Use of Dexmedetomidine as a prophylactic rather than treatment for Alcohol withdrawal syndrome – A case series

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Abstract
We report a case series of continuous use dexmedetomidine intraoperatively in three patients with known history of chronic alcoholism undergoing surgery under general anaesthesia to prevent the symptoms of alcohol withdrawal syndrome post operatively. Although used as a treatment drug, we used dexmedetomidine as a prophylactic measure to prevent alcohol withdrawal syndrome thus opening its path for further studies enlighting its role in pre-emptive anesthesia.

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1. Introduction

Alcohol is one of the most widely abused substances across the globe. It causes imbalance in the GABAergic and Glutaminergic system in the brain. Alcohol withdrawal syndrome (AWS) is principally a hyperexcitable response of the central nervous system which occurs due to abstinence from alcohol after a prolonged duration of its use. It is characterized by autonomic hyperactivity, hallucinations, and seizures, termed alcohol withdrawal delirium or delirium tremens when accompanied by a persistent altered sensorium and severe hyperadrenergic state. (Rayner et al 2012) Excess alcohol consumption increases the chances of opioid toxicity because both of them share the same pharmacokinetic (hepatic MEOS) pathway for their disposal. (Cushman et al 1987) Various pharmacological modalities have been utilised to relieve the symptoms of AWS in postoperative period. These include benzodiazepines most commonly (Amato et al 2010), anticonvulsants, propofol, clonidine and propanolol. But high doses are required in monotherapy leading to increased risk of aspiration and subsequently intubation. Dexmedetomidine is an alpha2 agonist which has sympatholytic, analgesic, antianxiety and sedative properties. (Bajwa et al 2011) We report a case series showing the efficacy of dexmedetomidine in preventing AWS if used intraoperatively and continued postoperatively for 24 hours duration.

2. Case Series

In this study, 3 patients posted for surgery were included. They were between the age group of 60-65 and known alcoholic. They were premedicated and induced with standard protocols. A loading dose of dexmedetomidine was given and anaesthesia was maintained with 50:50 O2:N20 mixture at fio2 0.4 with desflurane along with maintenance dose of dexmedetomidine for amnesia and analgesia. Morphine was given at a dose of 0.05 mg/kg. During the intraoperative period hemodynamics were stable and there was no
further opioid requirement. At the end of the surgery patients were reversed with neostigmine and glycopyrrolate and extubated when they started generating adequate tidal volume and shifted to Post Anaesthesia Care Unit. The patients were comfortable with no signs of AWS.

3. Discussion

Alcohol dependence is a major public health problem whose withdrawal results in severe signs and symptoms which can sometimes prove fatal. It occurs in approximately 8% of hospital admissions, some of which require mechanical ventilation. (Sarff et al 2010) Ethanol binds to post-synaptic GABA_A receptors, enhancing their inhibitory effect. The resulting chronic excitatory suppression, coupled with a direct inhibition of excitatory glutamate N-methyl-D-aspartate (NMDA) receptors, leads to anxiolytic and sedative effect. (Sarff et al 2010) When the inhibitory effects of ethanol are withdrawn, the brain becomes exposed to augmented levels of excitatory neurotransmitters.

There are several pharmacological approaches available: benzodiazepines, barbiturates, propofol, clonidine, propanolol and most recently dexmedetomidine and thus a significant variation in the management of alcohol withdrawal are seen.

Benzodiazepines are currently the first line drugs used for AWS. It binds to the GABA_A receptors and decreases neuron excitability. It has sedative, hypnotic, anxiolytic and muscle-relaxant properties. A recent meta-analysis has found that benzodiazepines are effective in reducing withdrawal symptoms and, in particular, in treatment and prevention of withdrawal seizures. (Amato et al 2010) But our patients were elderly who were more prone to side-effects like respiratory depression. Benzodiazepine use also increases the risk of hypoxemia in the elderly. (Munoz et al 1992) So, these patients require dose alteration and continuous monitoring. Moreover cross-tolerance with alcohol also limits benzodiazepines’ potential benefit.

Anticonvulsants are also being used to treat symptoms of alcohol withdrawal. They have different mechanism of action based on different receptors on which they act in the brain. There is no data suggesting that they should be used as the first line treatment replacing benzodiazepines. The adverse effects of their use in elderly individuals are also high. They are neither effective in preventing further seizures in withdrawal episodes nor can they be used prophylactically. (Minozzi et al 2010).

As haloperidol has its utility for treating severe agitation or hallucinations, it can be used as add on therapy with benzodiazepines. Its use in AWS has declined in previous years as it may increase the risk of seizures by lowering the seizure threshold. (Hedges et al 2013) Propofol acts through different pathways similar to benzodiazepines. It can be used to achieve conscious sedation in patients, but the chances of patients requiring intubation are very high. The dose required for using propofol for prolonged period increases the risk of propofol infusion syndrome and patients become prone to side-effects like hypertriglyceridemia and acute pancreatitis. (Mahajan et al 2010) To reduce autonomic symptoms sympatholytics like clonidine and beta blockers are used but they are not recommended for monotherapy. (Mayo-Smith et al 1997)

Dexmedetomidine is an alpha2 receptor agonist which produces sedation, anxiolysis, analgesia and sympatholysis. It was approved by FDA in 1999 for human use. (Reves et al 2010) It combines the properties of various other pharmacological modalities used previously. It has the advantage of providing sedation like benzodiazepines without causing respiratory depression. In addition it decreases symptoms of autonomic hyperactivity. Its action terminates quickly after discontinuing the drug making it easy to titrate as compared to Clonidine, another alpha 2 agent, has a plasma half life of 12-16 hours and benzodiazepines which have variable durations. It can cause an initial increase in the blood pressure causing bradycardia which stabilizes in a few minutes. Hence, it should be used with proper hemodynamic monitoring in the elderly who tend to have endogenous vagal blockade.

We used it intraoperatively expecting a decrease in the requirement of opioids because of its analgesic effect leading to faster recovery and shorter hospital stay which is beneficial for the patient. Opioids itself have a vast side-effect profile which includes delirium and hallucination. (Benyamin et al 2008) The chances of these side-effects get amplified in alcoholics as both of them have the same receptor site for metabolism. In addition many clinicians had used dexmedetomidine in alcohol withdrawal delirium refractory to conventional treatment, (Rayner et al 2012; Tolonen et al 2013) but no study has been reported for using it for prevention, so an attempt was made to use it intraoperatively on a prophylactic basis to avoid such symptoms.

Thus the utilization of dexmedetomidine was done in the above mentioned alcoholic patients undergoing surgery to decrease the symptoms of
alcohol withdrawal postoperatively and maintain a well sedated cooperative patient.

**Conclusion**

We conclude that dexmedetomidine can be considered for use in alcoholic patients intraoperatively thus decreasing the requirements of opioids as well as reducing the chances of patients landing up into alcohol withdrawal syndrome.

**Research Highlights**

Symptoms of AWS were prevented rather than waiting for them to occur and then manage.

Use of opioids was reduced thus minimizing their adverse effects.

Multiple drug therapy for treatment of AWS was prevented which use the deranged metabolic pathways in chronic alcoholics.

**Limitations**

We studied only 3 cases. Further studies with high sample size are required to validate the efficacy of dexmedetomidine in alcoholic patients by comparing it with the age long traditional drugs which are in use for alcohol withdrawal syndrome.

**References**


