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Late Onset Paradoxical Effect of Zolpidem after Anoxic Brain Injury: A Pediatric Case Report

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Background

Acquired Brain Injury is defined as an insult to the brain affecting its structure or function, that subsequently results in impairments of communication, cognition, sensorimotor function, behavior and consciousness. Anoxic brain injuries can be more disabling when compared to traumatic brain injury with more severe deficits, longer recovery times and prolonged rehabilitation course .[3]

Common causes of anoxic brain injury in children include[3]:

- Drowning
- Carbon Monoxide Poisoning
- Status Epilepticus and Status Asthmaticus
- Cardiac Arrest

With an increased time of hypoxia to neurons, there is an influx of calcium and efflux of potassium triggering irreversible apoptosis of neurons.

The Revised coma recovery scale (CRS-R), formerly known as JFK Coma Recovery scale, is the gold standard behavioral assessment used in disorders of consciousness.[4]
There are a paucity of reports of zolpidem as a neurostimulant for disorders of consciousness in children.

Case Description

This is a 16 year old boy with no prior medical conditions who sustained an unwitnessed prolonged pulseless cardiopulmonary arrest requiring multiple defibrillations and several doses of epinephrine before he converted to ventricular tachycardia. His cardiac and genetic workup were negative . His brain magnetic resonance imaging (MRI) revealed diffuse ischemic injury to the temporal, parietal and occipital regions and the basal ganglia. His hospital course was complicated by dysautonomia requiring clonidine, propranolol, and lorazepam and reducing stimuli, hypertonicity and agitation requiring gabapentin and baclofen, botulinum toxin injections, and serial casting, impaired sleep/wake cycles requiring melatonin and zolpidem, and decreased level of arousal
During his six week inpatient rehabilitation admission, he trialed multiple neuro- stimulants including amantadine, bromocriptine and zolpidem, but unfortunately, he did not emerge from a persistent unresponsive wakefulness state. Shortly after discharge, his parents noticed a significant change in his level of alertness, command following, and communication after taking zolpidem. During a follow up appointment, zolpidem administration confirmed improved CRS- R score from 6 to 14. This demonstrated improvement for a persistent state of unresponsive wakefulness state.

Discussion

Zolpidem, most known as a hypnotic sleep agent, selectively stimulates the Ω-1 receptors on the α1 and α5 subunits of a gamma aminobutyric acid (GABA) A receptor in the brain.[5] There is a high concentration of these receptors in the basal ganglia and striatum to the thalamus and motor cortices (see Figure 1). Moreover, it is hypothesized that the paradoxical effect of zolpidem in neurologic disorders is related to the agonism at GABA receptors in these locations. This may further lead to increased cerebral perfusion seen on single photon electroscopic computed topography.[2] Typically, there is a rather acute paradoxical effect contrarily to the delayed effect seen in this young patient.[1] The effect lasts for one to four hours due to the short half life of zolpidem.[1]

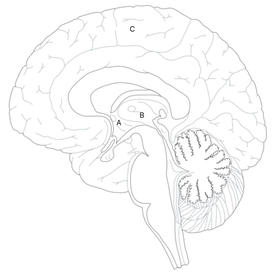

Figure 3: Mid-sagittal view of the brain demonstrating area of high concentration of GABA receptors. (A) basal ganglia which overlies the thalamus (B) and the (C) Primary Motor Cortex

Conclusion

Zolpidem may have a paradoxical effect in the pediatric brain injury population even after extensive time since initial injury.

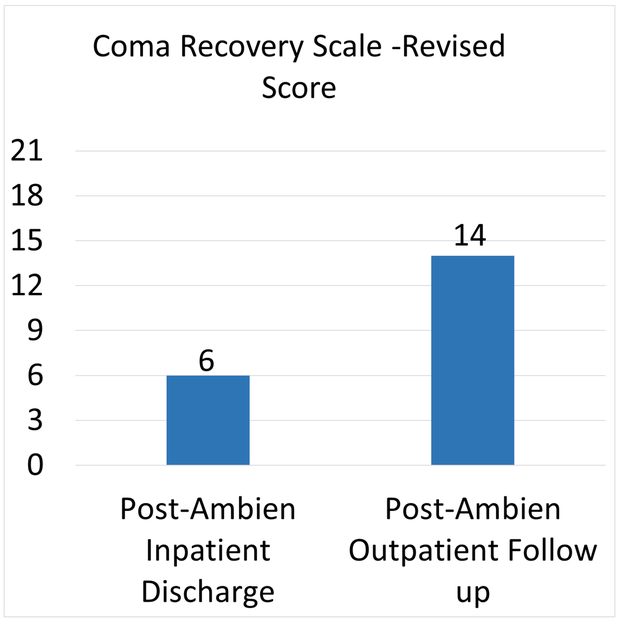

Figure 1: Change in Coma Recovery Scale-Revised score from discharge to score after the zolpidem trial in outpatient clinic.

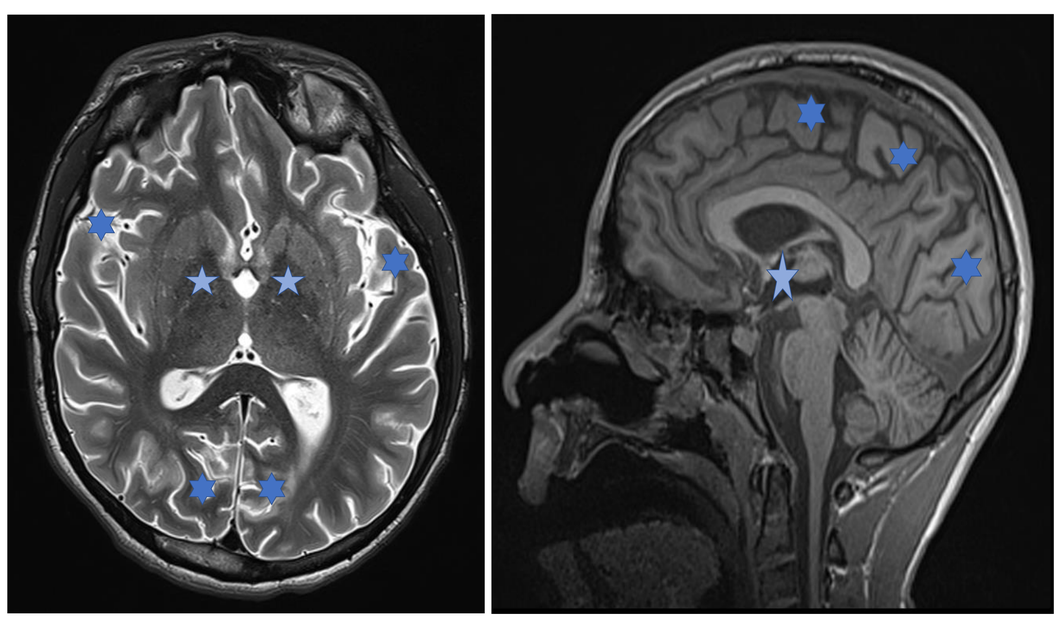

Figure 2: Patient's mid-sagittal T2 weighted magnetic response imaging with evidence of diffuse injury specifically basal ganglia, temporal, parietal and occipital lobes. ★ represents thalamus with basal ganglia overlying

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