

Treatment of Refractory Serotonin Syndrome with Dexmedetomidine

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Objectives: Dexmedetomidine, a centrally acting alpha-2-adrenergic agonist that inhibits norepinephrine and serotonin release, has gained popularity for its use for certain types of delirium and withdrawal. Herein, we describe a novel case of Dexmedetomidine use in the treatment of an adult patient with delirium due to serotonin syndrome. **Methods:** After unsuccessful treatment with Benzodiazepines, and Cyproheptadine, a patient was transferred to our institution with "refractory" serotonin syndrome. Upon arrival, the patient was confused, tremulous and minimally responsive to verbal stimuli, with unstable vital signs, and was started on a Dexmedetomidine infusion. **Results:** Within two hours of initiation, the patient's vital signs stabilized. Within 12 hours, mental status improved to baseline. **Conclusions:** Management of serotonin syndrome is based on cessation of the offending agent and supportive care. Dexmedetomidine has been shown to inhibit serotonin release in animal models. This case describes its successful adjunctive use in treating serotonin syndrome. *Journal of Nature and Science*, 1(2):e47, 2015.

Dexmedetomidine | Serotonin Syndrome | Case Report

Introduction

Dexmedetomidine is a centrally acting α -2 adrenergic agonist with both sedative and anxiolytic properties that inhibits the release of norepinephrine and serotonin²⁻⁴. It has been used in patients with delirium secondary to alcohol and substance abuse withdrawal¹. Evidence for the use of Dexmedetomidine in other causes of delirium is lacking. Herein is described a case of Dexmedetomidine use in the treatment of an adult patient with Serotonin Syndrome.

Case Report

A patient was transferred to our institution from an outside hospital after presenting 24 hours earlier with confusion, uncontrollable jerking movements, tachycardia, and hyperthermia. The patient's past medical history included depression, and osteoarthritis for which he was on Citalopram, Bupropion, Diphenhydramine, Fentanyl patch, Hydrocodone/Acetaminophen and Oxycodone/Acetaminophen.

Upon initial presentation, vital signs included an elevated blood pressure with systolic ranging from 160-188mmHg, regular heart rhythm with rate greater than 110 beats/minute, a temperature exceeding 101°F and pronounced jerking movements. The patient was diagnosed with serotonin syndrome by Neurology based on Hunter's Criteria, and received multiple doses of benzodiazepines (Lorazepam 8.5mg, Midazolam 2mg, Diazepam 10mg, Clonazepam 0.5mg, in total) and diphenhydramine 100mg (in total).

The jerking movements persisted and concern arose for the possibility of underlying seizure activity, and a Valproate load and infusion were given. However, the patient remained tremulous, delirious, hypertensive, tachycardic, and febrile. Cyproheptadine was started, as an initial dose of 12mg, followed by 2mg two hours later, and final 4mg dose four hours after that, with no symptom resolution. The patient was then transferred to our institution.

Upon arrival, the patient was still confused, agitated, and tremulous. Vitals revealed a blood pressure of 166/99 mmHg, heart rate of 110 beats/min, respiratory rate of 36 breaths/min. Dexmedetomidine 0.2mcg/kg/hr (no loading dose) was begun.

Within two hours of initiating the infusion the patient's vital signs improved (Figure 1). Heart rate decreased to 90 beats/min, blood pressure to 140mmHg systolic, and temperature to 99°F. Shortly thereafter, the agitation improved and the patient became alert, oriented and able to converse.

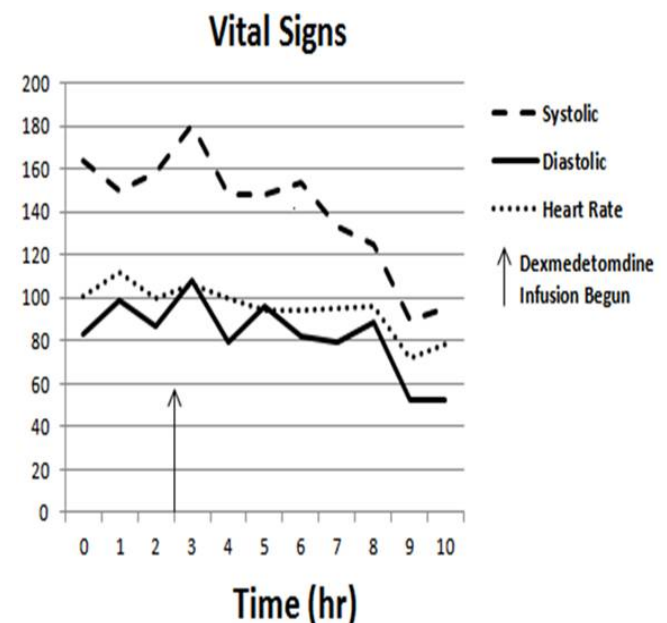


Figure 1. Vital signs before and after dexmedetomidine treatment

Discussion

Serotonin syndrome is an uncommon complication of therapy associated with many different of medications (monoamine oxidase inhibitors, analgesics, antibiotics, newer antidepressants, over the counter cold medications (dextromethorphan)⁵ and combinations of these different classes of medications. Selective serotonin-reuptake inhibitors are most commonly associated with this syndrome, while severe cases occur in combination with monoamine oxidase inhibitors.⁶ Serotonin syndrome is classically described as a clinical triad of mental status changes, autonomic hyperactivity (fevers, tachycardia, hyperreflexia, diaphoresis, diarrhea), and neuromuscular abnormalities (rigidity) which can be life threatening.⁵

Agonism of 5-HT_{1A} and 5-HT_{2A} receptors is believed to play a primary role in developing the syndrome. However, no single receptor has been implicated by itself, and the agonism or antagonism of different 5-HT receptors in concert likely contribute to development of serotonin toxicity.⁵⁻⁸ Other neurotransmitters also play a role. *N*-methyl-*D*-aspartate (NMDA), γ -aminobutyric acid (GABA), Noradrenaline (NA) and dopaminergic (DA) receptors also may play a role in this syndrome.^{5,6}

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Management is largely based on identifying and removing the offending agent, control of autonomic instability, and supportive care.⁵ It should be noted that even with discontinuation of the offending drug symptoms may persist due to extended half-lives of certain agents and their metabolites (ex. Fluoxetine).^{5,9} Benzodiazepines are a mainstay of therapy for mild Serotonin syndrome, and work by decreasing autonomic tone and anxiolysis.^{5,6,9} They have also shown survival benefit in animal models.⁹ Patients with moderate to severe serotonin syndrome may benefit from 5-HT_{2A} antagonists (i.e. Cyproheptadine) and most patients symptoms will abate within the first few doses.^{11,12} This data is based on case series, and randomized controlled trials are lacking. Nisijima et al. in 2003 evaluated outcomes comparing pre-treatment with diazepam and chlormethiazole compared to 5-HT_{2A} antagonists in rats. They found that rats treated with 5-HT_{2A} antagonists all survived. However, despite an improvement in

hyperthermia, most of those treated with diazepam and chlormethiazole died.¹⁰

With Dexmedetomidine, activation of the α_2 -adrenergic receptor mediates sedative (α_{2A}), cardiovascular (α_{2B}), dopaminergic neurotransmission, hypothermia and behavioral (α_{2C}) responses, leading to stimulation of parasympathetic outflow and inhibition of sympathetic outflow from the brainstem^{14,15} In addition to its approved use as a sedative, there is literature to support the use of Dexmedetomidine as an adjunct in treatment of alcohol and opioid withdrawal.

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