Use of Dexmedetomidine in a Patient Allergic to Clonidine Presenting for an Awake Craniotomy: A Case Report

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Abstract

Introduction: The use of dexmedetomidine with concurrent scalp block is increasingly being utilized as an effective and safe anesthetic approach for awake craniotomy (AC). Dexmedetomidine is an alpha-2 adrenergic receptor (α2-AR) agonist with dose-dependent sedative, analgesic, and anxiolytic properties while preserving respiratory function. The challenge with the use of dexmedetomidine arises when the patient in question has a clonidine allergy that is also an α2-AR agonist. Currently there aren't any published literature regarding the use of dexmedetomidine in a patient allergic to clonidine.

Case Presentation: A 48-year-old male with chronic obstructive pulmonary disease, obstructive sleep apnea, and body mass index of 54 with clonidine allergy presents for an AC. Given the goals of the surgery and patient comorbidities, we planned for monitored anesthesia care with intravenous (IV) dexmedetomidine, remifentanil, and propofol. We discussed the use of dexmedetomidine with the patient and the potential risk of allergic reaction given his allergy to clonidine. Patient understood the risk and consented to the anesthetic plan. AC was successfully performed with IV dexmedetomidine, remifentanil, and propofol.

Conclusion: Although both dexmedetomidine and clonidine have some functional similarities in terms of acting on the central and peripheral nervous system, there are marked differences between the two based on chemical structure, receptor affinity, and metabolism of the drug. This case highlights the successful use of dexmedetomidine in a patient with known allergy of rash to clonidine.

Introduction

Awake craniotomy (AC) with intraoperative brain mapping and monitoring of neurological function and cognitive performance has been shown to improve efficacy and safety of tumor resection. The primary aim of AC is to achieve maximum resection of tumors or epileptic foci while preserving brain function [1]. Relative contraindications for AC consist of anxiety disorder, poor neurological status, anticipated difficult airway, severe chronic obstructive pulmonary disease (COPD), obstructive sleep apnea (OSA), obesity, gastroesophageal reflux (GERD), and large tumor with midline shift [2]. Balancing relative contraindications with the potential benefit of AC present a challenge for the anesthesiologist. A multitude of tasks need to be accomplished by the anesthesiologist to avoid complications during an AC, including the maintenance of airway, analgesia, sedation, and management of hemodynamics. Therefore, it is critical that the anesthetic regimen for AC be individualized to the patient's comorbidities and the goals of the surgery.

There have been multiple publications demonstrating the successful use of dexmedetomidine in high-risk patients undergoing AC [2–5]. Dexmedetomidine is an alpha-2 adrenergic receptor (α2-AR) agonist with dose-dependent sedative, analgesic, and anxiolytic properties while preserving respiratory function.[6] Its actions make it an ideal anesthetic agent for an AC [5]. Concern with the use of dexmedetomidine arises when you encounter a patient with a documented allergy to clonidine, which is also an α2-AR agonist.

Currently there are no case reports or published work discussing the use or avoidance of dexmedetomidine in patients who are allergic to clonidine. In most situations, anesthesia providers would avoid dexmedetomidine in these patients to mitigate any potential adverse reaction, but in circumstances where dexmedetomidine can provide a major advantage to the anesthetic plan, the risk-benefit needs to be weighed.

The goals of this case report are to present a case where dexmedetomidine was successfully used in a patient with a reported allergy to clonidine and to explore the similarities and differences between clonidine and dexmedetomidine.

Written Health Insurance Portability and Accountability Act authorization has been obtained from the patient to publish this case report.

Case Presentation

We report a case of a super morbid obese 48-year-old male with a body mass index of 54, who presents for an AC for a 6cm lesion involving the left anterior temporal lobe, basal ganglia, inferior frontal lobe and the thalamus. Location of the cranial lesion incorporated sensorimotor and language areas. Therefore, during the resection phase of the surgery, along with neuromonitoring, patient would have to perform language and vocabulary tasks to optimize tumor resection and minimize neurological complications.

Patient's past medical history was significant for hemorrhagic stroke, hypertension, COPD on home inhalers, OSA, insulin dependent diabetes, and GERD. Due to the cranial lesion, patient was also experiencing seizures despite being on antiepileptics. Airway exam revealed Mallampati of 3, thick neck, and at least three fingerbreadth thyromental distance. Patient also had a documented allergy to clonidine and mentioned developing a rash while on clonidine.

Given the goals of the surgery and patient comorbidities, we planned for monitored anesthesia care with intravenous (IV) dexmedetomidine, remifentanil, and propofol. We researched the use of dexmedetomidine with clonidine allergy in PubMed and was unable to find any published literature regarding its use in a patient allergic to clonidine. We reached out to our institution's inpatient clinical pharmacist for guidance. Our clinical pharmacist confirmed the lack of published literature but did mention, based on experience, dexmedetomidine had been safely used in two prior patients who were also allergic to clonidine. With this information we discussed the use of dexmedetomidine with the patient and the potential risk of allergic reaction. Patient understood the risk and consented to the anesthetic plan.

Prior to taking the patient to the operating room, the patient had two peripheral IV access, was given a breathing treatment, 20mg of IV famotidine, 10mg of IV metoclopramide, and 4mg of IV ondansetron. Bilateral nares were prepped with neosynephrine in case nasopharyngeal airway would have to be used during the procedure for airway maintenance. Upon arrival to the operating room IV infusion of 0.4mcg/kg/hr of dexmedetomidine and 0.03mcg/kg/min of remifentanil was immediately started after

standard monitors (ECG, pulse oximetry, and noninvasive blood pressure cuff) and salter nasal cannula were placed. Given patient's history of diabetes and the need to check blood glucose throughout the case, hemorrhagic stroke, and hemodynamic effects of the IV anesthetic, radial arterial catheter was inserted in the operating room with 1% lidocaine local anesthetic. Video laryngoscopy, intubation equipment along with supraglottic airway, and emergency medications (epinephrine, diphenhydramine, levetiracetam, and lorazepam) were ready in the operating room.

During the 12-point scalp block and placement of urinary foley catheter increments of 5-10mg of propofol were given for patient comfort while maintaining a Richmond Agitation Sedation Score (RASS) of -1 to -2. Throughout the procedure, goal was to keep patient arousable so patient could communicate potential allergic symptoms. Prior to pinning of the head in the Mayfield, in addition to the increments of 5-10mg of propofol, propofol infusion was also started at a rate of 5ug/kg/min and titrated upward as tolerated to maintain target RASS. Patient tolerated the scalp block, positioning, and pinning well.

During the opening phase of the dura, patient tolerated upward of 0.7mcg/kg/hr of dexmedetomidine, 0.03 mcg/kg/min of remifentanil, and 12mcg/kg/min of propofol. Any increase in the propofol dosing led to airway obstruction. All IV infusions were paused once the dura was opened for the awake phase of the AC. Patient successfully underwent testing of language, memory, and motor during mapping and resection. Once resection was completed, dexmedetomidine and remifentanil infusions were reinitiated at 0.4mcg/kg/hr and 0.3mcg/kg/min, respectively, for the post-awake phase.

Throughout the procedure, patient's oxygenation was maintained with a salter nasal cannula without the need of oral or nasopharyngeal airway. Patient remained hemodynamically stable throughout the case without the need of any vasopressors. Toward the end of the post-awake phase, patient became hypertensive, which was resolved with IV labetalol. After the surgery concluded, patient was transferred to the post-anesthesia care unit for recovery and transferred to the intensive care unit for monitoring. Patient was discharged on post-operative day 6.

Discussion

This case report highlights the successful use of dexmedetomidine in a patient with history of an adverse reaction of rash with oral clonidine. Currently there are no publications discussing the use of dexmedetomidine in a patient with history of clonidine rash allergy.

Dexmedetomidine is a full agonist at the α2-AR and it selectively binds to presynaptic α2-AR located in the locus coeruleus of the brain stem for sedative action. It inhibits the release of norepinephrine from synaptic vesicles, which leads to an inhibition of post-synaptic activation of adrenoreceptors, which inhibit sympathetic activity, leading to sedation and anxiolysis. Its analgesic effect is mediated by binding to α2-AR in the spinal cord. Dexmedetomidine is 8-10 times more selective for the α2-AR than clonidine. The improved specificity for the α2-AR, especially for the 2A subtype, may make it a more effective sedative than clonidine. Clonidine is a partial agonist at the α2-AR. It stimulates central alpha receptors in the vasomotor center of the medulla oblongata and hypothalamus, which decreases the

efferent sympathetic tone to the heart, kidneys, and peripheral vasculature with concomitant increase in vagal activity [6].

Though both dexmedetomidine and clonidine work on α2-AR, there are noteworthy differences between the two (Table 1). Dexmedetomidine is an imidazole derivative, while clonidine is an imidazoline derivative as seen in Figure 1 [7–8]. When chemically comparing the two drugs, the Tanimoto coefficient, based on atom pairs is 0.180723 and maximum common substructure is 0.2609 [9]. Tanimoto coefficient is a similarity measure score comparing two chemical structures by means of their chemical fingerprint. Its score ranges of 0 to 1 with values closer to 1, indicating greater similarity between two compounds [10]. Based on the Tanimoto coefficient, the two drugs are not similar. Dexmedetomidine is water-soluble, while clonidine is insoluble in water. Majority of dexmedetomidine is metabolized in the liver, while less than 50% of clonidine is metabolized in the liver [7–8].

Although both dexmedetomidine and clonidine have some functional similarities in terms of acting on the central and peripheral nervous system, there are marked differences between the two based on chemical structure, receptor affinity, and metabolism of the drug. In this case presentation we are not concluding that it is clearly safe to use dexmedetomidine in patients with clonidine allergy; we would need more information and research to state that. But until we do have more research and publications, we want to highlight the importance of weighing the risk and benefit of the use of dexmedetomidine in situations where the medication's benefit may outweigh its risk. As anesthesiologist we often encounter patient allergies that are not confirmed with testing but documented, therefore, we have to acknowledge the documented facts. Our patient's reported reaction to clonidine was a type IV hypersensitivity reaction which is not life threatening and is often resolved with topical creams and avoidance of trigger. The advantage of using dexmedetomidine in the anesthetic plan allowed for a successful AC with sedation, anxiolysis, analgesia, while preserving patient's respiratory function.

GLOSSARY

AC = awake craniotomy

COPD = chronic obstructive pulmonary disease

OSA = obstructive sleep apnea

α2-AR = alpha-2 adrenergic receptor

GERD = gastroesophageal reflux

IV = intravenous

RASS = Richmond Agitation Sedation Score

Declarations

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Consent to Publish: Written Consent was obtained from patient to publish the case.

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Table

TABLE 1: COMPARISON OF DEXMEDETOMIDINE AND CLONIDINE

	DEXMEDETOMIDINE	CLONIDINE
Structure	Imidazole Derivative	Imidazoline Derivative
Molecular Weight (gram/mole)	200.2	230.09
pKa	7.1	8.05
Metabolism	Hepatic	<50% Hepatic
Excretion	95% Urine, 4% Feces	50% Urine, 20% Feces
Solubility in water	Soluble	Insoluble
Elimination Half Life (hours)	2	8
Protein Binding	94%	50%
Ratio of α2: α1 Receptor Binding	220:1	1620:1
Function at α2 Receptor	Full Agonist	Partial Agonist

Figures

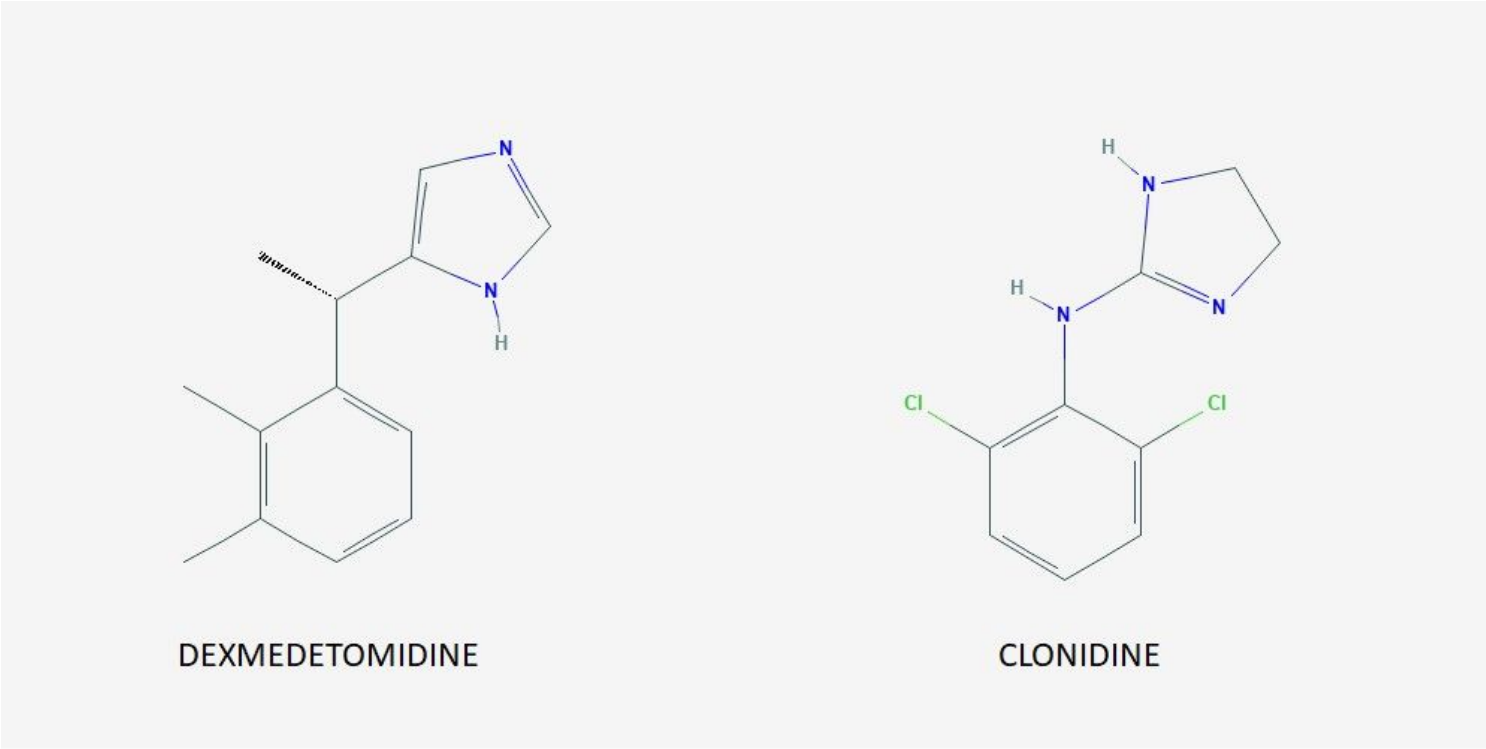

Figure 1

Chemical structure of dexmedetomidine and clonidine (PubChem Database)

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