Effects of Clonidine on Withdrawal from Long Term Dexmedetomidine in the Pediatric Patient

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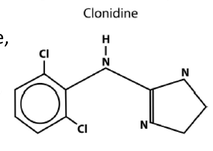
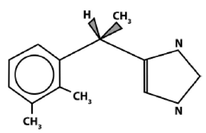
BACKGROUND

- Use of dexmedetomidine is increasing in pediatric critical care, cardiac critical care, and anesthesia[1,2]
  - Favorable adverse effect profile
  - Reduction in opioid and benzodiazepine use
  - Potential for reduction in mechanical ventilation days
  - Provided more effective sedation than midazolam[3]
- Adult studies of ≥24 hour infusions have shown minimal rebound hypertension and tachycardia after abrupt discontinuation
- Limited studies have evaluated dexmedetomidine use longer than 4-5 days in the pediatric population
- Upon discontinuation of long term dexmedetomidine, pediatric patients have experienced withdrawal symptoms such as: agitation, rebound hypertension, and rebound tachycardia[4-7]
- Due to similar mechanisms of action, clonidine is theorized to help reduce withdrawal from long term dexmedetomidine
- The Withdrawal Assessment Tool-1 (WAT-1) is a validated tool to objectively monitor opioid and benzodiazepine withdrawal symptoms in pediatric patients[8]





Dexmedetomidine

OBJECTIVES

Primary Objective:

To compare Withdrawal Assessment Tool-1 (WAT-1) scores among patients on clonidine to those not on clonidine, while being weaned from long term dexmedetomidine (≥5 days)

Secondary Objective:

To describe the withdrawal symptoms experienced after long term dexmedetomidine use (≥5 days)

STUDY DESIGN & METHODS

- Single center, retrospective chart analysis including patients admitted to the Pediatric Intensive Care Unit (PICU): Approved by University of Maryland School of Medicine IRB

Primary Outcome: Withdrawal

- WAT-1: Number of scores ≥3 and average score during the 24 hours post-wean

Secondary Outcomes:

- Rebound hypertension: 20% increase in value from baseline
- Rebound tachycardia: 20% increase in value from baseline

Inclusion Criteria: ≥2 weeks of age, ≥42 weeks gestational age, <18 years of age, supported on mechanical ventilation for acute pulmonary parenchymal disease

Selected Exclusion Criteria: Cyanotic heart disease, single ventricle, primary pulmonary hypertension, ventilator dependent on PICU admission, neuromuscular respiratory failure, pain managed on PCA or epidural catheter, transferred from outside ICU where sedatives have already been administered for >24 hours

RESULTS

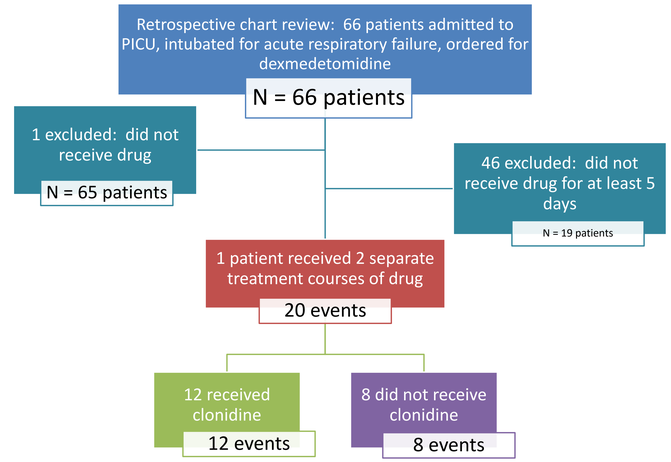


Table 1. Demographics

No. of events = 20	Clonidine N = 12	No Clonidine N = 8	p value
Male, n (%)	5 (50.0%)	5 (62.5%)	0.670
Age (years), median (IQR)	1.5 (0.67 – 3.3)	1.0 (0.85 – 1.3)	0.624
Weight (kg), median (IQR)	12.3 (8.0 – 19.0)	9.8 (8.5 – 12.3)	0.521
LOS (days), median (IQR)	29.1 (22.0 – 35.9)	19.9 (16.0 – 28.7)	0.270
ICU LOS (days), median (IQR)	16.6 (13.2 – 26.9)	12.9 (9.8 – 20.3)	0.181
Ventilator Days, median (IQR)	12.3 (10.5 – 20.3)	7.5 (6.5 – 14.4)	0.115

Table 2. Dexmedetomidine Use

No. of events = 20	Clonidine N = 12	No Clonidine N = 8	p value
Duration of Dex. (hours) median (IQR)	241.8 (185 – 406.3)	134.5 (117 – 144)	**0.003**
Cumulative Dose, mcg/kg median (IQR)	232.7 (158.3 – 336.1)	126.1 (102.1 – 157.5)	**0.031**
Mean Dose, mcg/kg/hour (range)	1.0 (0.53 – 1.81)	1.0 (0.42 – 1.73)	0.910
Maximum Dose, mcg/kg/hour	2.2	2.0	0.521

Table 3. Clonidine Use

	N = 12
Transdermal Formulation, n (%)	12 (100%)
Dose at Initiation (mcg/kg/day), mean (range)	9.0 (2.9 – 18.2)
Day No. of dexmedetomidine infusion when clonidine was initiated, mean (range)	7 (5-9)

RESULTS CONTINUED

No. of events = 20	Clonidine N = 12	No Clonidine N = 8	p value
Mean no. of WAT Scores ≥3 per patient (range)*	0.8 (0 – 6)	3.2 (0 – 8)	0.149
Mean Systolic Blood Pressure, mmHg (range)			
Pre-Wean	100.1 (86.5 – 116.6)	99.5 (83.6 – 130.0)	0.624
Post-Wean	102.6 (73.2 – 123.8)	104.7 (91.8 – 118.3)	0.851
Rebound Systolic Hypertension, n (%)	2 (16.7%)	0 (0.0%)	0.495
Mean Diastolic Blood Pressure, mmHg (range)			
Pre-Wean	52.7 (41.2 -62.5)	53.2 (46.4 – 65.0)	0.910
Post-Wean	56.3 (37.0 – 67.3)	58.7 (50.5 – 70.7)	0.678
Rebound Diastolic Hypertension, n (%)	4 (33.3%)	1 (12.5%)	0.603
Mean Heart Rate, bpm (range)			
Pre-Wean	108.4 (85.8 – 149.3)	108.6 (93.7 – 131.8)	0.851
Post-Wean	112.0 (88.5 – 151.5)	138.4 (117.8 – 168.3)	**0.003**
Rebound Tachycardia, n (%)	3 (25.0%)	4 (50.0%)	0.356

*Clonidine group, N = 11; No clonidine group, N = 6

CONCLUSIONS

- Patients received clonidine when on dexmedetomidine for longer duration
- Patients who received clonidine trended towards having fewer elevated WAT scores compared to the no clonidine group
- Significant tachycardia after dexmedetomidine wean was observed in the no clonidine group
- Including only patients with respiratory failure may limit generalizability of study
- Need larger sample size to reach power
- Overall, clonidine may be helpful in reducing withdrawal symptoms associated with weaning of long term dexmedetomidine in pediatric patients

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