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Review Article

Delirium: Assessment and Management - A Review

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I N F O

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A B S T R A C T

Delirium is described as a syndrome characterized by disturbed consciousness, cognitive function or perception, which is acute in onset and has fluctuating course. This article serves to provide a brief review of this condition with respect to diagnostic classification, epidemiology, etiopathogenesis and types. Furthermore, a focused discussion on its assessment and management in routine clinical practice has been documented.

Keywords: Delirium, Acute Confusional State, Assessment, Management

Introduction

Toxic psychosis, ICU psychosis, organic brain syndrome, encephalopathy, encephalitis, acute organic state, acute organic psychosis, acute confusional state, acute brain failure are few names that have been provided in the literature for delirium.

As per NICE (2010),[1] delirium has been defined as "A common clinical syndrome characterized by disturbed consciousness, cognitive function or perception, which has an acute onset and fluctuating course." DSM-5 (2013)[2] describes delirium as "Disturbance of attention or awareness that is accompanied by a change in baseline cognition that cannot be better explained by a pre-existing or evolving neurocognitive disorder."

ICD-11 states "Delirium is characterized by disturbed attention (i.e., reduced ability to direct, focus, sustain, and shift attention) and awareness (i.e., reduced orientation to the environment) that develops over a short period of time and tends to fluctuate during the course of a day, accompanied by other cognitive impairment such as memory deficit, disorientation, or impairment in language, visuospatial ability, or perception."[3]

Among these entire definitions disturbance in attention and awareness, acute onset and fluctuating course seem prominent and common features.

Clinical Features and Diagnostic Critera

As there is no recognized physiologic measure, diagnosis of delirium is made on the basis of history, physical examination, mental status examination and enquiring about onset, course of illness from family members as patient is not able to give all these information.[4]

Clinical history may indicate toward abrupt/ acute onset, fluctuating severity over 24 hours with disturbed sleep

wake cycle in which mainly sleep is fragmented, with sleeplessness in night with characteristic reversal of sleep wake cycle,[5] diffuse cognitive deficits mainly attention, orientation, memory, visuo-spatial ability,[6] with disturbance in psychomotor behaviour i.e. hyperactive, hypoactive or both,[7,6] hallucinations (more commonly visual) and delusions (not well formed, paranoid).[8] Language impairment and disorganized thinking may be seen.[8,9]

ICD 10,[10] ICD 11[3] and DSM 5[2] have used all these features in their respective guidelines, detailed in Table 1.

Table 1.Diagnostic criteria for delirium in ICD 10, ICD 11, DSM 5

ICD 1010	ICD 113	DSM 52
For a definite diagnosis, symptoms, mild or severe, should be present in each one of the following areas: • Impairment of consciousness and attention • Global disturbance of cognition • Psychomotor disturbances • Disturbance of the sleep-wake cycle • Emotional disturbances	All definition Criteria should meet "Delirium is characterized by disturbed attention (i.e., reduced ability to direct, focus, sustain, and shift attention) and awareness (i.e., reduced orientation to the environment) that develops over a short period of time and tends to fluctuate during the course of a day, accompanied by other cognitive impairment such as memory deficit, disorientation, or impairment in language, visuospatial ability, or perception"	• Disturbance in attention (i.e., reduced ability to direct, focus, sustain and shift attention) and awareness (reduced orientation to the environment) • The disturbance develops over a short period of time (usually hours to a few days), represents an acute change from baseline attention and awareness, and tends to fluctuate in severity during the course of a day • An additional disturbance in cognition (e.g. memory deficit, disorientation, language, visuospatial ability, or perception) • The disturbances in Criteria A and C are not better explained by a pre-existing, established or evolving Neurocognitive disorder and do not occur in the context of a severely reduced level of arousal such as coma • There is evidence from the history, physical examination or laboratory findings that the disturbance is a direct physiological consequence of another medical condition, substance intoxication or withdrawal (i.e. due to a drug of abuse or to a medication), or exposure to a toxin, or is due to multiple etiologies

Table 2.Predisposing and Precipitating Factors of Delirium[14,16,17]

<table>
<tr><th colspan="2">Predisposing Factors</th><th>Precipitating Factors</th></tr>
<tr><td>Patient's Factors
• Old Age
• Male
• Dementia
• Previous delirium</td><td rowspan="3">Medical Causes
• Infections
• Severity of illness
• Chronic renal or hepatic disease
• Stroke
• Neurological disease
• Fractures or trauma
• Hypotension and Hypo perfusion
• Hypoxia or anoxia
• Malnutrition and nutritional deficiencies
• Acute vascular problems (e.g., myocardial infarction, pulmonary embolism)
• Endocrinopathies</td><td rowspan="2">• Immobility
• Dehydration
• Use of bladder catheter
• Use of physical restrained
• Hypoxia
• Intercurrent illness
• Malnutrition
• Change of Environment</td></tr>
<tr><td>Pharmacological Factors
• Polypharmacy
• Alcohol or Benzodiazepine dependence
• Specific Drugs</td></tr>
<tr><td>Perioperative
• Course of postoperative period
• Type of operation (for example, hip replacement)
• Emergency operation
• Duration of operation</td><td rowspan="2">Medicines (High Risk)
• Benzodiazepines
• Opioid analgesics
• Antiparkinsonian agents
• Antidepressants
• Centrally acting agents
• Corticosteroids
• Lithium</td></tr>
<tr><td>Environmental Factors
• Hypothermia/Hyperthermia
• Visual Impairment
• Hearing Impairment
• Impaired ADL and Mobility</td><td>Water and Metabolic derangements
• Hypo- or hyper-glycemia
• Hyponatremia
• Hypokalemia
• Dehydration
• Hypoalbuminaemia
• Hypocalcaemia</td></tr>
</table>

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Epidemiology

Delirium is most common in mechanically ventilated patients in the ICU with prevalence up to 80%[11] giving it the name "ICU Psychosis." Among general hospital adult inpatients prevalence of delirium is 17.6 to 19.6%.[12] Among all admissions to ICU and in advanced cancer and palliative care prevalence of delirium is ≥50%.[13] Likewise, prevalence among patients presenting to emergency departments is up to 10%, in all admissions to general hospitals 10% to 30%, among inpatients in general medical settings ≥33%, among hip fracture patients 66%, in old people and nursing homes, delirium is found in about 60% people.[14]

Etiology

Delirium can be multifactorial. Practically any physiological derangement can cause delirium in a susceptible individual. In a prospective study of delirium in elderly patients, Francis and colleagues identified five leading causes of delirium: a) Fluid/ Electrolyte disturbance b) Infection c) Medication toxicity d) Metabolic derangement e) Sensory and environmental disturbance.[15]

Neurobiology

Several hypotheses have been given to explain several clinical features and Neurobiological basis of delirium prominent ones are neurotransmitter hypothesis, neuroinflammatory hypothesis, neuronal ageing hypothesis, oxidative stress hypothesis, neuroendocrine hypothesis, circadian rhythm dysregulation hypothesis and others.

- Neurotransmitter hypothesis: Involvement of Cholinergic & dopaminergic pathways, glutamate, serotonin and GABA-ergic pathways.[18]
- Neuroinflammatory hypothesis: Activation of peripheral immune system, release of pro-inflammatory cytokines (IL-6, 8, 10, TNF) by the brain parenchyma, neopterin, S100 beta protein.[19,20]
- Neuronal ageing hypothesis: Age related cerebral atrophy and neuronal loss, changes in neuro-transmitter systems, reduction of the blood brain flow as well as regional blood flow, reduction in the cerebral metabolic rate of oxygen and decreased oxygen supply and thus reduced redox activity.[21-23]
- Oxidative stress hypothesis: increase in consumption of oxygen or reduced availability of oxygen and altered cerebral metabolism and thus a state of oxidative stress.[24]
- Neuroendocrine hypothesis: activation of the hypo-thalamic-pituitary system, malfunction of the glucocorticoid receptors in the hippocampus and limbic system, which regulates the negative feedback on the HPA axis.[25,26]
- Circadian rhythm dysregulation hypothesis: De-synchronization of circadian rhythm including sleeplessness, reversal of sleep-wake cycle, and fragmentation of sleep.[27]
- Other etiological theories- Neural dysconnectivity hypothesis, Orexinergic neurons in the peri-fornical nucleus, involvement of vitamin B complex, folate, lipids and anti-oxidants.[28,29]

In current understanding delirium is thought to be cumulative effect of these entire hypothesis altogether.

Subtypes

Delirium was first divided by Liptzin & Levkoff,[30] depending upon the motor activity into three major types: hyperactive, hypoactive and mixed. Hyperactive delirium comprising of patients with restlessness, wandering behaviour, increased psychomotor activity, loss of control of activity, increased speech, aggression uncooperation, hyper alert, increased startle response, hallucinations. Hypoactive delirium characterized by apathy, listlessness, decreased activity levels, decreased speed, social withdrawal, hypo-alert, hype-somnolence. Mixed delirium has features of both and is the most common of all three varieties.

Assessment

A comprehensive assessment of delirium must include following components:

- Clinical History: Proper history should be elicited from available informants regarding all clinical features as previously mentioned in this article.
- General and Systemic Examination: Complete general and systemic examination should be done keeping in mind all possible etiologies as motioned in the Table 2
- Rating Scales
- Lab workup

Rating Scales

Several Scales have been developed for assessment of level of consciousness, screening, diagnosis, severity and aetiology of delirium.

- To see whether the patient is arousable and in a state to be assessed for delirium
  - Richmond Agitation and Sedation Scale (RASS)
- Scales for screening
  - MMSE (Mini Mental State Examination)
  - CAM ICU/ CAM
  - NEECHAM confusion scale
  - Delirium Observation screening scale
  - Intensive care delirium screening checklist
  - Global attentiveness rating
- Diagnostic scales
  - Delirium symptom interview
  - Saskatoon delirium checklist
  - Delirium rating scale

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- Memorial delirium assessment scale

- Scale to assess severity of delirium
  - Delirium Rating Scale
  - Delirium-O-Meter
  - Delirium Severity Scale

- Aetiology
  - Delirium aetiology checklist

Lab Iinvestigations

Lab investigation for delirium includes routine investigation and level two investigations which should be done if indications are present. Routine investigations include full blood count, CRP, urea and electrolytes, glucose, calcium, LFTs, KFTs and ECG. If indicated, chest X-ray, urinalysis, blood cultures, pulse oximetry, arterial blood gases, vitamin B12 and folate, thyroid function tests, specific cultures (e.g. sputum, urine), CT of the head, lumbar puncture, EEG can also be done.[14,31]

EEG in delirium shows generalized slowing except for delirium tremens. Slow posterior rhythms, diffuse delta/theta waves, poor background rhythm organization, loss of reactivity[32] are characteristic of delirium. However, EEG is not recommended for making diagnosis.6 Evoked potentials are also abnormal.[33]

Differential Diagnosis

About 1/ 3 to 2/ 3 cases are missed across range of therapeutic settings and specialists.34 Causes cited for the same are non-recognition, fluctuating symptom.[35,36] Diagnosis is more likely to be missed or misdiagnosed in elderly, patients with sensory impairments, patients with pre-existing dementia, delirium of hypoactive type[37] or due to lack of sensitivity of screening instruments.[38] Delirium is often confused with dementia, depression, and schizophrenia/psychosis superficially and therefore must be differentiated from the same. Differential diagnosis details are given in Table 3.

Management

Management of Delirium should be done by treatment of all possible underlying causes and includes:

1. Prevention
2. Non Pharmacological Management
3. Pharmacological Management

Prevention

NICE in 2010,1 provided detailed guidelines about prevention of delirium, it is summarized as follows:

- Avoid polypharmacy: Carry out a medication review: both the type and number of medications

Table 3.Differential diagnosis of Delirium l [6]

	Delirium	Dementia	Depression	Schizophrenia
Clinical Picture	Fluctuating levels of consciousness, decreased attention	Memory impairment with normal level of consciousness	Sadness of mood, loss of pleasure and interest in usual activities	Hallucinations, delusions, disorganised behaviour
Onset	Acute	Insidious	Variable	Variable
Course	Fluctuating; short with diurnal variations	Steadily progressive and chronic	over months, morning worsening	Variable
Consciousness & Orientation	Clouded; Disoriented	Clear until late stages	Generally Unimpaired	Unimpaired but may be perplexed in acute stage
Thinking	Disorganized	Impaired judgment	Intact	disorganized
Attention and Memory	Poor short term memory; inattention	Poor short term memory without marked inattention	Poor attention but memory intact	Poor attention but memory intact
Psychomotor Activity	Depending on subtype; generally increased	Normal	Reduced	Variable
Sleep Wake Cycle	Disturbed/reversed sleep-wake cycle	Disturbed; may be fragmented	Early morning awakening or Hypersomnia	Poor sleep
EEG	Abnormal in 80-90%; Generalized Diffuse slowing in 80%	Abnormal in 80-90%; Generalized Diffuse slowing in 80%	Generally Normal	Generally normal

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- Use Anticholinergic, Opioid and sedatives carefully
- Maintain hydration status
- Train caregivers and nursing staff to recognize delirium
- Regular assessment especially in elderly
- Avoid moving people within and between wards or rooms unless absolutely necessary
- Address immobility or limited mobility
- Address pain by: looking for non-verbal signs of pain, starting and reviewing appropriate pain management
- Address poor nutrition, if people have dentures ensuring they fit properly
- Address sensory impairment by: resolving any reversible cause (e.g. impacted ear wax), hearing and visual aids.
- Promote good sleep patterns and sleep hygiene by:

o avoid procedures during sleeping hours, if possible
o scheduling medication rounds to avoid disturbing sleep
o Reducing noise to a minimum during sleep periods

Non Pharmacologiacl Management

Non Pharmacological management is as important as pharmacological management in patients of Delirium as it can help in reducing Polypharmacy which is again an individual etiological cause of delirium. Non pharmacological management includes providing support and orientation, providing an unambiguous environment and maintaining competence.[16]

Providing Support and Orientation

- Short and clear communication with the patient; frequent reorientation especially about family members and treating team
- Place clock, calendar and days schedule with the patient
- Objects from home should be brought to make hospital familiar
- Use TV or Radio to help maintain contact with the outside world
- Involve attendants to give a feeling of safety

Providing an Unambiguous Environment

- Remove unnecessary objects from the room
- Minimize unnecessary sensory stimulation
- Maintain adequate lighting even In night to avoid a perceptual abnormality
- Keep room temperature I comfortable range

Maintaining Competence

- Correct any possible sensory impairments using hearing or visual aids
- Encourage patients involvement In treatment and promote self-care
- Maintain possible activity levels
- Avoid intervention during sleep hours

Pharmacological Management

Pharmacological management is required is delirium only if it is due to drug withdrawal (alcohol/ benzodiazepines) or when there is physical aggression causing harm to patient or others. Mainly antipsychotics ad benzodiazepines are used, where benzodiazepines are used for alcohol/ benzodiazepine withdrawal delirium.

Typical Antipsychotics

Among typical antipsychotics most evidence is for Haloperidol. As per NICE 2010,[1] Haloperidol for short-term (usually for 1 week or less) can be given, to start at the lowest clinically appropriate dose and titrate cautiously according to symptoms.[1] Similarly, short term Haloperidol 2.5 mg to 10 mg oral/ IM per day has been recommended by other studies.[39-41] It has certain advantages such as, can be given orally or I/M,[42] lesser propensity to cause metabolic side effects, reduces overall mortality and can be helpful in paediatric delirium.[43] However, it should be used with precaution in presence of ECG changes.[44]

Atypical Antipsychotics

Atypical Antipsychotics can also be used, however, evidence is still not robust and agents like Clozapine may even cause delirium. Among atypical maximum evidence is for Risperidone, Olanzapine, with emerging evidence on Quetiapine.[6] Second-generation antipsychotics, such as Risperidone, Clozapine, Olanzapine, Quetiapine, Ziprasidone, and Aripiprazole, may be considered. But these agents are associated with increased mortality in patient of dementia.

For patients with Parkinson's disease and delirium who require antipsychotic medications, Clozapine or Quetiapine have some support in the literature.

Other Psychotropics

Other molecules that have also been used are Donezepil, Rivastagmine, Melatonin and Sodium Valproate.

Modified Electroconvulsive Therapy

It has been used as a last resort for delirious patients with severe agitation who are not responsive to pharmacotherapy.

Delirium Tremens

When delirium is associated with sedative-hypnotic and alcohol withdrawal, Benzodiazepines can be given as Symptom triggered, Front loading and Fixed dose reduction regimen.[45] In symptom triggered 20-30 mg Chlordiazepoxide stat, then as needed hourly based on Symptoms. In front-loading bolus dose of 10 mg IV Diazepam equivalent every 5-20 minutes until (a) light sedation (drowsy but verbally responsive) is achieved (b) CIWA-Ar scores are < 10, Then

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5-20 mg every hour as maintenance can be given.45 In Fixed dose reduction dose of Benzodiazepine can be calculated if for example, 20 Units consumed/day, then Dose of Chlordiazepoxide given is 20mg QID which is gradually tapered off.[46] In delirium tremens, Prophylactic Thiamine minimum of 300 mg daily for 5 days, and then followed by Oral Thiamine in assisted withdrawal.46 In literature up to 300 to 1500 mg/day Thiamine has been suggested in various articles.[47,48] However, there is lack of consensus with respect to exact dosage of Thiamine required in patients presenting with Delirium tremens and is a potential area of research.

Conclusion

Delirium is an acute confusional state which affects the global outcome and prognosis of severely ill patients. It substantially surges health-care utilization and costs; therefore, prevention, early recognition and effective treatment of delirium are indispensable in this condition. Swift screening and proactive management is the cornerstone of reducing the incident and prevalence. Along with pharmacological, non-pharmacological interventions are imperative.

Conflict of Interest: None

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