Amphetamine (Adderall) and venlafaxine (Effexor) Drug Interaction with Dexmedetomidine

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Background: Dexmedetomidine (DEX), a selective α2-adrenoreceptor agonist is commonly used to provide sedation in the ICU. Drug-induced sleep endoscopy (DISE) is an extremely useful tool for assessing the dynamic airway in an asleep patient with obstructive sleep apnea (OSA). DEX provides an optimal agent for sleep endoscopies in this patient population given its reliability as a sedative agent most closely mimicking REM sleep with negligible respiratory depression. Most common adverse effects of dexmedetomidine infusions are bradycardia and hypotension.

Case presentation: We present an intriguing case of a 68-year-old male with a history of OSA status-post right-sided hypoglossal nerve stimulator, chronic neck pain, headaches, depression and adult-ADHD who underwent two DISEs requiring DEX at rates as high as 3 mcg/kg/hr along with 10mg incremental boluses of propofol to successfully induce sleep. Once the patient was finally asleep he was noted to be hypotensive and bradycardic unresponsive to ephedrine requiring a combination of fluids, glycopyrrolate and phenylephrine to support his blood pressure. His home medications included dextroamphetamine/amphetamine (Aderall) 20mg thrice daily, venlafaxine (effexor) 150mg twice daily, and buprenorphine (subutex) 4-8mg SL thrice weekly as needed.

Discussion: The patient had complex neuropharmacology at play. Amphetamines increase the activity of dopamine and norepinephrine in the brain but may also affect serotonin, histamine and other neuropeptides. Venlafaxine is a commonly used antidepressant that is a selective serotonin-norepinephrine reuptake inhibitor, which at high doses may also inhibit dopamine uptake and can potentially increase the activity of Adderall.

On review of the literature, there are no reports of drug interactions between psychopharmacologic drugs (including SNRIs and therapeutic amphetamines) with dexmedetomidine. We theorize that the patient's chronically altered neurobiology may help explain the patient's apparent resistance to dexmedetomidine. In terms of drug safety, atipamezole, a reversal agent for both the sedative and sympatholytic properties of dexmedetomidine, is currently only approved for use in veterinary medicine.

Drug-drug interaction between amphetamines and DEX have not been previously reported. Plausible methods of amphetamine interaction with DEX could involve interaction at the alpha-2 receptor. Amphetamines may modulate the re-uptake of norepinephrine and thus decrease the effect of DEX as reported in a rat model (1). The interaction between amphetamines and clonidine has been reported to be caused by inhibition of binding of clonidine to the alpha-2 receptor (2). It may be likely that inhibition of DEX by amphetamines occurs at the membrane level.

Furthermore, a less known fact about dexmedetomidine is its interaction with the cytochrome P450 enzymes, including inhibition of CYP2D6 which is involved in the metabolism of amphetamines. While this may not play a role in brief procedural sedation as in our patient, it merits further investigation in the intensive care unit population where prolonged infusions of dexmedetomidine are common.

Conclusion: Dexmedetomidine is increasingly used in the operating room, out-of-OR environments, and intensive care units but its interactions with other neurotransmitter altering therapeutics remain unknown.

References:

1) Neuropharmacology (2004) 29, 1282-1293
2) Gen. Pharmaco. (1989) 20(3), 351-358