J Anesth (2013) 27:135–136
DOI 10.1007/s00540-012-1458-7

LETTER TO THE EDITOR

Benzodiazepine misadventure in acute alcohol withdrawal: the transition from delirium tremens to ICU delirium

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Received: 2 July 2012 / Accepted: 13 July 2012 / Published online: 5 August 2012

Keywords Alcohol withdrawal · Dexmedetomidine · ICU delirium · Benzodiazepines

To the Editor:

In the May issue of the *Journal of Anesthesia*, Demuro et al. [1] describe a case series of patients receiving dexmedetomidine for alcohol withdrawal. The authors highlight that benzodiazepines may be associated with hemodynamic instability and respiratory depression. An additional complication, intensive care unit (ICU) delirium, may be an underdescribed complication of benzodiazepines in alcohol withdrawal. While not studied in alcohol withdrawal, analysis has shown an association of lorazepam use with the transition to delirium in mechanically ventilated patients, and a higher incidence of delirium with midazolam compared with dexmedetomidine [2, 3]. We recently encountered a case of severe alcohol withdrawal transitioning to ICU delirium following extensive benzodiazepine exposure. We are curious if the authors have any data regarding benzodiazepine requirements or ICU delirium assessment before/after dexmedetomidine initiation.

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A 38-year-old woman with past medical history of hepatitis C and alcohol abuse presented to the emergency department with pruritus and visual hallucinations after several days of abstaining from alcohol. During the first 8 h of admission, she received 31 mg of intravenous lorazepam with minimal improvement in symptoms. She was transferred to the ICU, where she was intubated and given escalating doses of continuous infusion benzodiazepines with intermittent propofol (Fig. 1). In spite of this intense regimen, the patient remained agitated and conscious enough to exit her ICU bed and stand unassisted with the endotracheal tube (ET) in place. On day 5, adjunctive phenobarbital and clonidine were added. On day 8, it was believed that the patient's withdrawal syndrome had improved and she was transitioned to scheduled lorazepam bolus doses. However, over the next 3 days she was unable to be liberated from mechanical ventilation due to fluctuating mental status and agitation despite the addition of haloperidol. The patient was positive for ICU delirium as assessed by the confusion assessment method for the ICU (CAM-ICU). In an effort to manage the delirium and agitation, a dexmedetomidine infusion was started on day 11 at 0.2 μg/kg/h and titrated to a dose of 1.0 μg/kg/h. Over the next 24 h, the patient's agitation improved and she was extubated on day 12. Dexmedetomidine was weaned off after 34 h, and she was transferred to the general medicine floor the following day without further need for any benzodiazepine doses. At the time of discharge from the ICU, the patient had received a total of 183.5 mg intravenous lorazepam, 24 mg oral lorazepam, and 1,221 mg intravenous midazolam.

This case illustrates the potential complications of benzodiazepines in severe alcohol withdrawal. We witnessed a patient transition from severe alcohol withdrawal, to delirium tremens, and finally to ICU delirium following

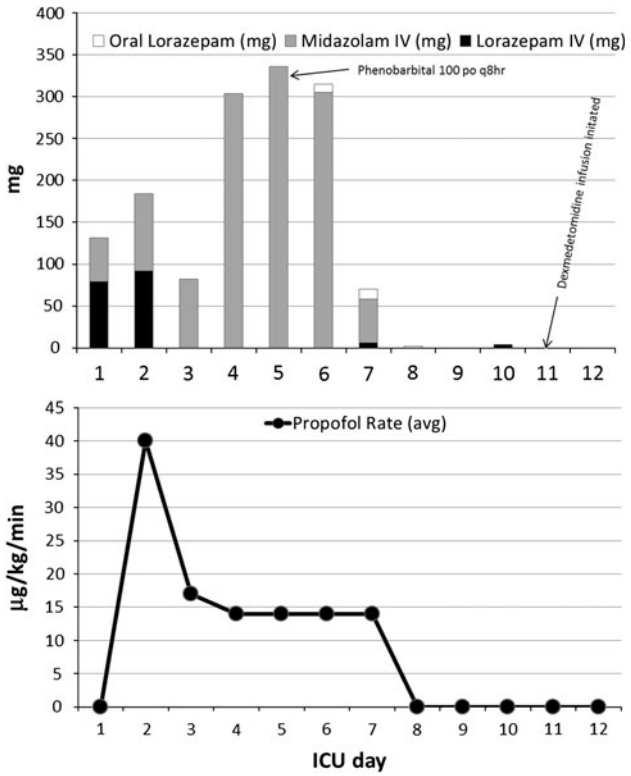

Fig. 1 Benzodiazepine and propofol usage by day. *IV* intravenous, *mg* milligram, *µg* microgram, *kg* kilogram, *po* by mouth, *ICU* intensive care unit, *avg* average

the administration of over 1,000 mg of parenteral midazolam and lorazepam. Dexmedetomidine's role may extend beyond prevention of intubation and benzodiazepine-sparing effects in patients with alcohol withdrawal, as demonstrated in Demuro's case series. Special consideration should be paid to the management of perceived "agitation" which occurred well outside of the normal time course of alcohol withdrawal. We suggest that clinicians consider the use of dexmedetomidine to avoid potentiation of ICU delirium from additional exposure to gamma-aminobutyric acid (GABA)nergic agents in this situation.

Conflict of interest Dr. Johnson has served as a member of Hospira Speakers Bureau. Drs. Yamanaka, Fraidenburg, and Kane have no conflicts of interest to disclose.

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