Pharmacist Impact on Protocol Driven Dexmedetomidine in Severe Alcohol Withdrawal

Shelbie McCoy, PharmD, BCCCP
Cox Medical Center Branson

Background

- Severe alcohol withdrawal (AW) results in frequent and prolonged intensive care unit (ICU) stays [1].
- Therapies used to manage AW, primarily benzodiazepines (BZDs), may also result in prolonged ICU stay and increased risk for mechanical ventilation (MV)[1,2].
- Dexmedetomidine, an alpha-2 receptor agonist, is used when symptoms persist despite use of BZDs. There is less respiratory depression and MV but increased delirium tremens (DTs) and seizures can occur [2-13].
- Due to continued BZD shortages, phenobarbital has been reviewed as a safe and effective alternative to BZD or as salvage therapy in AW [14-17].
- In 2016, Cox Medical Center Branson implemented protocol driven dexmedetomidine to outline its use in severe AW.
- A review in 2017 showed dexmedetomidine use and ICU length of stay (LOS) increased despite the protocol with reduced BZD administration. Phenobarbital was not a treatment option during this time.

Describe and report the impact of pharmacist guided interventions on ICU LOS after updating the dexmedetomidine protocol in severe AW management

Evaluate differences in MV frequency and dexmedetomidine duration and adverse events

Patient Population

Inclusion Criteria:

- Age > 18 years
- Admission or transfer to the ICU with a diagnosis and implementation of the severe alcohol withdrawal order set
- Use of dexmedetomidine in addition to the severe alcohol withdrawal order set

Exclusion Criteria:

- ICU stay < 24 hours
- Severe benzodiazepine order set and/or dexmedetomidine order set used for indications other than alcohol
  - i.e. other illicit substances in the absence of positive alcohol levels or alcohol history
- Dexmedetomidine ordered but not charted as given

Interventions

- Re-education of BZD symptom-triggered protocol (Riker Sedation-Agitation Scale)
- Fixed-dose phenobarbital implemented at physician discretion if BZD and haloperidol failed
- Dexmedetomidine duration reduced (72 hrs to 48 hrs) with lorazepam intravenous push taper x 48 hrs

Results

Primary Outcome	
ICU LOS (days), (n= 19 vs 22)	9.05 vs 7.13; NS
ICU LOS adjusted (days), (n=18 vs 18)	7.67 vs 7.17; NS
Secondary Outcomes (n= 19 vs 22)	
Mean Dexmedetomidine duration (hrs)	77.92 vs 63.36 ; NS
Adverse Events Overall (%)	73.68 vs 45.45; NS
HR < 60	63.15 vs 31.8; NS
HR < 50	15.78 vs 4.54; NS
MAP < 65	10.52 vs 13.63; NS
Rate above 1.5 mcg/kg/hr	26.31 vs 9.09; NS
LE (mg) prior to dexmedetomidine initiation	34.39 vs 64.64; NS
LE (mg) after dexmedetomidine initiation	54.85 vs 128.26; *p=.01*
MV(%)	26 vs 9; NS
Phenobarbital Adverse Events (%), 12/22	0

*NS: not significant

Author Disclosures

Authors of this presentation have nothing to disclose concerning possible financial or personal relationships with commercial entities that may have a direct or indirect interest in the subject matter of this presentation.

Methods

Design

- Single center, retrospective, descriptive study

Phase I:

- Washout Period:
  - Four week trial of protocol to assess safety
- Data included:
  - Baseline patient demographics and clinical status
  - Primary and secondary endpoints

Phase II:

- Descriptive statistics utilized to analyze pre and post revised protocol implementation

Differences in Baseline Characteristics

Increased frequency of DTs	63% vs 95%; *p=.01*
Increased mean drinks/day	18.85 vs 60; *p=.03*
Increased seizure history	11% vs 32%; *p=.14*

Patients in both groups were primarily male (~90%), 50 years of age, with an average alcohol level > 0.25 g/dL on admission and SOFA score ~3

Discussion

Limitations

- Small sample size
- Single center study
- Un-blinded

Future Direction

- Re evaluate protocols as a system
- Continue phenobarbital protocol
- Discussion regarding expansion of phenobarbital protocol due to BZD shortages

Conclusion

- Pharmacist intervention, while not statistically significant, did not result in prolonged ICU LOS or increased MV

References

1. Kattimani S, et al. Clinical management of alcohol withdrawal: A systematic review. *IND Psychiatry J.* 2013 Jul-Dec; 22(2): 100-108.
2. Ferreira, JA, et al. Approach to the complicated alcohol withdrawal patient. Journal of Intensive Care Medicine. 2015 Oct; 32 (1):3-14.
3. Beg, M, Fisher, S, et al. Treatment of Alcohol Withdrawal Syndrome with and without Dexmedetomidine. *Ferm J.* 2016 Spring; 20(2): 49–53.
4. Rayner S, et al. Dexmedetomidine as adjunct treatment for severe alcohol withdrawal in the ICU. *Ann Intensive Care.* 2012; 2: 12.
5. Jamil Darroca, Nitin Puri, et al. Dexmedetomidine Infusion as Adjunctive Therapy to Benzodiazepines for Acute Alcohol Withdrawal. Volume: 42 Issue: 11, page(s): 1703-1705
6. Mueller SW, Preislaki CR, Kiser TH, et al. A randomized, double-blind, placebo-controlled dose range study of dexmedetomidine as adjunctive therapy for alcohol withdrawal. *Crit Care Med.* 2014;42:1131-1139.
7.Muzyk A, Revollo J, Rivelli S. The use of dexmedetomidine in alcohol withdrawal. *J Neuropsychiatry Clin Neurosci.* 2012;24:E45-E46.
8. Rayner SG, Weinert CR, Peng H, Jepsen S, Brocard AY. Dexmedetomidine as adjunct treatment for severe alcohol withdrawal in the ICU. *Ann Intensive Care.* 2012; 2:12.
9. Frazee EN, Personett HA, Leung JG, Nelson S, Dierkhising RA, Bauer PR. Influence of dexmedetomidine therapy on the management of severe alcohol withdrawal syndrome in critically ill patients. *J Crit Care.* 2014; 29: 298-302.
10. Baddigam K, Russ P, Rosso J, Tobias J. Dexmedetomidine in the treatment of withdrawal syndromes in cardiothoracic surgery patients. *J Intensive Care Med.* 2005;20: 118-123.
11. Darroca J, Puri N, Prince F, Lomonaco A, Syverti A, Gerber DR. Dexmedetomidine infusion as adjunctive therapy to benzodiazepines for acute alcohol withdrawal. *Ann Pharmacother.* 2008; 42: 1703-1705.
12. VanDeWiele LA, Foster CJ, MacLaren R, Kiser TH, Fish DN, Mueller SW. Evaluation of early dexmedetomidine addition to the standard of care for severe alcohol withdrawal in the ICU: a retrospective controlled cohort study [published online October 16, 2014]. *J Intensive Care Med.*
13. Ludtke K, Stanley K, Yount N, Gerkin R. Retrospective review of critically ill patients experiencing alcohol withdrawal: dexmedetomidine versus propofol and/or lorazepam continuous infusions. *Hosp Pharm.* 2015; 50:208-213.
14. Gold JA, Rinaldi B et al. A strategy of escalating doses of benzodiazepines and phenobarbital administration reduces the need for mechanical ventilation in delirium tremens. Critical Care Medicine 2007:35:724-730.
15. Hayner CE, Wuestefeld NL. Phenobarbital treatment in a patient with resistant alcohol withdrawal syndrome. Pharmacotherapy 2009;29(7):875-878.
16. Michaelsen HI, Anderson IE, Fink-Jensen A, Allerup P, Ulrichsen J. Phenobarbital versus diazepam for delirium tremens: a retrospective study. *Dan Med Bull.* 2010;57:A4169.
17. Rosenson J., Clements C, et al. Phenobarbital for acute alcohol withdrawal: a prospective randomized double-blind placebo-controlled study. The Journal of Emergency Medicine, Vol.44, No. 3, pp.592-598, 2013.