2019

Impact of atypical antipsychotics on sedation requirements in mechanically ventilated, critically ill patients

Michael Genday PharmD

Dustin D Linn PharmD, BCPS, BCCCP

Jim Roy PharmD, BCPS, BCCCP

Impact of atypical antipsychotics on sedation requirements in mechanically ventilated, critically ill patients

Michael Genday, PharmD; Dustin Linn, PharmD, BCPS, BCCCP; Jim Roy, PharmD, BCCCP
Parkview Regional Medical Center
Fort Wayne, Indiana

BACKGROUND

- Antipsychotics have historically been given to treat delirium in the intensive care unit. Their role is controversial with more recent data reporting a lack of efficacy when used, especially in hypoactive etiologies.
- Estimated prevalence rates for delirium in the intensive care unit are as high as 50%.
- Studies have shown that prevalence rates for hypoactive delirium are as high as 80% of cases.
- Pharmacologic treatment options for delirium include antipsychotics such as haloperidol, quetiapine, olanzapine, risperidone, and ziprasidone.
- Atypical antipsychotics may be beneficial when weaning deeper sedation for extubation as it provides lighter sedation.
- Whether antipsychotics directly impact continuous sedation requirements as part of the ventilation process is unknown.

OBJECTIVE

- To determine if atypical antipsychotics lower continuous infusion sedation requirements while also assessing risk.

METHODS

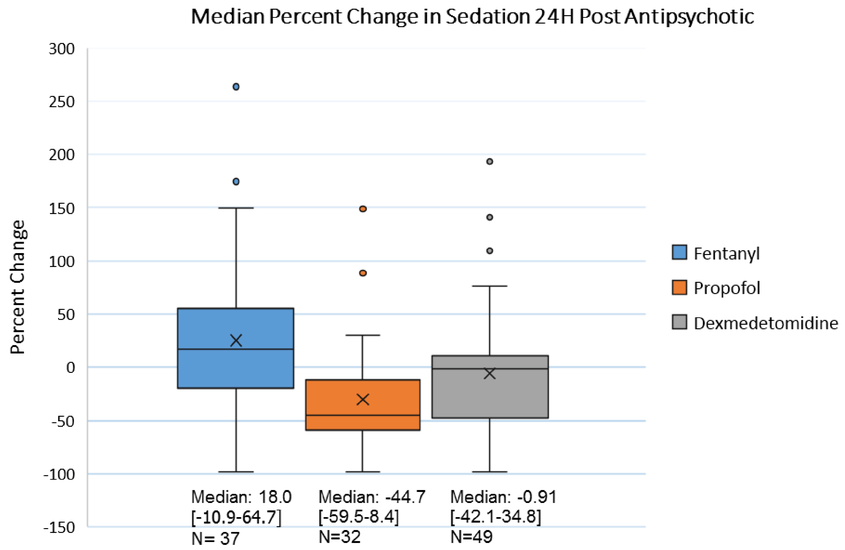
- **Retrospective chart review study**
- **Inclusion:** Mechanically ventilated patients who received a dose of an atypical antipsychotic while receiving continuous sedation
- **Exclusion:** Age less than 18
- Outcomes were compared over the specified date range:
  - August 1st, 2018 to August 1st 2019
- **Primary Outcome:** Percent change in total sedation dose 24 hours before and after the administration of an atypical antipsychotic
- **Secondary Outcomes:**
  - Change in RASS score 6 & 24 hours before and after antipsychotic administration
  - QTc > 500 ms after administration
  - Percent of subjects at RASS goal (0 or -1) before and after antipsychotic administration

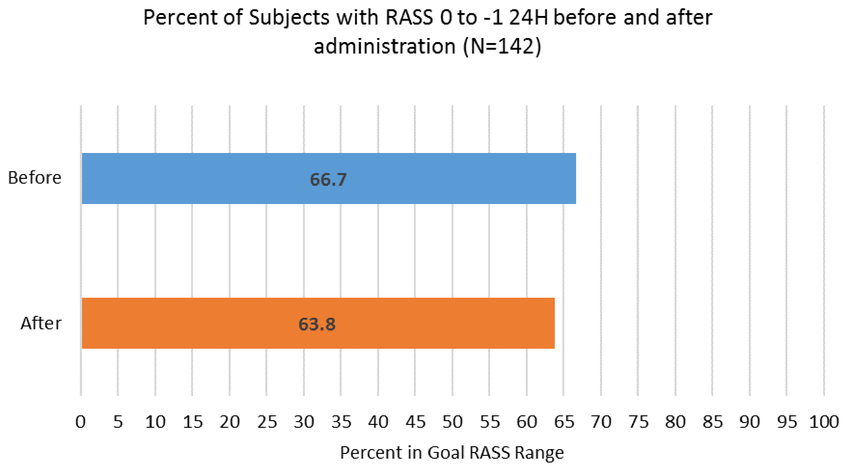
RESULTS

Baseline Characteristics of Total Population

		(n=142)
Age (Years ± SD)		55.7 ± 12.7
Mean ICU Length of Stay (Days, ± SD)		16.1 ± 12.8
Antipsychotic Duration (Days, ± SD)		7.2 ± 7.7
Positive CAM-ICU Prior to antipsychotic administration		96/125 (76.8%)
Admission Location (n, %)	CVICU Surgical ICU Medical ICU	12 (8.5%) 47 (33.3%) 82 (57.7%)
Antipsychotic Started(n, %)	Olanzapine Quetiapine	31 (21.8%) 111 (78.1%)
Antipsychotic Dose First Given	Olanzapine: 2.5 mg 5 mg Other (10, 25, 50 mg)	 7 (22.5%) 15 (48.3%) 9 (29.0%)
	Quetiapine: 25 mg 50 mg Other (2.5, 5, 12.5, 100 mg)	 50 (45.0%) 37 (33.3%) 24 (21.6%)

RESULTS

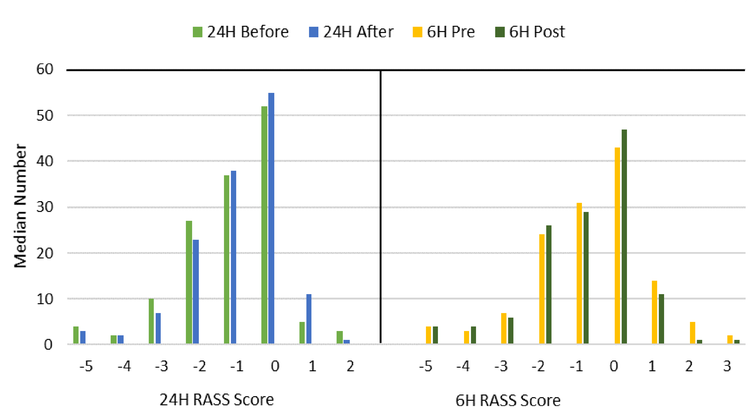




Ventilator Timeline (N=121)

Median Time Between:	Days [IQR]
Intubation and antipsychotic administration	5.8 [2.5-8.9]
Antipsychotic administration and extubation	3.3 [1.6-5.9]
Intubation and Extubation	9.1 [5.2-20.7]

RESULTS



DISCUSSION & CONCLUSIONS

- Sedation in the intensive care unit is often a multi-factorial process that involves several different medications at varying times throughout an ICU stay.
- Propofol is a highly sedating medication that is often used at the beginning of an ICU stay in order to adequately sedate the patient.
- The larger decrease in propofol received after the administration of an antipsychotic argues for a relationship between antipsychotics and reduced propofol requirements.
- Almost no change in dexmedetomidine dose was found which would is consistent with the current practice of using it as a primary sedative and also to wean off a ventilator.
- The slight increase in fentanyl administration may argue against a correlation between antipsychotics and reduced sedation requirements.
- When administering antipsychotics to ventilated patient's, RASS score's would be expected to be closer to 0 or -1. The lack of a significant change found indicates proper sedation was used prior to antipsychotics being given.
- There was only 1 reported incidence of QTc prolongation over 500 ms.
- Considering the multi-factorial disorders of a critically ill patient, administering an antipsychotic may be correlated with a reduction in sedative doses, particularly propofol, to promote lighter sedation with a reduced risk for delirium.
- Going forward, appropriate dosing regimens, timing, and guidance on the preferred antipsychotic should be assessed.

Limitations:

- Different doses of antipsychotics were administered making a dose related comparison to sedation requirements difficult.
- QTc was not measured frequently enough to assess adequate safety data.
- Retrospective data limits ability to assess positive behavioral changes that may have been reduced or increased with antipsychotic use.

REFERENCES

1. Devlin JW, Skrobik Y, Gélinas C, et al. Clinical practice guidelines for the prevention and management of pain, agitation/sedation, delirium, immobility, and sleep disruption in adult patients in the ICU. Crit Care Med 2018;46(9):e825-e873.
2. ASHP therapeutic guidelines on stress ulcer prophylaxis. Am J Health-Syst Pharm. 1999; 56:347-79.
3. Ely EW, Shintani A, Truman B, et al. Delirium as a predictor of mortality in mechanically ventilated patients in the intensive care unit. JAMA 2004;291:1753-1762.
4. Krag M, Marker S, Perner A, et al. Pantoprazole in patients at risk for gastrointestinal bleeding in the ICU. N Engl J Med 2018; 379:2199-2208. DOI: 10.1056/NEJMoa1714919
5. Girard TD, et al. Haloperidol and ziprasidone for treatment of delirium in critical illness. *N Engl J Med.* 2018. ePub 2018-10-22:1-12.

Disclosure
The authors of this presentation have the following 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:
Michael Genday: Nothing to disclose Dustin Linn: Nothing to disclose Jim Roy: Nothing to disclose