

OVERVIEW OF DELIRIUM

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OVERVIEW OF DELIRIUM

- LEARNING OBJECTIVES

- Definition/synonyms
- Epidemiology across health care settings
- Pathophysiology/proposed theories on etiology of delirium + subtypes
- Risk factors for development of delirium
- Recognizing/Diagnosing delirium
- Practical treatment strategies
- Challenges/future research

DEFINITION/SYNONYMS

- Official definition provided by the ***DSM-V Manual*** requires ALL the following to be present:

- Disturbance in attention and awareness
- Disturbance develops acutely and tends to fluctuate in severity

.....and ONE of the following

- Disturbance not better explained by pre existing dementia
- Disturbance does not occur in the context of severely reduced level of arousal or coma
- Evidence of an underlying organic cause[es]

DEFINITION/SYNONYMS

- IMPORTANT TAKE AWAY POINTS FROM DSM-V CRITERIA

-There have to be **noticeable deficits** in ***attention span*** [the patient/resident is easily distracted] and ***awareness*** as relates to interaction with the current environment.

-Above deficits are **sudden in onset** [hours to days] and noticeably fluctuate.....at one time the patient/resident is at baseline and the next moment they are not [*CNAs/Family usually volunteer this information*].

-Underlying dementia cannot explain the above changes

-Search for an underlying etiology to explain the changes

SYNONYMS FOR DELIRIUM

- Delirium is also known as
 1. Acute confusional state
 2. Altered Mental Status
 3. Toxic/Metabolic Encephalopathy
 4. Acute Mental Status Change

Delirium in Hospitalized Older Adults N Eng J Med 2017;377:456-1466

GRS 10 teaching slides.

EPIDEMIOLOGY OF DELIRIUM

Occurrence of Delirium varies across different settings;

-In the ER, it is present in 10-15% of patients

-On the medical floor, 1/3rd of hospitalized patients > 70yrs have delirium

-In the ICU setting, incidence is higher and is quoted as > 70%

Delirium in Hospitalized Older Adults N Eng J Med 2017;377:456-1466

Geriatric review Syllabus 9th edition

EPIDEMIOLOGY OF DELIRIUM

- In the palliative care setting, it is even higher at around 85%
- In the nursing home setting, up to 15% of residents admitted to the SNFs have delirium.
- Community dwelling older adults not spared; delirium does occur primarily in older adults recently discharged from the hospital with a prevalence quoted as between 1-2%.

Delirium in Hospitalized Older Adults N Eng J Med 2017;377:456-1466

Geriatric review Syllabus 9th edition; chapter on Delirium

Delirium during Postacute Nursing Home admission and Risk for Adverse Outcomes JAGS 2017 65:1470-1475

EPIDEMIOLOGY OF DELIRIUM

- **Rates of *unrecognized delirium* [that missed by treating MDS/CNP/PAs/RN but diagnosed by a trained assessor] remained unchanged over a 15 year span.....55-70% in 2000-2001 and 60% in 2015.....

- Delirium is expensive.....

-Yearly health care costs related to delirium care in the USA quoted as \$182 billion in 2011, increased from the previous estimate of \$164 billion/year.

-About 2.6million adults > 65yrs develop delirium each year.

Joining forces against Delirium-From Organ System Care to Whole Human Care. N Engl J Med 2020;382(6) 499-501

Delirium in Older Persons: Advances in Diagnosis and Treatment JAMA 2017;318(12):1161-1174

EPIDEMIOLOGY OF DELIRIUM

- Delirium is devastating.....

- Persistent delirium up to 6 months post hospital discharge is around 21%.

- It independently increases the risk of death at least 2 fold.

- Delirium results in functional decline with potential loss of independence.....therefore more than doubles the risk of NH placement

- Delirium causes more than a 12 fold increase in risk of incident dementia.

Delirium during Postacute Nursing Home admission and Risk for Adverse Outcomes JAGS 2017 65:1470-1475.

Geriatric review Syllabus 9th edition; chapter on Delirium

PATHOPHYSIOLOGY AND SUBTYPES

- Delirium is thought to be the “*final common pathway of multiple mechanisms*”.
- Some authors indeed describe delirium as “*Acute brain failure*”drawing a parallel with the complex processes that precipitate acute heart/congestive failure.
- Myriad of theories exist but commonest are the **Cholinergic deficiency** and the **Inflammation theories**.

Delirium Pathophysiology: An updated hypothesis of the etiology of acute brain failure. International Journal of Geriatric Psychiatry, November 2018, Vol.33(11), pp.1428-1457

PATHOPHYSIOLOGY-CHOLINERGIC DEFICIENCY

- Based on the fact that medications with strong anticholinergic activity can trigger delirium.....examples of such medication are, Darifenacin, Oxybutynin, Benadryl, SSRIs/Paroxetine, TCA's/Amitriptyline + Nortriptyline, Benztropine
- Interestingly, medications that increase levels of acetylcholine example rivastigmine/galantamine have not shown efficacy in treating and preventing delirium.
- Simple to use tool to calculating “Cholinergic burden” of a medication available online at acbcalc.com....just type in the medication!

PATHOPHYSIOLOGY-INFLAMMATION

- Posits that during states as infection/inflammation [post op], WBCs adhere the BBB [blood brain barrier] cells and trigger disruption of the usually tight cell-cell adhesion allowing:
 1. Increased permeability across the BBB.
 2. Increased transport of WBCs/peripherally released cytokines [IL-1RA, IL-6, IL-8, IL-10, TNF alpha].
 3. Decreased perfusion and longer diffusion distances for oxygen.

End result:

Neuronal ischemia and Neuronal Apoptosis.

Delirium Pathophysiology: An updated hypothesis of the etiology of acute brain failure. International Journal of Geriatric Psychiatry, November 2018, Vol.33(11), pp.1428-1457

PATHOPHYSIOLOGY-ADDITIONAL THEORIES

- Neuronal aging hypothesis
- Oxidative stress hypothesis
- Neuroendocrine hypothesis
- Circadian rhythm dysregulation hypothesis
- Neurotransmitter hypothesis [implicates additional neurotransmitters: DA, GABA, 5HT, NE, GLUT, H1/H2, etc]

Delirium Pathophysiology: An updated hypothesis of the etiology of acute brain failure. International Journal of Geriatric Psychiatry, November 2018, Vol.33(11), pp.1428-1457

PATHOPHYSIOLOGY DELIRIUM

- WHEW!!! QUITE COMPLEX!!

To make sense of all the theories, the Systems Integration Failure Hypothesis summarizes as follows.....

“alterations in neurotransmitter function, combined with a failure of the complex, highly organized and interconnected brain systems lead to a failure in the CNS’s functional integration and appropriate processing of information and response mechanisms”

Delirium Pathophysiology: An updated hypothesis of the etiology of acute brain failure. International Journal of Geriatric Psychiatry, November 2018, Vol.33(11), pp.1428-1457

PATHOPHYSIOLOGY

- Eventually there is an uncoupling of 5 core domains which characterize delirium phenotype.
 1. Attention deficits.
 2. Cognitive deficits/Illogical thought process.
 3. Circadian rhythm dysregulation.
 4. Emotional dysregulation.
 5. Psychomotor function alteration/impairment.

Delirium Pathophysiology: An updated hypothesis of the etiology of acute brain failure. International Journal of Geriatric Psychiatry, November 2018, Vol.33(11), pp.1428-1457

DELIRIUM PHENOTYPES/SUBTYPES

- Traditionally there are 3 subtypes of Delirium

-Hyperactive- 25% of cases, easy to recognize

-Hypoactive-50% of cases; usually missed/under recognized

-Mixed-25% of cases

More recently 2 additional variants have been described:

“Catatonic variant”, an extreme form of hypoactive type.

“Excited variant” an extreme form of hyperactive delirium usually associated with abuse of sympathomimetic drugs.

RISK FACTORS FOR DEVELOPMENT OF DELIRIUM

- Categorized into **PREDISPOSING** and **PRECIPITATING** factors.
- PREDISPOSING factors are usually inherent/intrinsic to the patient/resident
- PRECIPITATING factors are usually extrinsic

**Delirium will develop when the aggregate of these factors crosses a critical threshold.....

** More the predisposing factors mean less precipitating factors are required the tip the patient/resident over.

RISK FACTORS FOR DEVELOPMENT OF DELIRIUM

- PREDISPOSING FACTORS INCLUDE

- Advanced age
- Dementia/Mild cog impairment
- Poor vision/hearing
- Impairment in ADLs
- Multimorbidity

Joining forces against Delirium-From Organ System Care to Whole Human Care. N Engl J Med 2020;382(6) 499-501

Hazzard's Geriatric Medicine and Gerontology 6th Edition. Chapter on Delirium.

RISK FACTORS FOR DEVELOPMENT OF DELIRIUM

- PREDISPOSING FACTORS INCLUDE [continued]

- Chronic Kidney disease

- Malnutrition

- Male gender

- Alcohol abuse

- Electrolyte anomalies

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Hazzard's Geriatric Medicine and Gerontology 6th Edition. Chapter on Delirium.

RISK FACTORS FOR DEVELOPMENT OF DELIRIUM

- PRECIPITATING FACTORS INCLUDE

- Medications [Hypnosedatives, anticholinergics, opioids, etc etc].

- Urinary/fecal disorders [retention/"cystocerebral syndrome" & impaction].

- Anemia.

- Anesthesia [route doesn't matter, total dose does!!].

- Surgery [Incidence rates: 50% post hip Fx repair, AAA, CABG and 15% post elective non cardiac surgery].

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RISK FACTORS FOR DEVELOPMENT OF DELIRIUM

- PRECIPITATING FACTORS INCLUDE [continued]

- Uncontrolled pain.

- Bedrest/use of physical restraints.

- Use of indwelling devices.

- Acute exacerbation of chronic illness [COPD exa/resp failure].

- Acute illness/infections [MI, ICH, Stroke, Diverticulitis, UTI, Cholecystitis, etc].

- Lack of drugs/withdrawal

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RISK FACTORS FOR DEVELOPMENT OF DELIRIUM

- Pneumonic to help remember common causes of Delirium:

- D**.....Drugs
- E**.....Electrolyte disturbances
- L**.....Lack of drugs
- I**.....Infection
- R**.....Reduced sensory input
- I**.....Intracranial
- U**.....Urinary/fecal
- M**.....Myocardial/pulmonary.

Geriatric review syllabus 9th Edition

Delirium in Hospitalized Older Adults N Eng J Med 2017;377:456-1466

RECOGNIZING/DIAGNOSING DELIRIUM

- Tools have been developed that help with the diagnosis of Delirium.
- The most validated is the ***CAM [Confusion Assessment Method]*** first published in 1990 and translated into 19 languages and counting.....
- Sensitivity of 94-100% and Specificity of 90-95%
- Has a good interrater reliability

Confusion Assessment Method: A new method for detection of delirium Ann Intern Med. 1990;113(12):941-948.

RECOGNIZING/DIAGNOSING DELIRIUM

- The CAM has 4 components

Feature 1: Acute Onset or Fluctuating Course [regards mental status]

Feature 2: Inattention [difficulty focusing, counting backwards, etc]

Feature 3: Disorganized thinking [Incoherent, rambling, illogical ideas]

Feature 4: Altered Level of consciousness [Alert, vigilant, lethargic, stuporous, comatose, uncertain]

DIAGNOSIS OF DELIRIUM : **1 AND 2** with **3 or 4**

Confusion Assessment Method: A new method for detection of delirium Ann Intern Med. 1990;113(12):941-948.

RECOGNIZING/DIAGNOSING DELIRIUM

- Facts about the CAM...

-It has several forms:

3D-CAM [takes about 3 mins to complete]; good sensitivity/specificity.

CAM-ICU [used for non verbal/ICU patients].

B-CAM [used for verbal/ED patients].

CAM-S [recently developed to assess severity of delirium and some important clinical outcomes].

FAM-CAM [adapted for use in the home setting; lower sensitivity].

Confusion Assessment Method: A new method for detection of delirium *Ann Intern Med.* 1990;113(12):941-948.

CAM-S: development and validation of a new scoring system for delirium severity in 2 cohorts. *Ann Intern Med.* 2014;160(8):526–533.

RECOGNIZING/DIAGNOSING DELIRIUM

- Other screening tools:

4AT [Brief, easy to administer, sensitivity of 89.7% specificity 84.1%]

Nu-DESC [Nursing Delirium Symptoms checklist; low sensitivity of 72% and specificity 80%; limitation: potential for over emphasis on hyperactive delirium and under diagnosing hypoactive delirium]

mRASS [low sensitivity 64-70%]

***Delirium Observation scale is being developed for use in NHs but yet to be validated.

Delirium in Older Persons: Advances in Diagnosis and Treatment JAMA 2017;318(12):1161-1174

RECOGNIZING/DIAGNOSING DELIRIUM

- Other potential diagnostic tools:

-EEG:

Helps in differentiating non-convulsive status epilepticus from Delirium. May be reasonable to consider EEG if

1. Hx of seizures/TBI/Stroke.
2. On meds that lower the seizure threshold eg Tramadol, Buspar, Fluoroquinolones.
3. Clinical signs that suggest a seizure.

****Biomarkers:*

Studies looking into the effectiveness of biomarkers [neurotransmitter based, metabolic, inflammatory, neurodegenerative] have been done. Unfortunately, none ready for prime time/clinical use.

DIAGNOSING DELIRIUM

- ***We should therefore probably screen for delirium if our residents demonstrate:***

- Confused speech/thoughts.

- Easy distraction during conversations/tasks.

- New difficulty focusing/following conversations they normally would.

- New aggression/restlessness/somnolence.

- Getting in and out of confused periods.

PRACTICAL TREATMENT STRATEGIES

- Most effective approach is **TO PREVENT** the development of Delirium.
- Once present/established, Delirium will run its course.....
- Multiple studies have looked at Delirium prevention but have focused more in the acute care/hospital setting.
- These studies have emphasized **Multicomponent Nonpharmacologic Interventions.**

Delirium in Older Persons: Advances in Diagnosis and Treatment JAMA 2017;318(12):1161-1174

SOME EVIDENCE BASED STRATEGIES TO PREVENT DELIRIUM.

- **In Delirium, prevention is the best antidote.**
- Please see section under nonpharmacologic management of Delirium for strategies as outlined in points 1 through 10.

SOME EVIDENCE BASED STRATEGIES TO PREVENT DELIRIUM.

- Approaches that don't work to prevent Delirium.

....prophylactic use of antipsychotics.

.....prophylactic use of anticholinergics.

***some literature suggests Ramelteon *may* work in this regard. No conclusive evidence.

AGS Abstracted Clinical Practice Guidelines for Postoperative Delirium in Older Adults J Am Geriatr Soc 63:142-150, 2015.

Antipsychotic Medications for Prevention and Treatment of Delirium in Hospitalized Adults: A Systematic Review and Meta-Analysis. J Am Geriatr Soc 64:705-714, 2016.

TREATING DELIRIUM

- Majority the studies that have looked at this have been in the ACUTE/HOSPITAL setting.
- Two potential approaches to addressing Delirium are:
 - Non pharmacologic measures
 - Pharmacologic intervention.

The general consensus is to emphasize use of a **multi component non pharmacologic approach for geriatric patients** unless alcohol withdrawal is the etiology for the delirium.

TREATING DELIRIUM

- A Multicomponent non pharmacologic approach entails addressing the following:
 1. Early mobilization with PT/OT [esp if post op in the skilled wing].
 2. Ensuring good pain control [esp of post op/fall with injuries].
 3. Ensuring frequent re orientation with use of reminders [clocks, calendars, TV, notes, staff].
 4. Ensuring minimal interruptions to sleep at night.
 5. Ensuring residents have their corrective lens on and hearing aids in all the times [if practicable] especially during the daytime.

TREATING DELIRIUM/MULTICOMPONENT NONPHARM APPROACH...continued.

6. Paying attention to hydration/intake.
7. Paying attention to bowel movements [avoiding constipation esp if on opioid pain medications post op].
8. Paying attention to oxygenation if needing oxygen for respiratory failure.
9. Paying attention to medication use/flagging potential delirium precipitation medications for redress by the team.

AGS Abstracted Clinical Practice Guidelines for Postoperative Delirium in Older Adults J Am Geriatr Soc 63:142-150, 2015.

TREATING DELIRIUM/MULTICOMPONENT NONPHARM APPROACH....continued.

10. Encouraging the presence of and involvement of family members in the care of the resident.

11. Considering moving patients with delirium to rooms closer to the nurses' station to increase supervision.

** A pilot in NH adapting "HELP using CNAs by Boockvar & Colleagues showed that this validated program was feasible in the NH setting.

Delirium in the elderly. Psychiatr Clin N Am 41 (2018)

An Adapted Hospital Elder Life Program to Prevent Delirium and Reduce Complications of Acute illness in Long Term Care Delivered by Certified Nursing Assistants J Am Geriatr Soc 2016 64(5):1108-13

TREATING DELIRIUM

- For a Multi component non pharmacologic approach to work:

Nursing homes/Health care Institutions must have a commitment to educate staff about recognizing Delirium and effectively implementing the components previously discussed.

There has to be effective communication across different disciplines...MD, RN, Pham. D, CNA, PT/OT/SLP.

AGS Abstracted Clinical Practice Guidelines for Postoperative Delirium in Older Adults J Am Geriatr Soc 63:142-150, 2015.

TREATING DELIRIUM

- Pharmacologic approach.

Multiple papers/literature highlight using this approach as 2nd line.

Pharmacologic agents do NOT TREAT Delirium.

Black box warning on multiple pharmacologic agents for increased risk of cerebrovascular/cardiovascular events with their use in residents with Dementia.

Agents typically used are the typical and atypical antipsychotic medications.

Antipsychotic Medications for Prevention and Treatment of Delirium in Hospitalized Adults: A Systematic Review and Meta-Analysis. *J Am Geriatr Soc* 64:705-714, 2016.

Efficacy and Tolerability of Atypical Antipsychotics in the Treatment of Delirium: A systematic review of Literature. *Psychosomatics* 2019;60 :18-26.

TREATING DELIRIUM/PHARMACOLOGIC APPROACH

- Consideration for use of medications for Delirium may be necessary if the resident is *“severely agitated” AND “threatening substantial harm to self and/or others”*.
- Even so, “lowest effective dose” for the “shortest possible duration” should be used.
- ***Before using medications, nonpharmacologic measures should have been tried FIRST and should be unsuccessful or not possible to implement.***

TREATING DELIRIUM/PHARMACOLOGIC APPROACH.

- Commonly used agents are Haldol [typical antipsychotic/1st generation], Quetiapine, Olanzapine, Risperidone, Ziprasidone [atypical antipsychotics/2nd generation].
- The 2nd generation agents may be an option for patients at risk for extra pyramidal side effects [Parkinson's dx, Dementia with Lewy body] or with Haldol Intolerance.

Efficacy and Tolerability of Atypical Antipsychotics in the Treatment of Delirium: A systematic review of Literature. *Psychosomatics* 2019;60 :18-26.

AGS Abstracted Clinical Practice Guidelines for Postoperative Delirium in Older Adults *J Am Geriatr Soc* 63:142-150, 2015.

TREATING DELIRIUM/PHARMACOLOGIC APPROACH.

- Benzodiazepines should be ideally reserved for ONLY ALCOHOL WITHDRAWAL RELATED DELIRIUM.
- Current guidelines ***recommend against*** giving an antipsychotic or benzodiazepine to residents with hypoactive delirium or who are not agitated.

AGS Abstracted Clinical Practice Guidelines for Postoperative Delirium in Older Adults J Am Geriatr Soc 63:142-150, 2015.

TREATING DELIRIUM-SPECIAL CONSIDERATION

- HOSPICE PATIENTS:

In residents on hospice with mild to moderately severe delirium, use of a non-pharmacologic approach compared with antipsychotics [Haldol, Risperidone] may be a probably better approach as suggested by Meera R Agar et al in the study below.

Efficacy of Oral Risperidone, Haloperidol or Placebo for Symptoms of Delirium Among Patients in Palliative Care, A Randomized Clinical Trial.

JAMA Intern Med. 2017;177(1)34-42

CHALLENGES/FUTURE RESEARCH

- The apparent lack of effective “pharmacologic treatment” for Delirium.
- Residents with hypoactive delirium may be missed and may not be able to fully articulate complaints/concerns.
- Current models for non-pharmacologic interventions may be difficult to implement [cost/capital wise and human resource].
- Future research should probably focus on isolating biomarker[s] that can be targeted to shorten/prevent or better risk stratify patients.

CONCLUSION

- Delirium is costly to the US Healthcare system and has a complex pathophysiology.
- Vigilance is required to diagnosis this medical condition.
- There are multiple validated tools for diagnosis.
- Effective preventative strategies have been proposed.
- Management is classified into nonpharmacologic and pharmacologic with a preference for the non pharmacologic approach.
- Future research is need to further advance the pharmacologic care of patients with Delirium.