the best tool for rating the severity of delirium.
3. Haloperidol is the first choice in treating the behavioural symptoms of delirium.
4. About 30–40% cases of delirium are preventable and therefore preventative strategies are beneficial.
5. Rivastigmine, an anticholinesterase inhibitor, can be used to treat delirium in patients with dementia of Lewy body.

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Patient consent: The people mentioned in this article are fictitious and none of the details are taken from specific cases.

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Answers

1. T; 2. F; 3. T; 4. T; 5. T