

## Postoperative delirium – Review Article

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### Abstract

Postoperative delirium is a common but often a missed complication following major surgery in elderly patients. Early diagnosis, treatment with non-pharmacological means, and drug treatment reduces complications, so also hospitalization cost. Awareness about common precipitating factors, preventive measures, treatment & training of healthcare workers is essential regarding this problem as it can be prevented in about 40% patients.

**Keywords:** Postoperative, Elderly, Delirium, Review

### Introduction

Postoperative delirium is the most common postsurgical complication occurring in 5% to 50% of older patients.<sup>(1)</sup> Delirium is unrecognized in more than 50% patients.<sup>(2)</sup> Delirium can lead to prolonged hospitalization, loss of functional independence, reduced cognitive function, other postoperative complications and death.<sup>(3)</sup>

Clinicians are familiar with managing organ dysfunction like that of kidneys and lungs but are less familiar with delirium representing acute brain failure.<sup>(4)</sup> Delirium is preventable in up to 40% of patients.<sup>(5)</sup> This review is presented to help clinicians in this regard.

### Definition

Neurobehavioral disturbances manifest in three distinct forms: emergence delirium (ED), postoperative delirium (PD), and Postoperative cognitive Dysfunction (POCD).<sup>(6)</sup>

**Delirium** is defined as presence of disturbed consciousness and a change in cognition or the development of a perceptual disturbance that is not better accounted for by a pre-existing, established, or evolving dementia.<sup>(6)</sup> As per International Classification of Diseases 10th edition (ICD-10) psychomotor disturbances, disturbance of the sleep-wake cycle, and emotional disturbances are also included along with cognitive dysfunction.

**ED** occurs during emergence from anaesthesia and sedation, with no lucid interval, lasting approximately 30 minutes.

**PD** lasts hours or longer and may or may not have lucid interval, usually peaking between one and three days postoperatively. Most cases recover within 4 weeks, but can persist till hospital discharge in 50% of cases.<sup>(2)</sup>

**POCD** refers to subtle cognitive impairment noted on neuropsychological tests, typically assessing attention and memory.<sup>(6)</sup>

PD is the most severe form of postoperative neurobehavioural disturbance.

### Epidemiology

**ED** occurs in about 5-21% of adults. It typically affects young, healthy, often anxious males, undergoing lengthy invasive surgery. Preoperative benzodiazepine seems to be the strongest risk factor.<sup>(7)</sup>

**PD** affects 3-53% of patients undergoing major surgery and 83% of critically ill patients.<sup>(8)</sup> Risk for delirium is more following emergency surgery.<sup>(4)</sup>

**Etiology:** Altered central cholinergic mediator levels appears to be the most important cause. Noradrenergic hyperactivity, Change in interleukin levels, decreased GABA ergic activity and cerebral perfusion might also contribute.<sup>(9)</sup>

**Predisposing Factors:** Preexisting dementia appears to be the most predictable risk factor.

**Risk Factors for Postoperative Delirium** <sup>(4,10)</sup>

**A. Patient related Factors:** These factors cannot be modified :

Age > 65 years

Pre-existing dementia

Cognitive impairment

Cerebral, Cardiovascular disease

Intra operative and post-operative complications

Severe illness or co-morbidity burden (e.g. Renal failure)

Genetic factors <sup>(6)</sup>

**Additional factors** (modifiable to some extent):

Auditory or visual impairment

Alcohol abuse

Sleep deprivation

Depression

Functional impairment

**B. Surgery related Factors :**

Major surgeries like cardiovascular surgeries

Infection

Inadequately controlled pain

Renal insufficiency

Anemia

Hypoxia or hypercarbia

Poor nutrition

Dehydration

Electrolyte abnormalities (hyper-, or hyponatremia)  
 Limited mobility  
 Use of benzodiazepines, anticholinergics, antihistaminics, antipsychotics etc.  
 Constipation, Presence of urinary catheter

Predisposing factors are intrinsic to patients, and determine vulnerability to brain insults.<sup>(11)</sup> Preventive measures should be implemented in patients with two or more risk factors.

**Diagnosis of Postoperative Delirium:** PD can be hypoactive in 25%, hyperactive in 50% or as a mixed form in 25% of cases.<sup>(12)</sup>

#### Common symptoms of delirium<sup>(4)</sup>

1. Decreased\*, or increased arousal
2. Delayed awakening from anesthesia\*.
3. Abrupt change in cognitive function over hours or days is a hall mark,<sup>(13)</sup> including problems with attention, concentration, memory and disorientation.
4. Difficulty in conversations and following suggestions
5. Disorganized thinking and speech (slow,\* or rapid).
6. Quick-changing emotions, irritability
7. Delusions, hallucinations.
8. Slowed movements,\* restlessness.
9. Sleep/wake cycle changes.
10. Decreased appetite\*.
11. New incontinence of urine or stool\*.
12. Rapidly fluctuating symptoms.

(\*The Hypoactive delirium symptoms and Signs)

Pre-operatively assess and document cognitive function in older adults at risk of PD. For diagnosing hypoactive delirium, timely help of competent professionals is necessary. Health care professionals should be trained to use a screening instrument.

#### Delirium Screening

Confusion assessment method (CAM) is used as a screening tool (short form) and as a diagnostic instrument (long form plus the algorithm). CAM has a sensitivity of 94% and specificity of 89%.<sup>(14)</sup>

Other tools include the Delirium Rating Scale, and the Delirium Symptom Interview,<sup>(15,16)</sup> NEECHAM Confusion Scale and the Estimation of Physiologic Ability and Surgical Stress (E-PASS).<sup>(17)</sup> Bedside tests like executive clock drawing task<sup>(18)</sup> & Mini-mental state examination can be used for screening as well as for follow up.<sup>(19)</sup> Severity of delirium can be graded, and may have prognostic value.<sup>(12)</sup>

#### CAM- scale for diagnosis of delirium<sup>(20)</sup>

1. **Acute Onset and Fluctuating Course:** Is there evidence of an acute change in mental status from the patient's baseline & fluctuating behavior during the day?
2. **Inattention:** Do the patients have difficulty in focusing attention, are they easily distracted, or have

difficulty in keeping track of what is being said? Ask them to recite backwards the days of the week.

3. **Disorganized Thinking:** Is the speech incoherent, or is there an unclear or illogical flow of ideas or unpredictable switching between subjects?
4. **Altered Level of Arousal:** Is patient alert, vigilant, lethargic, difficult to rouse, or can't be roused?

Diagnosis of delirium requires presence of criteria no. one and two plus either three or four.

**CAM ICU** protocol is used for ICU patients. It combines assessment Of patient's sedation using Richmond 10 point sedation score with evaluation of CAM.<sup>(21)</sup>

Hypoactive delirium is difficult to detect and needs validated methods for diagnosis and has increased mortality.<sup>(22)</sup>

At present, there is insufficient evidence to make a routine recommendation for delirium screening.<sup>(23)</sup> Risks include misdiagnosis, increased cost of evaluation, and inappropriate treatment with antipsychotic medications.

**Prevention of Delirium:** PD can be prevented in 40% susceptible patients.<sup>(5)</sup>

#### Intraoperative Measures to prevent Delirium:

Intraoperative oxygenation, hemodynamic stability, electrolyte balance & appropriate drug dosages are helpful in prevention of PD.<sup>(24)</sup> In another study, regional anesthesia, instead of general anesthesia, for orthopedic procedures has been proven successful in reducing the incidence of PD in elderly patients.<sup>(25)</sup>

Single dose of Ketamine (0.5 mg/ Kg) given upon induction was associated with lower serum levels of C-reactive protein and incidence of delirium in patients undergoing cardiac surgery. Neuroprotective effects of Ketamine might be responsible.<sup>(26)</sup>

In a randomized controlled trial that compared light and deep sedation in patient with hip fracture, deep sedation was associated with increased rates of PD.<sup>(25)</sup> BIS monitoring helps to avoid deep levels. Titrated level of anaesthesia reduces PD.<sup>(27)</sup>

Recent trials have shown that patients receiving dexmedetomidine, rather than benzodiazepines<sup>(28)</sup> and non-opioid analgesic alternatives in comparison with opioid-only pain regimens<sup>(29)</sup> were less likely to experience delirium.

But at present there is no adequate information to make a recommendation about specific anesthetic agents, general vs. regional anesthetics, systemic arterial pressure monitoring, intra-operative blood transfusion, and use of dexamethasone.<sup>(4)</sup>

**Non- Pharmacological Measures:** Some studies demonstrated benefit of non-pharmacologic approaches for prevention and for de-escalation of agitation.<sup>(30,31)</sup> Perioperative proactive geriatric consultation for patients with hip fracture reduced the risk of delirium by 40%.<sup>(5)</sup> Commonly used **preventive interventions**<sup>(4,10)</sup> are:

1. Orientation protocol: provide patients with repeated orientation to their surroundings.

2. Sensory enhancement: Provide them glasses, hearing aids.
3. Sleep protocol: Ensure day & night time sleep, relaxation measures.
4. Ambulate the patient at least twice a day when possible.
5. Adequate and continuous pain control.
6. Adequate nutrition and hydration.
7. Nonessential catheters, nasal-gastric tubes, additional intravenous access lines should be removed
8. Review medications and necessary interventions as needed, avoid benzodiazepines and anticholinergics.<sup>(6)</sup>

Daily Assessment by Multidisciplinary Team for reinforcement of preventive interventions reduced the incidence and duration from 15% to 10% but there was no change in hospital stay duration.<sup>(32)</sup> Supportive strategy has also reduced delirium related complications like decubitus ulcers, falls, urinary tract infection etc.<sup>(33)</sup>

#### **Medications as risk factors for Postoperative Delirium**<sup>(34)</sup>

Following drugs are associated with higher incidence of PD.

Drugs with anticholinergic properties

**Tricyclic antidepressants:** amitriptyline, doxepin, imipramine

Diphenhydramine, hydroxyzine

**Antimuscarinics:** oxybutynin, tolterodine

**Antispasmodics:** scopolamine

First-generation antipsychotics: chlorpromazine, thioridazine

Cimetidine, Ranitidine

**Skeletal muscle relaxants:** cyclobenzaprine

**Antiemetics:** promethazine

Antipsychotics –Paroxetine, Olanzapine

Corticosteroids, Methylprednisolone

Meperidine

**Benzodiazepines:** alprazolam, diazepam, lorazepam, midazolam.

**Sedative hypnotics:** Zolpidem, Zaleplon

Polypharmacy increase the risk of delirium. Use of multiple medications (5 or more) has been associated with an increased risk of delirium.<sup>(35)</sup>

**Pharmacologic Prevention:** PD may be preventable in some patients, though its severity and duration may be limited in others, especially if promptly recognized and managed.

Prescribing antipsychotic medications to prevent PD has contradictory support in the literature. Risperidone in patients undergoing cardiac surgery showed a decrease in the incidence PD,<sup>(36)</sup> while studies using Haloperidol, Ziprasidone, and Quetiapine have shown conflicting results.<sup>(37)</sup> Antipsychotics are not recommended to prevent delirium as potential harms of these drugs are considerable (community acquired pneumonia, arrhythmias etc.).<sup>(38)</sup>

**Sedation in the ICU:** Sedation should only be used if clinically indicated, and at the lowest tolerated dose.<sup>(39)</sup>

If a patient is alcohol or benzodiazepine addict, benzodiazepine is used even though there is a risk of delirium precipitation.<sup>(4)</sup> Dexmedetomidine is not superior to other sedatives as per recent analytical study.<sup>(40)</sup> Clonidine may be of beneficial.<sup>(41)</sup>

**Evaluation of Postoperative Delirium:** Review history and repeat physical examination to rule out organic causes and search for treatable causes.<sup>(4)</sup>

**Laboratory evaluation:** Estimate Serum electrolytes (sodium, potassium, calcium, phosphate, magnesium), blood glucose, arterial blood gases.

**Find out any source of infection:** particularly urosepsis, pneumonia, blood culture, surgical infection (USG). Clinician should be aware of the fact that clinical signs of sepsis may be modified in elderly patients.

**Screening for Drugs:** Avoid drugs responsible for delirium in patients with multiple risk factors for delirium or reduce their dosages and frequency.

Delirium due to withdrawal should not be confused with postoperative delirium. Delirium due to withdrawal needs special treatment, for example Thiamine for alcoholic psychosis.

**Imaging:** CT head is advised only if there is any focal neurological deficit, or there is no obvious cause.<sup>(42)</sup>

**Pharmacological treatment:** Use antipsychotics at the lowest effective dose for the shortest possible duration to treat patients who are severely agitated or distressed, and not for hypoactive patients. Haloperidol is the most frequently used drug.<sup>(43)</sup> For mild agitation initial dose is 0.5 -2.5 mg I.V., for moderate agitation 5 mg, and for severe agitation 10 mg can be administered at the outset<sup>(44)</sup> and can be repeated after six hours. I.M. dosing is less preferred. Watch for dyskinesia, Torsade de pointes, hyperthermia.<sup>(44)</sup> Newer antipsychotics are not tried for PD.<sup>(45)</sup> Benzodiazepines should not be used as a first-line treatment of agitated patient as they promote delirium, but are recommended for alcohol withdrawal.<sup>(46)</sup>

Delirium due to sedation or analgesic withdrawal can be managed by adding dexmedetomidine<sup>(47)</sup> and that due to cholinergic syndrome by using Physostigmine 10-39 microgm/kg<sup>(48)</sup>

To summarize, we should remember ABCDE<sup>(49)</sup> bundle of delirium prevention & management. (**A**, **B** –Awakening and Breathing, **C** –Choice of sedation and minimizing relaxant use, **D**–delirium assessment and proper management, **E** – Early mobilization and exercises, **F** – Family member involvement).

**Outcome of the patients with PD:** Delirium may be associated with complications like fall, pulled lines or tubes, prolonged bladder catheterization, aspiration pneumonia and prolonged hospital stay. Mortality increases by at least 10–20% for every 48 hours of delirium.<sup>(9)</sup> Delirium doubles risk of post-discharge re-hospitalization and death, and that of dementia up to 10-fold.<sup>(50)</sup>

## Conclusion

Delirium is a common, highly morbid, but often undiagnosed post-operative complication. Management requires knowledge for screening, diagnosis, risk factor assessment, non-pharmacologic and pharmacologic interventions aimed at preventing and treating delirium and POCD. Guidelines can be adapted within each health care system.

Relationship among PD and subsequent cognitive decline need to be explored in future prospective trials.

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