

Clinical aspects of delirium

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ABSTRACT Delirium is a common and frequently missed condition in elderly people admitted to hospital, and represents a considerable financial and health burden. It is important to recognise both those suffering from and those at high risk of delirium at the time of admission to hospital, which allows preventative and therapeutic measures to be instituted. Management of delirium is a multi-component and multidisciplinary undertaking, with important considerations throughout hospital stay and following discharge.

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INTRODUCTION

Delirium is among the most common of all acute disorders in older hospital inpatients, with admission prevalence of 14–24% and an incidence during hospital stay of 6–56%. It is a serious condition, with inpatient mortality rates of 6–18% and mortality at one year of 35–40%. Early recognition is of vital importance, as the condition's presence should prompt specific investigation and management steps to be undertaken by the multidisciplinary team. Despite these features, delirium is under-recognised and under-diagnosed by health professionals.

In addition to causing great distress for both patients and carers, delirium results in increased morbidity and mortality, increased length of hospital stay, loss of independence and increased institutionalisation. As a result, it represents a considerable financial burden on healthcare providers, which will likely continue to rise as the population ages. This makes the effective prevention, recognition and management of delirium a key priority for healthcare providers and clinicians alike.

Two comprehensive reviews (Inouye, 2006; Young and Inouye, 2007) have recently been published and this article draws on these as well as guidelines produced in 2006 by the British Geriatrics Society and the Royal College of Physicians of London and other reference material, in order to provide an overview of delirium targeted at a general audience with an aim to provide practical management advice.

PATHOLOGY

The pathogenesis of delirium is poorly understood, but in addition to a background of ageing-related changes in the brain and neurodegenerative disease (e.g. Alzheimer's disease), three important acute factors that are likely to contribute are: the role of particular neurotransmitters;

inflammation; and disruption of the hypothalamic–pituitary–adrenal axis.

There is well-established evidence of disruption in cholinergic and dopaminergic neurotransmitter pathways in delirium. Cholinergic system underactivity appears to be a crucial factor, explaining the propensity of drugs with anticholinergic properties to precipitate or contribute to delirium. Dopamine excess is also important, potentially as a consequence of its regulatory action on cholinergic pathways. The role of dopaminergic excess provides a theoretical basis whereby dopamine antagonists (antipsychotic drugs) may effectively treat some aspects of delirium. Other neurotransmitters may also play a role in the pathogenesis of delirium, but their effects are less well characterised.

There is evidence of inflammatory activity and raised levels of a range of cytokines in delirium, which impair cerebral function through disruption of neurotransmitter pathways and other mechanisms. Elevation of peripheral pro-inflammatory cytokines can induce apathy, malaise and withdrawal via effects on central nervous system neurotransmission. This is a normal response to illness ('sickness behaviour'), and delirium may in part reflect an exaggerated form of this process.

Sustained hyperactivity of the hypothalamic–pituitary–adrenal axis (as a result of illness-related stress combined with ageing-related impaired cortisol regulation), with resulting hypercortisolaemia and consequent impairment of neural function, may be another important underlying mechanism.

AETIOLOGY

There are several well-characterised predisposing and precipitating factors for the development of delirium (see Table 1). A useful concept is to think of one or

TABLE 1 Predisposing and precipitating factors for delirium (adapted from Inouye 2006 and Young and Inouye 2007)

Predisposing factors for developing delirium	Precipitating factors for delirium
Old age	Any acute illness (e.g. infection)
Severe or terminal illness	Psychoactive medication
Cognitive impairment (including dementia)	Other drugs (e.g. anticholinergics)
Past history of delirium	Malnutrition
Frailty	Dehydration
Admission with infection or dehydration	Iatrogenic events (e.g. introduction or abrupt withdrawal of medication)
Visual or hearing impairment	Use of urinary catheter
Polypharmacy	Use of physical restraint
Surgery	Immobility
History of alcohol excess	Constipation
Renal or hepatic impairment	Sleep deprivation

more predisposing factors resulting in increased susceptibility to delirium. A highly susceptible patient (for example, a frail, malnourished 85-year-old with dementia) needs only a relatively minor precipitating event to trigger delirium. Delirium can develop in patients without predisposing factors, but in these circumstances the precipitating insult must be of much greater magnitude (e.g. severe bronchopneumonia as opposed to a mild urinary tract infection).

Because of the complex aetiology of delirium, systematic assessment of the potential role of multiple predisposing and precipitating factors, rather than focusing on a single presumed 'cause', is essential for effective management.

CLINICAL FEATURES

There are two crucial steps for a diagnosis of delirium to be made:

1. Detecting cognitive impairment or altered arousal
2. Establishing that these changes are of acute onset (days, weeks) and/or show a fluctuating course

Other features such as hallucinations, delusions and sleep-wake cycle disturbance are also common. Thus, delirium diagnosis requires a combination of bedside assessment and additional information-gathering from the referral letter, relatives, carers and staff who know the patient.

Delirium can be subdivided into hyperactive (characterised by agitation and hypervigilance), hypoactive (characterised by drowsiness and apathy) or mixed variants, depending on the level of psychomotor disturbance. Hypoactive delirium is more common but is

TABLE 2 Confusion Assessment Method (adapted from Inouye et al. 1990)

Diagnosis of delirium requires criteria 1 AND 2 to be present plus EITHER criteria 3 OR 4

1. **Acute onset and fluctuating course** (history from staff, family or carers essential)
2. **Inattention** (tested formally with digit span, counting down from 20 to 1, months of the year in reverse order; or informally: easily distractable with difficulty maintaining thread of conversation)
3. **Disorganised thinking** (rambling, incoherent or irrelevant conversation)
4. **Altered level of consciousness** (either increased vigilance in hyperactive delirium or lethargy or stupor in hypoactive delirium)

also more frequently overlooked, and clinicians should specifically consider this diagnosis in all vulnerable patients who are sleepy and lethargic. Hypoactive delirium has a higher mortality rate than hyperactive delirium and also carries a higher risk of the complications of immobility, such as pressure sores and infection.

SCREENING AND ASSESSMENT

Despite (or perhaps because of) its high frequency, impaired cognition (acute, chronic or acute-on-chronic) is often overlooked in older people at the time of their hospital admission or during the course of their stay. This raises the need for screening tools to increase recognition and assess the level of cognitive dysfunction. Recent guidelines published by the British Geriatrics Society and the Royal College of Physicians of London recommend the use of two screening tools, namely the 10-point Abbreviated Mental Test (AMT) or the 30-point Mini Mental State Examination (MMSE). These tools are quick and simple to perform and can be repeated throughout the course of an admission to determine improvement or deterioration in cognition.

Tools such as the Confusion Assessment Method (see Table 2) have been developed to differentiate delirium from chronic causes of cognitive impairment, such as dementia, and from milder acute changes in mental status. In cases of uncertainty of diagnosis, a pragmatic approach is to consider delirium to be present until proven otherwise (given the frequency of delirium, any confusional state has a high likelihood of being delirium, and not treating it as such may result in simple but crucial management steps being omitted). Mortality and morbidity are higher in patients with unrecognised delirium. Delirium is extremely common (30–40%) and a major source of distress in dying patients, so all such patients should be screened for the condition and, within the limits of what is appropriate, managed as with other cases of delirium.

PREVENTION

It is estimated that up to one third of all cases of delirium are preventable. It is possible to identify those at high risk of delirium (see Table 1 for predisposing factors). Good clinical care for these patients should routinely include steps to prevent the onset of delirium. This requires early assessment and intervention by a multidisciplinary team.

Prevention includes steps to identify and promptly treat risk factors for delirium (such as infection), provide orientation to time and place, encourage early mobilisation, ensure continuity of care and avoid frequent changes of environment (e.g. ward changes), correct visual and hearing impairment, ensure good fluid intake and nutrition and maintain a good sleep pattern. Urinary catheterisation, constipation, sedation and restraints should all be avoided. All patients should have drug therapy reviewed, with particular attention to reducing or stopping anticholinergic medication, inappropriate diuretics or psychoactive medication.

There is little evidence at present to support pharmacological measures to reduce the incidence of delirium in hospitalised patients. However, one randomised placebo-controlled study carried out on patients undergoing hip surgery demonstrated that prophylactic low-dose haloperidol reduced the severity and duration of post-operative delirium, despite having no effect on the overall incidence.

MANAGEMENT

An acute alteration of mental status may indicate a life-threatening underlying process such as shock, hypoxia or hypercapnia. Delirium should therefore always be regarded as a medical emergency, and the standard Airway, Breathing, Circulation, Disability approach to the sick patient should routinely be applied in the first instance if delirium is suspected.

Subsequently, the key step in the management of delirium involves the identification (by appropriate history, examination and investigation) and treatment of precipitating factors, and mitigation of the effects of predisposing factors where possible. In particular, consider drugs or drug withdrawal, infection, electrolyte disturbance, dehydration or constipation.

It is also essential to treat any distress and agitation, to communicate clearly with the patient and carers, and to prevent and/or treat complications. As a general rule, all cases of delirium in older people should be strongly considered for early referral to a specialist geriatrics service.

Symptomatic management of delirium can be divided into pharmacological and non-pharmacological measures.

Non-pharmacological measures

- Reorient patients to environment and time (verbal cues, clocks, calendars)
- Try to identify reasons behind disturbed behaviour/wandering, e.g. pain, urinary retention
- Involve family and/or carers, ensure family are aware of the cause of disturbed behaviour
- Encourage early mobility (early involvement of multidisciplinary team)
- Maintain fluid intake and nutrition
- Correction of sensory impairment (e.g. spectacles and hearing aids)
- Avoid constipation
- Normalise sleep-wake cycle (by discouraging daytime naps and ensuring undisturbed night-time rest in a quiet room with low-level lighting)
- Ensure continuity of care and avoid frequent ward or room transfers
- Avoid urinary catheterisation
- Avoid physical restraint
- Adopt a non-confrontational approach to the agitated patient, e.g. acknowledge patient's feelings while avoiding endorsement of the content of their speech, change the subject of conversation. Avoid arguments

Pharmacological measures

All drug therapy should be reviewed and medications contributing to delirium should be withheld, such as anticholinergics, inappropriate diuretics, opiates, benzodiazepines. However, chronic benzodiazepines and higher doses of tricyclic antidepressants (e.g. 50 mg of amitriptyline or above) should usually not be withdrawn immediately: consult a pharmacist.

In hyperactive delirium, it may be necessary to consider the use of sedative medication. Such medication should be kept to a minimum and only considered under the following circumstances:

- To allow essential investigation or treatment
- To prevent the patient endangering themselves or others
- For relief of distress in an agitated or hallucinating patient

Always consider the use of non-pharmacological interventions as an alternative or adjunct.

There is limited trial evidence available to guide the choice of drug treatment. Theoretical considerations would support dopamine antagonists to counteract the dopaminergic excess found in delirium, and what little evidence there is supports haloperidol as the agent of choice. This should be used in low doses initially (0.5 mg orally) with step-wise escalation to control behaviour (recommended maximum of 5 mg daily). Haloperidol may also be indicated in non-agitated patients who are experiencing distressing hallucinations and delusions.

The atypical antipsychotic drugs risperidone and olanzapine are no longer recommended because of evidence of increased risk of stroke.

Benzodiazepines (such as lorazepam 0.5–1.0 mg initially) worsen cognitive function and may prolong delirium. They should therefore usually only be used as second-line agents, but should be considered first in the setting of Parkinson's disease or Lewy Body Dementia as these patients are particularly susceptible to dopamine antagonists. Benzodiazepines such as diazepam or chlordiazepoxide are also the drugs of choice for the management of delirium secondary to alcohol or benzodiazepine withdrawal.

MANAGEMENT OF COMPLICATIONS

Complications in delirium result from:

- immobility (e.g. pressure sores, nosocomial infection, venous thromboembolism)
- instability (falls)
- iatrogenic disease (over-sedation)
- malnutrition and dehydration

Early recognition, evaluation and treatment of these complications using the skills of the multidisciplinary team are essential to reduce the morbidity and mortality associated with delirium.

DISCHARGE AND FOLLOW-UP

Delirium is frequently an indication of underlying physical and mental frailty, and discharge planning needs to take account of this, with appropriate multidisciplinary assessment and follow-up.

There is increasing evidence that delirium is a marker for current or future dementia. For example, elderly patients (with no history of dementia) have been shown to have lower MMSE scores both at six months and one year after an episode of delirium, compared with patients with no history of delirium. A prospective cohort study following hospital discharge demonstrated an incidence of dementia of 18.1% per year for individuals who had delirium during hospital stay versus 5.6% per year for those without delirium.

There is therefore a strong case to be made that all older patients who have had an episode of delirium should be followed up and screened for dementia. This can be done in primary care or in the outpatient clinic and, although such follow-up assessments are uncommon at present, they are likely to be part of normal practice in the future. Follow-up assessment should combine

history taking, basic cognitive screening (with the MMSE and clock-drawing test) and an assessment of possible longer-term decline using the Informant Questionnaire for Cognitive Decline in the Elderly (see *Delirious about dementia* and *Delirious about dementia toolkit*, British Geriatrics Society).

Those who have suffered delirium are at increased risk of further episodes of delirium, and it is important that the diagnosis is clearly documented to allow appropriate preventative measures to be taken on future admissions.

Delirium is an unpleasant and distressing experience, and one neglected aspect of care now increasingly recognised is that patients often retain unsettling memories of the experience. Appropriate explanation and support (for the patient and family) should therefore always be provided once delirium has resolved.

KEY POINTS

- Delirium is extremely common, with high rates of morbidity and mortality. Early recognition and appropriate management are therefore of vital importance.
- Key steps in management include the assessment and amelioration of precipitating and predisposing factors in addition to symptomatic treatment with pharmacological and non-pharmacological measures. Early recognition of complications is also important.
- Delirium has hyperactive, hypoactive and mixed variants. Hypoactive delirium is more common, more serious and more easily overlooked.
- Up to one-third of delirium is preventable with proactive management of risk factors and high-quality clinical care.
- Delirium is a potential marker for current or future dementia, and patients should be followed up to detect this at an early stage.

FURTHER READING

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