Dravet Syndrome and Anesthetic Implications of Cannabidiol

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Introduction

Dravet Syndrome:
- Early, severe epileptic encephalopathy
- Mutation in neuronal sodium channel gene SCN1A
- Resistant to anti-epileptic medications
- Exacerbated by many treatments

Cannabidiol:
- An experimental cannabinoid anti-epileptic medication known to cause prolonged emergence

Case Presentation

- 6 year-old 20.3 kg male with Dravet Syndrome and obstructive sleep apnea presents for laparoscopic gastric tube placement
- Baseline daily tonic-clonic seizures, with weekly cluster seizures lasting 24-48 hours
- Medications: clobasam, stiripentol, and a vagal nerve stimulator
- Frequency of seizures caused recent weight loss
- Requires the gastric tube to optimize nutrition during periods of increased seizure activity
- Patient in status epilepticus on arrival to pre-op holding, having seizures every 20 minutes for the past 24 hours
- 20 mg of rectal diazepam the night before was ineffective
- 8 mg of midazolam IV was incrementally administered with no further seizures for the next 45 min
- Decision made to proceed based on medically intractable nature of his seizures, and inability to further optimize pt.
- Potential for prolonged emergence from the interaction of cannabidiol with volatile and IV anesthetics - a previous patient on the same regimen required 10 hours for emergence.

- BIS monitor used to assess anesthetic depth and minimize anesthetic dosage
- IV induction with propofol 2 mg/kg, fentanyl 1 mcg/kg, and midazolam 2 mg
- Anesthesia maintained with 4-5% desflurane
- Pt extubated awake at the end of the procedure and taken to the PACU
- Within 5 minutes, eyes were open and pt responded to verbal command
- Pt admitted to the PICU for monitoring and discharged home on post-operative day 1 without further seizures

Discussion

- Cannabidiol: an experimental cannabinoid shown to inhibit epileptiform activity in vitro and seizure severity in vivo
- Mouse models have shown that cannabinoids control cellular respiration and energy production
- Cannabinoids activate type 1 cannabinoid receptors on mice neuronal mitochondria
- Activation of these receptors decreases complex 1 function
- Decreased complex 1 function increases volatile anesthetic sensitivity and propofol sensitivity
- Use of BIS monitor and careful titration of short acting anesthetics helps avoid prolonged emergence
- Recreational marijuana and other cannabinoids may have similar anesthetic implications
- Myocardial depression and sedative-hypnotic effects are additive with those caused by inhaled anesthetics
- Recent legalization of marijuana in Colorado and Washington make understanding these interactions important to understand

References