

# Opioid class rotation in mechanically ventilated children

Texas Children's Hospital, Department of Pediatrics and Pediatric Critical Care Medicine, Baylor College of Medicine

Sara Hyatt, DO  
Barbara-Jo Achuff, MD  
Danielle Guffey, MS  
Jean Raphael, MD

## BACKGROUND

Opioids are commonly used in the pediatric intensive care unit (PICU) to alleviate pain, minimize the stress response and provide sedation for procedures and/or intubation. While it is the goal to use adequate doses of analgesia, it has been shown that prolonged use of opioids has led to tolerance, hyperalgesia and eventual iatrogenic withdrawal syndrome. The latter results in extended mechanical ventilation and overall prolonged ICU stay, none of which benefits the patient.

Rotation of opioid agents may mediate tolerance and lower the total effective dose, which may optimize outcomes.

## PURPOSE

The purpose of this study is to determine whether opioid class rotation decreases the total opioid dose exposure, therefore improving health outcomes.

## METHODS

We conducted a retrospective review at a quaternary pediatric intensive care unit from June 2018 to July 2020. The cohort was extracted via Virtual Pediatric Systems and uploaded into Tableau®.

### Inclusion criteria:

- Ages 0 to 18 years old
- Admitted with primary diagnosis of acute or acute on chronic respiratory failure
- Mechanical ventilation for  $\geq 5$  days
- Use of at least one opioid during mechanical ventilation period

### Exclusion criteria:

- Patients with tracheostomy
- Extracorporeal membrane oxygenation
- Continuous renal replacement therapy

## DATA

	Without Rotation		With Rotation		p-value
	(N=181)	(%)	(N=37)	(%)	
<b>Gender</b>					0.859
Female	96	(53.0)	19	(51.4)	
Male	85	(47.0)	18	(48.6)	
<b>Race</b>					0.048
Asian	6	(3.3)	4	(10.8)	
Black or African American	38	(21.0)	4	(10.8)	
Hispanic or Latino	92	(50.8)	16	(43.2)	
Other/Mixed	3	(1.7)	1	(2.7)	
Unspecified	0	(0.0)	1	(2.7)	
White	42	(23.2)	11	(29.7)	
<b>Mortality</b>					0.014
Survived	176	(97.2)	32	(86.5)	
Died	5	(2.8)	5	(13.5)	
<b>Past Medical History</b>					<0.001
No	89	(49.2)	5	(13.5)	
Yes	92	(50.8)	32	(86.5)	

Table 1: Patient Demographics

	Without Rotation		With Rotation		p-value
	(N =181)		(N =37)		
	Median	(IQR)	Median	(IQR)	
Age (years)	2.6	(1.9,4.4)	4	(2.9,6.5)	0.001
Weight (kg)	7.5	(4.5,12.7)	11.6	(8.9,20.1)	<0.001
Mechanical ventilation days	8	(6.0,10.0)	13	(9.0,17.0)	<0.001
ICU LOS	11	(9.0,16.0)	22	(13.0,27.0)	<0.001
Hospital LOS (DC-Admit)	18	(13.0,25.0)	29	(22.0,41.0)	<0.001
Dexmedetomidine	87	(34.6,150.8)	306.5	(136.9,486.9)	<0.001
Benzodiazepine	12.3	(2.1,51.8)	117.6	(59.0,226.1)	<0.001
Opioid (MMeq/kg)	70	(36.9,108.8)	211.7	(151.0,275.0)	<0.001

Table 2: Demographics; continuous and and outcome variables

Drug	Coefficient	95% CI	p-value
Opioid	51.12	(7.21-95.03)	0.023
Benzodiazepam	1.80	(1.13-2.46)	<0.001
Dexmedetomidine	76.87	(45.36-108.38)	<0.001

Table 3: Adjusted quantile regression in rotated participants

## RESULTS

A total of 218 patients were included in the study, with a total of 243 mechanical ventilator (MV) events and 227 hospitalizations. Of those, 17% (n=37) had opioid class rotation. The median age and weight were 2.7 years (IQR 2, 4.9) and 8.3kg (IQR 4.8, 13.3) respectively with MV median of 8 days (IQR 6,11).

Class rotation participants were found to be older (p = 0.001), weighed more (p <0.001), had longer MV (p <0.001) and were more medically complex (p <0.001).

Increased total opioid dose was found in rotators versus non-rotators, 211 vs. 70 MMeq/kg, p<0.001. After adjusting for age, gender, weight, race, and MV days, the rotation group remained statistically significant with increased total opioid dose (p = 0.023), 136% higher than those without.

## CONCLUSION

Although thought to alleviate high dose exposure, pediatric patients with respiratory failure requiring mechanical ventilation who undergo an opioid agent rotation have a 136% higher total opioid dose exposure than those without rotation.

## REFERENCES

- Fisher, Deborah, Mary Jo Grap, Janet B. Younger, Suzanne Ameringer, and R.K. Elswick. "Opioid Withdrawal Signs and Symptoms in Children: Frequency and Determinants." *Heart & Lung* 42, no. 6 (November 2013): 407-13.
- Galinkin, Jeffrey, Jeffrey Lee Koh, Committee On Drugs, and Section on Anesthesiology and Pain Medicine. "Recognition and Management of Iatrogenically Induced Opioid Dependence and Withdrawal in Children." *Pediatrics* 133, no. 1 (January 1, 2014): 152-55.
- Giordano, Vito, Joy Edobor, Philipp Deindl, Brigitte Wildner, Katharina Goeral, Philipp Steinbauer, Tobias Werther, Angelika Berger, and Monika Ollschar. "Pain and Sedation Scales for Neonatal and Pediatric Patients in a Preverbal Stage of Development: A Systematic Review." *JAMA Pediatrics* 173, no. 12 (December 1, 2019): 1186-97.
- Harris, Julia, Anne-Sylvie Ramelet, Monique van Dijk, Pavla Pokorna, Joke Wietenga, Lyvonne Tume, Dick Tibboel, and Erwin Ista. "Clinical Recommendations for Pain, Sedation, Withdrawal and Delirium Assessment in Critically Ill Infants and Children: An ESPNIC Position Statement for Healthcare Professionals." *Intensive Care Medicine* 42, no. 6 (June 2016): 972-86.
- Keogh, S. J., D. A. Long, and D. V. Horn. "Practice Guidelines for Sedation and Analgesia Management of Critically Ill Children: A Pilot Study Evaluating Guideline Impact and Feasibility in the PICU." *BMJ Open* 5, no. 3 (March 30, 2015): e006428-e006428. Martyn, J.A. Jeevendra, Jianren Mao, and Edward A. Bittner. "Opioid Tolerance in Critical Illness." Edited by Julie R. Ingelfinger. *New England Journal of Medicine* 380, no. 4 (January 24, 2019): 365-78.
- Mehta, Sangeeta. "Protocolized Sedation in Critically Ill Children." *JAMA* 313, no. 4 (January 27, 2015): 363-64.
- Playfor, Stephen, Ian Jenkins, Carolyne Boyles, Imti Choonara, Gerald Davies, Tim Haywood, Gillian Hinson, et al. "Consensus Guidelines on Sedation and Analgesia in Critically Ill Children." *Intensive Care Medicine* 32, no. 8 (August 2006): 1125-36.