Supplemental materials

Effect of enteral guanfacine on dexmedetomidine use in the intensive care unit

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Supplemental methods description

A medication use report was used to identify patients for inclusion and chart review was used to screen for exclusion

Methods and rational for exclusion

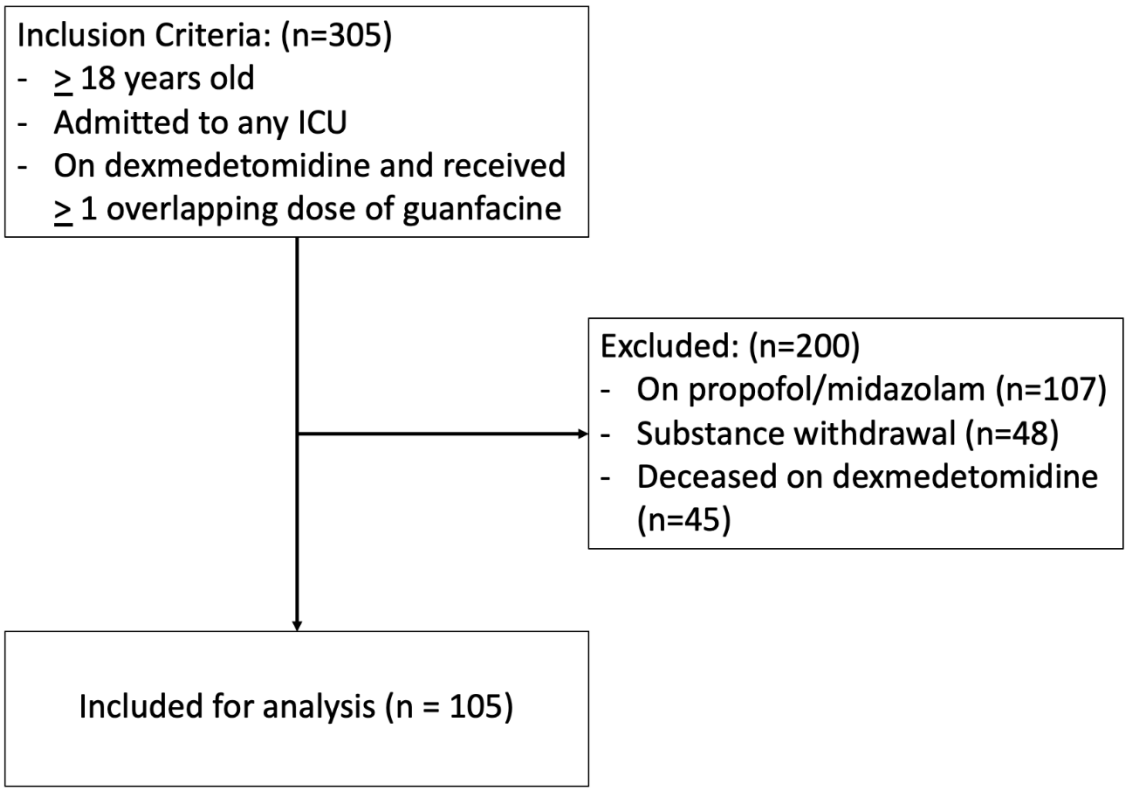
Exclusion criteria	Methods/Rationale
Alcohol or substance withdrawal	This was determined by chart review and progress note documentation. Alcohol and substance withdrawal symptoms are similar to dexmedetomidine withdrawal symptoms, potentially confounding results.
Taking guanfacine prior to admission	This was determined by chart review of the prior to admission medication list. Prior to admission guanfacine use may confound efficacy due to potential tolerance.
Received propofol or midazolam continuous infusions at the time of guanfacine initiation	This was determined by chart review of the medication administration record. Use of continuous sedative infusions may induce deep sedation, masking the potential effects of guanfacine and dexmedetomidine withdrawal symptoms.
Deceased on dexmedetomidine	This was determined by chart review and progress note documentation. Including such patients may confound the primary outcome and confound the effects of guanfacine.

Secondary outcomes and definitions

Outcome	Definition / Rationale
Discontinuation of dexmedetomidine within 72 hours of guanfacine initiation	Discontinuation of dexmedetomidine infusion order in the electronic medical record within 72 hours of guanfacine initiation. An analysis at 72 hours was included given steady state concentrations of guanfacine may take between 50-150 hours to be reached. We chose to look at the earlier timeframe at which guanfacine steady state concentrations were reached (48 and 72 hours) to provide a pragmatic insight to dexmedetomidine weaning, as many providers aim to discontinue dexmedetomidine either

	immediately or shortly after starting an oral transition agent.
Dexmedetomidine withdrawal	Based on daily provider progress note indicating dexmedetomidine withdrawal, as the objective symptoms of withdrawal (tachycardia, insomnia, hypertension, agitation, etc.) may also be present in other disease state processes in critically ill patients.
Bradycardia	Heart rate $\leq$ 60 beats per minute
Hypotension	MAP <65, systolic blood pressure <90mmHg, or blood pressure requiring initiation of vasopressors
Escalation in ventilation	Escalation in ventilation defined as need for initial intubation or re-intubation not related to other procedures while on guanfacine therapy
ICU Delirium	Positive CAM-ICU score at any time during guanfacine therapy, documented every four hours as assessed by the bedside nurse
Medication Dosing – Rescue psychoactive medications	Data was collected on use of as needed antipsychotics (haloperidol, quetiapine, olanzapine, risperidone), hydroxyzine, benzodiazepines, valproic acid and propofol infusion as these are the commonly used rescue agents at our institution. Data presented in supplemental table 1
Medication Dosing – Scheduled psychoactive medications	Data was collected on scheduled use of Antipsychotics (haloperidol, quetiapine, olanzapine, risperidone), benzodiazepines, valproic acid, gabapentin/pregabalin, SSRI/SNRI/DNRI and/or nocturnal dexmedetomidine cycling as these are commonly used as adjunct therapies at our institution. Data presented in supplemental table 1

Supplemental Figure 1. Patient flow chart



Supplemental Table 1: Medication dosing and use

Concomitant Clonidine – n (%)	5 (5)
Clonidine daily dose – mg, median (IQR)	0.9 (0.5-0.9)
Use of as needed rescue agents – n (%)	58 (55)
Antipsychotics[a]	47 (45)
Hydroxyzine	43 (41)
Benzodiazepine	13 (12)
Valproic acid	2 (2)
Propofol infusion	1 (1)
Other[b]	3 (3)
Scheduled psych meds – n (%)	56 (53)
Antipsychotics[a]	43 (41)
Benzodiazepine	2 (2)
Valproic acid	12 (11)
Gabapentin/Pregabalin	24 (23)
SSRI/SNRI/DNRI[c]	11 (10)
Dexmedetomidine cycling[d]	14 (13)
Other[e]	7 (7)
Opioid daily use – morphine equivalents (MME), median (IQR)	13 (4-42)

[a] *- includes both typical and atypical antipsychotics (patients received haloperidol, quetiapine, olanzapine, risperidone)*

[b] *- Use of medications on a as needed basis for management of agitation/ restlessness not listed in previous categories*

[c] *- Selective serotonin reuptake inhibitor (SSRI), Serotonin norepinephrine reuptake inhibitor (SNRI), Dopamine norepinephrine reuptake inhibitor (DNRI)*

[d] *– Use of nocturnal dexmedetomidine from 2100-0600 to facilitate sleep*

[e] *- Buspirone (2), doxepin (1), lithium (1), mirtazapine (3)*