

# The use of dexmedetomidine for refractory agitation in substance abuse patient

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## Abstract

Psychomotor disturbance in Intensive Care Unit (ICU) continues to be a challenging issue in view of its various ranges of predisposing factors and this includes withdrawal from chronic substance abuse. A combination of opioids, benzodiazepines and antipsychotics are often used to treat such neurochemical disturbances. We report a case of 43 year-old man with 10 years history of substance abuse who presented with acute opioids

intoxication. He required mechanical ventilation but exhibited significant agitation in the ICU. The conventional combination of midazolam and morphine, and later propofol infusion failed to control his agitations following admission. However, his symptoms improved and he was extubated within the first 24 hours of stay after dexmedetomidine infusion.

**Key words:** Dexmedetomidine, substance abuse, withdrawal, agitation.

## Introduction

In the Intensive Care Unit (ICU), patients are vulnerable to develop psychomotor disturbances with increase in both motor and psychological activities, often accompanied by loss of action control and disorganization of thought. Various terms have been used including agitation, anxiety and delirium. (1) Predisposing factors such as alcohol and substance abuse, male gender, advancing age, dementia and sensory impairment can further aggravate the symptoms. (1-3) It is a recognized problem that may complicate patients' recovery and until now remain a challenging issue as it is

difficult to diagnose and treat.

## Case Report

A 43 year-old male, presented to the Emergency Department in a post-ictal state after an episode of sudden generalized tonic-clonic seizure. On examination both pupils were equal at 3 mm and reactive to light, and his Glasgow Coma Scale (GCS) was 8 (E3V1M4). The air entry of both lungs was equal with no added sounds but he had shallow spontaneous breathing with respiratory rate of 18-25 breaths/min. His oxygen saturation on room air was 80%. The blood pressure was at 128/70 mmHg with a pulse rate of 70 per min. Arterial blood gas (ABG) analysis showed severe metabolic acidosis; pH 7.011, bicarbonate 8.5 mmol/L and lactate 12.8 mmol/L. He was intubated following a total of 14 mg midazolam, 100 mg suxamethonium and 30 mg rocuronium and was transferred to the ICU.

In the ICU, his oxygenation had improved. Intravenous infusions of midazolam and morphine both at 4 mg/hr were started. However, he remained restless without spontaneous eyes opening. Propofol infusion was added starting at 50

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mg/hr to control his agitations. There was no history of medical illness but he has been sniffing recreational drugs for the past 10 years. The renal and liver profiles were within normal range but his urine was tested positive for opioids. The blood toxicology analysis was negative for benzodiazepines, paracetamol and salicylates. However levels of amphetamines, opioids, cocaine and ketamine were not included.

Three hours later, the metabolic acidosis had improved slightly; pH 7.35, bicarbonate 22.9 mmol/L and lactate 2.4 mmol/L. He had spontaneous eyes opening but with pin point pupils and not focusing, E4VtM4. He was still irritable, restless and needed restraint, with blood pressure of 140/92 mmHg and a pulse rate of 88 per min. In view of the persisting symptoms, we decided to give a loading dose of 50 µg dexmedetomidine intravenously over 10 minutes followed by 0.3 µg/kg/hr infusion. Propofol infusion was terminated. A total of 1.2 mg of intravenous naloxone at 0.4 mg incremental doses was given to reverse the opioids effect as the pupils remained pin point. Over the next six hours, he gradually became less irritable, more arousable, obeyed commands and became cooperative while his metabolic status normalized. His haemodynamics were stable throughout the night with blood pressures ranging from 125-130 mmHg systolic and 70-80 mmHg diastolic and a pulse rate of 65-78 per min. He was then extubated at 17 hours after ICU admission and dexmedetomidine infusion was tapered down and discontinued.

## Discussion

All drugs of abuse act on the mesocorticolimbic dopamine system via different pathways. (4) Alpha2-adrenergic agonists have long been recognized as a potential agent for the treatment of substance withdrawal. The use of clonidine in the

attenuation of alcohol withdrawal symptoms has previously been evaluated. (5,6) Dexmedetomidine, a newer centrally acting alpha2-adrenergic agonist with an imidazole structure, is an active d-isomer of medetomidine, an agent that has been used as a sedative and analgesic in veterinary medicine for years. As dexmedetomidine is eight times more selective than clonidine, it is conceivable that dexmedetomidine may also be a useful agent for the treatment of substance withdrawal. (3,4)

Recently, dexmedetomidine is recognized as an alternative drug for sedation in critically ill patients. Its role in the prevention and treatment of delirium in the ICU has been demonstrated and its use in alcohol withdrawal has been reported. (2-4) Clinical trials that compared dexmedetomidine to benzodiazepine and propofol infusion showed less incidence of delirium and shorter duration of ventilator time. (3,4)

In this case report, dexmedetomidine's array of clinical manifestations, especially sedation and anxiolysis was an advantage and its undesirable effect on the cardiovascular system was not seen. To date, its use as sedation in the ICU is getting more popular but is limited to the recommended infusion duration of less than 24 hours as approved by FDA in 1999. The concern for its withdrawal symptoms similar to other alpha2-adrenergic agonists still exists.

## Conclusion

Dexmedetomidine with its pharmacokinetic advantage as an alpha agonist exerts the desired effects of sedation, analgesia, anxiolysis and sympatholysis with less respiratory depression. In this case, it offered useful and effective sedation in the management of refractory agitation in a substance abuse patient. However, more clinical evidence is needed for recommendation of its use on agitated patients in the ICU.

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