Standardized antipsychotic administration for control of peri-extubation agitation in adult medical intensive care unit patients

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BACKGROUND

- Delirium affects many critically ill patients, worsens health outcomes, and places a significant financial burden on the hospital system.[1] In mechanically ventilated intensive care unit (ICU) patients, delirium often leads to agitation that may impede extubation, or increase the risk of re-intubation due to the patient's inability to protect their airway.[2]
- While antipsychotics, such as haloperidol, are used routinely in ICUs to manage agitated delirium in the peri-extubation period, dosing regimens vary greatly and are based on prescriber preferences.
- The benefit of antipsychotics during peri-extubation remains ill-defined. As a retrospective quality initiative (QI), we sought to assess the benefits of a standardized dosing schematic and its impact on patient outcomes and medication exposure.

METHODS

Group 1

Historical control group

Adult patients extubated within the medical ICU between 7/1/21 and 2/8/22

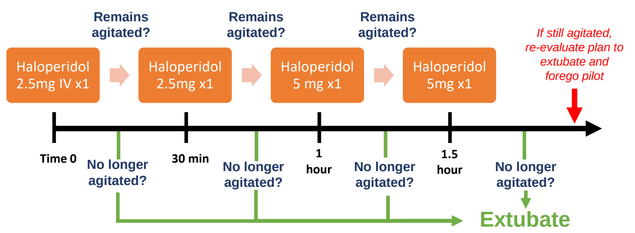
Exclusion criteria: no antipsychotic admin pre-extubation, COVID-19 +, DNAR-B or C, death during ICU stay

Group 2

Haloperidol QI group

Patients identified by the primary team as at risk for agitated delirium between Feb and May 2022 were considered for a **standardized haloperidol dosing schematic**

Figure 1: Standardized haloperidol dosing schematic



If clinically appropriate, the most recent dose used pre-extubation may be continued as every 6 hours x 4 doses (for 24 hours total)

Primary Outcome

- Milligrams of antipsychotic (in haloperidol equivalents, HE) administered within 24 hours post-extubation*

Secondary Outcomes

- Rate of re-intubation within 24 hours
- Richmond Agitation Sedation Scale (RASS) score within goal post-extubation
- Milligrams of benzodiazepine (BZD) (in midazolam equivalents, MDE) administered 24 hours post-extubation

*Haloperidol equivalents based on 1mg haloperidol = 37.5mg quetiapine = 2.5mg olanzapine[3]

RESULTS

Table 1: Baseline characteristics (n=34)

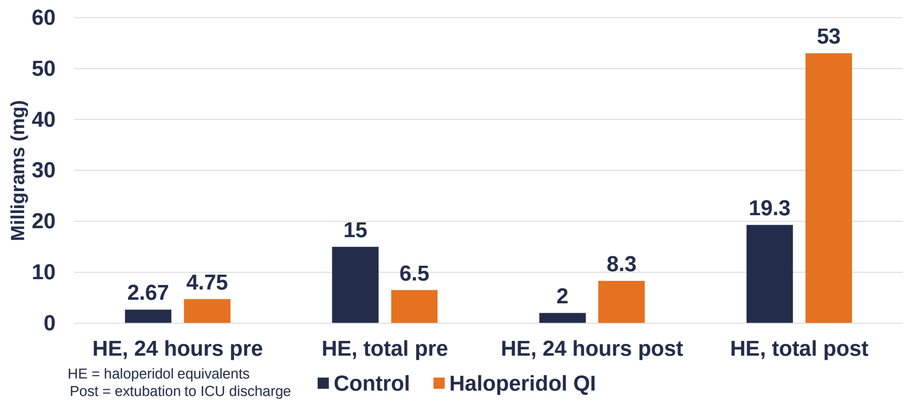
	Control (n=23)	Haloperidol QI (n=11)
Age, median (IQR) – yr	58 (54-70)	42 (30-62)
BMI, median (IQR) – kg/m²	26 (22-41)	27 (20-30)
Female sex, (%)	13 (57%)	3 (27%)
Race, no. (%) - White - Black	20 (87%) 3 (13%)	9 (82%) 2 (18%)
Intubation duration, median (IQR) – days	4.9 (2.8-8.2)	2.2 (1.6-3.9)
CAM-ICU positive prior to extubation, no. (%)	16 (70%)	8 (73%)
RASS -2 to 1 (i.e. Desired level of sedation & agitation control) prior to extubation, no. (%)	17 (74%)	9 (82%)
Mg BZD administered pre-extubation, median MDE (IQR) – mg	21 (1-178)	15 (1-165)
Mg opioids administered pre-extubation, median MME (morphine milligram equivalents) (IQR) – mg	15 (1.5-297)	70 (0-185)
ICU length of stay, median (IQR) – days	9 (6-15)	7 (4-14)
Time between extubation and ICU discharge, median (IQR) – days	2.5 (0.5-3.3)	3.5 (1.4-5.6)
Restraint utilization prior to extubation, no. (%)	10 (44%)	7 (64%)
History of alcohol withdrawal, no. (%)	2 (9%)	1 (9%)

Table 2: Primary and secondary endpoints

	Control (n=23)	Haloperidol (n=11)	p-value
Primary outcome			
Mg antipsychotic administered within 24 hours post-extubation, median HE (IQR) – mg	2 (0-8.4)	8.3 (1-16.8)	0.385
Secondary outcomes			
Re-intubation within 24 hours, no. (%)	1 (4%)	0 (0%)	0.483
RASS score within goal post-extubation, no (%)	21 (91%)	10 (91%)	0.970
Mg BZD administered within 24 hours post extubation, median MDE (IQR) – mg	0 (0-0)	0 (0-0)	1.000

Post = extubation to ICU discharge; results considered statistically significant if $p \leq 0.05$

Figure 2: Milligrams HE pre- and post-extubation (median)



DISCUSSION

- In this interim analysis, a haloperidol QI dosing schematic was associated with decreased total amount of antipsychotic exposure pre-extubation, but increased exposure in both the 24-hour time period post-extubation, as well as, the total time between extubation and discharge from the ICU. No patients in the haloperidol QI group required re-intubation.
- Seven of the 11 patients (64%) in the haloperidol QI group required only one 2.5 mg dose prior to extubation. All remaining patients (4/11 or 36%) required a second 2.5 mg dose.
- Notably, the total antipsychotic exposure post-extubation was markedly higher in the haloperidol QI group. Per the QI project, patients were selected subjectively by the primary team. This may have selected for patients at higher risk of demonstrating agitation in the days after extubation. On average, the QI group spent one additional day in the ICU prior to discharge. Also, there was a higher median opioid exposure pre-extubation in the QI group, which places those patients at higher risk for developing delirium.
- Limitations of this quality improvement project include a small sample size and the retrospective nature of the study. Reliance on retrospective chart documentation led to the inability to compare the degree of agitation between groups, or the timing of RASS assessments in the relation to symptoms of agitation.

CONCLUSION

- In this interim analysis, a standardized haloperidol schematic given to patients at risk for agitated delirium pre-extubation may decrease the total amount of antipsychotic exposure pre-extubation, but increase exposure post-extubation. Further investigation must be made into the possible benefits of prophylactic haloperidol in high risk patients.
- This quality improvement project remains ongoing.

REFERENCES

1. Devlin, John W, 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, Critical Care Medicine: September 2018 - Volume 46 - Issue 9 - p e825-e873 doi: 10.1097/CCM.0000000000003299
2. Wilson, Jo Ellen, et al. "Delirium." Nature Reviews Disease Primers 6.1 (2020): 1-26. doi: 10.1038/s41572-020-00236-z
3. "Psychiatric Pharmacy Essentials: Antipsychotic Dose Equivalents." CPNP: College of Psychiatric and Neurologic Pharmacists (CPNP), https://cpnp.org/guideline/essentials/antipsychotic-dose-equivalents

This quality improvement project was approved by the QI-IRB at UVA Health