Therapeutic Effects of Intranasal Insulin Aspart on Cognitive Function in Post-Operative Delirium

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Disclosure

• I have no actual or potential conflict of interest in relation to this program

Objectives

• Define delirium and discuss possible complications
• Discuss current delirium treatment recommendations and the potential benefit of intranasal insulin to improve cognitive function
• Describe the purpose and methodology of this research project
• Communicate the current results and future directions of this study
Background

• Delirium is defined as a change in cognition characterized by an acute onset of inattention
  – Not due to dementia
  – Direct physiologic consequence of a general medical condition, an intoxicating substance, medication use, or more than one cause

• There are multiple types of delirium and different forms of presentation
  – Hyperactive form
  – Hypoactive form
  – Mixed

American Psychiatric Association (2013). DSM-V.

Consequences of Delirium

• One study found that a single episode of delirium resulted in:
  – A doubled odds ratio for death
  – An increase in the risk of admission
  – An increase in dementia
  – Increased length of mechanical ventilation
  – Increase in total length of ICU and hospital stay

• Cost:
  – Single episode:
    • 18% increase in nursing costs
    • 22% increase in total costs
  – The estimated annual cost of delirium in the US is estimated to be between 38 and 152 billion dollars.


Current Treatment Recommendations

• Atypical antipsychotics may reduce the duration of delirium in adult ICU patients

• There is no published evidence that treatment with haloperidol reduces the duration of delirium in adult ICU patients

• We do not recommend administering rivastigmine to reduce the duration of delirium in ICU patients

• In adult ICU patients with delirium unrelated to alcohol or benzodiazepine withdrawal, continuous IV infusions of dexmedetomidine rather than benzodiazepine infusions be administered for sedation to reduce the duration of delirium in these patients

Is Delirium Diabetes Type III?

- CNS insulin resistance
  - Impaired brain insulin signaling may be the cause of cognitive decline (Alzheimer’s disease)
- Circulating insulin accesses the CNS receptors to exert pivotal functions
  - Insulin affects distinct cognitive processes by triggering the formation of psychological memory content
  - Enhancing CNS insulin action has been shown to improve memory functions in animals as well as in humans
- Options to overcome central nervous insulin resistance by pharmacologic interventions
  - Intranasal insulin is an effective means of introducing insulin to the brain while minimizing the systemic effects

Study Objective

- Evaluate the use of intranasal insulin aspart on cognitive function in patients with postoperative delirium

Study Design & Outcomes

- Randomized, Double Blind, Placebo Controlled Trial
  - 40 IU insulin aspart (0.4 mL) intranasally as a single dose
  - 0.4 mL 0.9% sodium chloride intranasally as a single dose
- Primary outcome measure
  - Duration of Confusion Assessment Method-Intensive Care Unit (CAM-ICU) positive delirium
- Secondary outcome measures
Surveys and Questionnaires

- **Telephone Interview for Cognitive Impairment (TICS)**
  - The TICS assessment has been standardized and validated for use with adults, ages 60 to 98 years.

- **Confusion Assessment Method-Intensive Care Unit (CAM-ICU)**
  - The most widely used tool for identifying delirium at the bedside has been the Confusion Assessment Method (CAM).
  - CAM-ICU is an adapted screening tool for use in nonverbal patients and has been validated in 2 major investigations for its specificity and reliability in determining delirium.

- **Daily Patient Survey (DPS)**
  - “Are you experiencing any nasal irritation?”
  - “Are you experiencing anything new, different, or unusual today?”

**TICS**

- The TICS Total score can be interpreted by means of four qualitative impairment ranges:
  - Nonimpaired
  - Ambiguous
  - Mildly Impaired
  - Moderately to Severely Impaired

**TICS Results**

- **Suggested Qualitative Interpretive Ranges for TICS Total Score Range**
  - 20-41 Nonimpaired
  - 22-29 Mildly impaired
  - ≤20 Moderately to Severely Impaired
Patient Inclusion Criteria

- Men and women aged 18 to 85
- Completion of TICS prior to surgery
  - Without evidence of moderately to severely impaired cognitive function
- Signed informed consent
- Development of post-operative delirium as measured by the CAM-ICU assessment
- Exclusive use of either total intravenous anesthesia (TIVA) or inhalation anesthesia

Study Design

1. Patient identification & Informed consent
2. Baseline cognitive testing (TICS) & inclusion criteria assessment
3. Post-operative CAM-ICU positive delirium occurs & Patient randomization
4. Medication Administration
5. CAM-ICU Assessments, Glucose, Patient survey assessing nasal irritation
6. Thirty day follow-up assessment (TICS)
Study Progress

- Patients Screened: N=236
- Informed Consent Provided: N=54
- Development of CAM-ICU Positive Post-Operative Delirium: N=5

Preliminary Data

- Trend towards decreased duration of delirium with treatment group “A” (n=2) compared to treatment group “B” (n=3)
  - The study team is evaluating ways to increase recruitment and capture more participants.
  - All data will be analyzed by a statistician.

Self-Assessment Questions
Question 1

• Which of the following characteristics of delirium differentiates it from dementia (major neurocognitive disorder)?

A. Inattention
B. Acute onset
C. Memory deficit
D. Disorientation

Question 2

• Based on the current recommendations, which option below is preferred as the first-line treatment for an adult ICU patient with delirium?

A. Lorazepam 1 mg PO
B. Haloperidol 0.5 mg PO
C. Rivastigmine 1.5 mg PO
D. Quetiapine 25 mg PO

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