The Effect of Intraoperative Methadone During Pediatric Cardiac Surgery on Postoperative Opioid and Sedation Requirements

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Clinical Conundrum

- Difficult pain control in this patient population
  - Sternotomy very painful
  - Many are not opioid naive
- Long ICU course
  - Sedation often required
  - Prolonged opioid infusions
- Many patients required opioid weans to Methadone

Why not start with Methadone at beginning of perioperative course, instead of the end?

Why Methadone?

Multiple Sites of Action

Long half-life

Hemodynamically stable

Methadone in Cardiac Surgery

Intraoperative Methadone for the Prevention of Postoperative Pain

A Randomized, Double-blinded Clinical Trial in Cardiac Surgical Patients

Glenn S. Murphy, M.D., Joseph W. Szokol, M.D., Michael J. Avram, Ph.D., Steven B. Greenberg, M.D., Jesse H. Marymont, M.D., Torin Shear, M.D., Kruti N. Parikh, B.S., Shivani S. Patel, B.A., Dhanesh K. Gupta, M.D.

Methadone in Pediatric Surgery

Comparison of morphine and methadone for prevention of postoperative pain in 3- to 7-year-old children

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Methadone in Pediatric Surgery

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ORIGINAL ARTICLE

Analgesic effects of methadone and magnesium following posterior spinal fusion for idiopathic scoliosis in adolescents: a randomized controlled trial

David P. Martin[1,2] · Walter P. Samora III[3] · Allan C. Beebe[3] · Jan Klamar[3] · Laura Gill[3] · Tarun Bhalla[1,2] · Giorgio Veneziano[1,2] · Arlyne Thung[1,2] · Dmitry Tumin[1] · N'Diris Barry[1] · Julie Rice[1] · Joseph D. Tobias[1,2]

Methadone in Pediatric Surgery

Contents lists available at ScienceDirect

Journal of Pediatric Surgery

journal homepage: www.elsevier.com/locate/jpedsurg

Multimodal anesthesia with the addition of methadone is superior to epidural analgesia: A retrospective comparison of intraoperative anesthetic techniques and pain management for 124 pediatric patients undergoing the Nuss procedure

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Study Design

- Retrospective Chart Review
- 198 Patients who underwent cardiac surgery between June 2017 and August 2018
- Divided patients into two groups: Neonatal and Non-neonatal

Patient Selection

Inclusion criteria	Exclusion Criteria
• Age <18 yo • Cardiac Surgery with cardiopulmonary bypass between June 2017 and August 2018	• ECMO pre- or postoperatively • Use of preoperative Methadone • No Methadone after practice change in Jan 2018

Study Endpoints

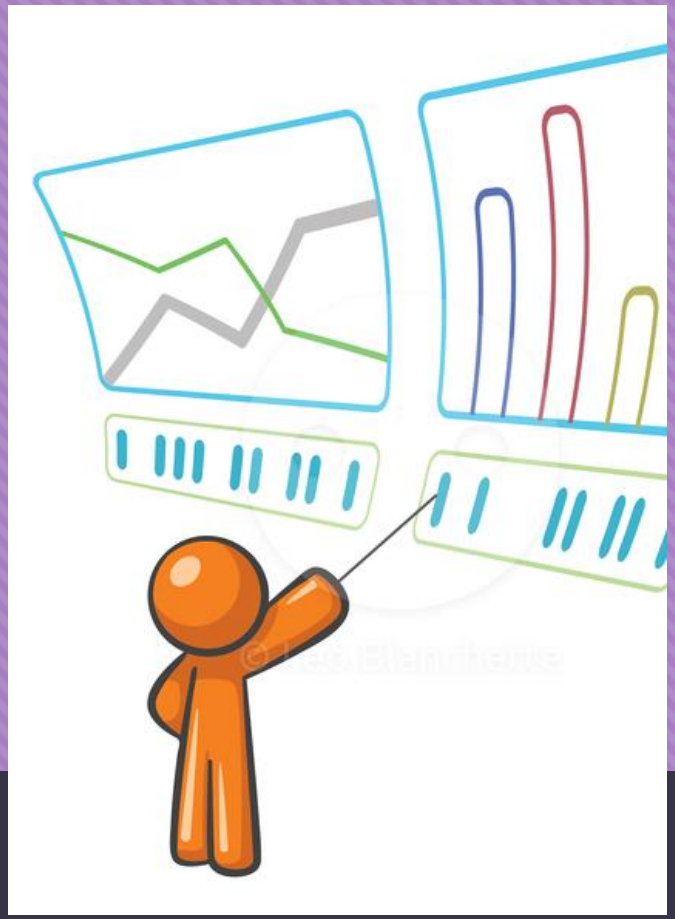
Primary Endpoint

- Perioperative Opioid Use

Secondary Endpoints

- Pain Scores
- Perioperative sedation requirements
- Pain and Sedation Scores
- Extubation in OR
- Time to first dose of Oral Oxycodone
- Need for Naloxone

Results



Patient Demographics

Neonates			
	Pre (n=21)	Post (n=23)	p-value
Age (days)	10.76 (6.39)	11.35 (5.49)	0.7454[1]
Sex	5 (23.81%)		0.7403[2]
Female	5 (23.81%)	7 (30.43%)	
Male	16 (76.19%)	16 (69.57%)	
Race			0.8032[2]
Black	2 (9.52%)	4 (17.39%)	
Other	3 (14.29%)	4 (17. 39%)	
White	16 (76.19%)	15 (65.22%)	
Weight (kg)	3.70 (0.54)	3.31 (0.61)	0.0331[1]
ASA Score			0.003[2]
2	1 (4.76%)	0 (0%)	
3	5 (23.81%)	0(0%)	
4	14 (66.67%)	23 (100%)	
5	1 (4.76%)	0 (0%)	

Non- Neonates			
	Pre(n=69)	Post (n=85)	p-value
Age (years)	2.54 (3.86)	3.48 (4.92)	0.7556[1]
Sex			0.1956[2]
Female	36 (52.17%)	35 (41.18%)	
Male	33 (47.83%)	50 (58.82%)	
Race			0.8281[2]
Black	18 (26.09%)	26 (30.59%)	
Other	15 (21.74%)	18 (21.18%)	
White	36 (52.17%)	41 (48.24%)	
Weight (kg)	14.61 (17.62)	17.04 (16.04)	0.5746[1]
ASA Score			0.0800[2]
2	3 (4.35%)	6 (7.06%)	
3	38 (55.07%)	59 (69.41%)	
4	27 (39.13%)	20 (23.53%)	
5	1 (1.45%)	0 (0%)	

The numbers are reported as number of patients (percentage). The shaded values highlight the differences within the neonatal group of weight and ASA scores between those who did and did not receive Methadone. P-value calculated with [1]Wilcoxon and [2]Fisher Exact test.

Neonatal Patients

- Age <30 days
- 44 total patients
  - 21 pre-Methadone intervention, 23 post-Methadone intervention

Intraoperative Medication Use

	Pre	Post	p-value
Opioids (MME/kg)	2.89 (1.47)*	1.98 (1.96)*	0.0112[1]
Midazolam (mg/kg)	0.27(.17)	0.25(.19)	0.6773[3]
Ketamine (mg/kg)	1.25(1.00)	1.10(1.22)	0.4430[1]
Acetaminophen (mg/kg)	6.99 (5.74)	9.08 (4.71)	0.2084[1]
Dexmedetomidine (mcg/kg)	3.03 (1.58)*	2.03 (1.86)*	0.0056[1]

Numbers reported as mean (standard deviation) or number of patients (percentage) as appropriate. P-value calculated with [1]Wilcoxon, [2]Fisher Exact, or [3]Equal Variance t-test as appropriate.

*indicates values with statistically significant difference (p-value <0.05)

First 24-hour Postoperative Medication Use

	Pre	Post	P-value
Opioids (MME/kg)	4.30(2.83)	2.97(2.00)	0.1154[1]
Midazolam (mg/kg)	0 (0.00)	0.04 (0.14)	0.0956[1]
Ketamine (mg/kg)	0.31(0.71)	0.31(0.71)	0.5938[1]
Acetaminophen (mg/kg)	34.43(20.54)	37.99(19.41)	0.3333[1]
Dexmedetomidine (mcg/kg)	9.45(6.41)	7.13(5.80)	0.2144[1]
Lorazepam (mg/kg)	0.02(0.07)	0.01(0.03)	0.2582[1]

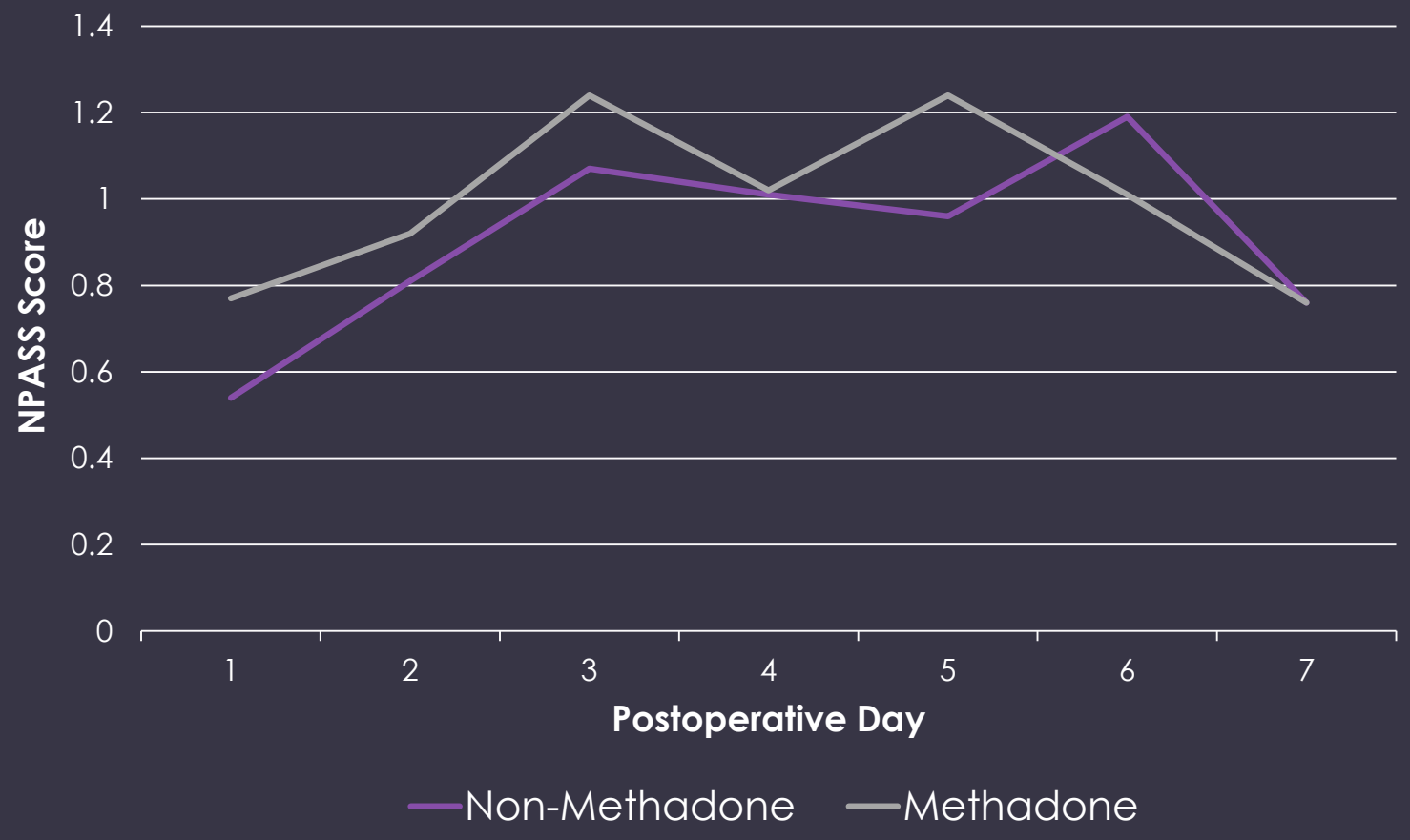
First 7-days Postoperative Medication Use

	Pre	Post	P-value
Opioids (MME/kg)	103.65(67.16)	111.44 (85.04)	0.9065[1]
Midazolam (mg/kg)	0.003 (0.1)	0.04 (0.14)	0.1863[1]
Ketamine (mg/kg)	3.09 (5.40)	4.00 (4.09)	0.1206[1]
Acetaminophen (mg/kg)	110.63 (74.32)	89.16 (75.67)	0.1921[1]
Dexmedetomidine (mcg/kg)	71.57 (61.64)	61.40 (51.16)	0.4520[1]
Lorazepam (mg/kg)	0.07 (0.11)	0.06 (0.14)	0.3219[1]

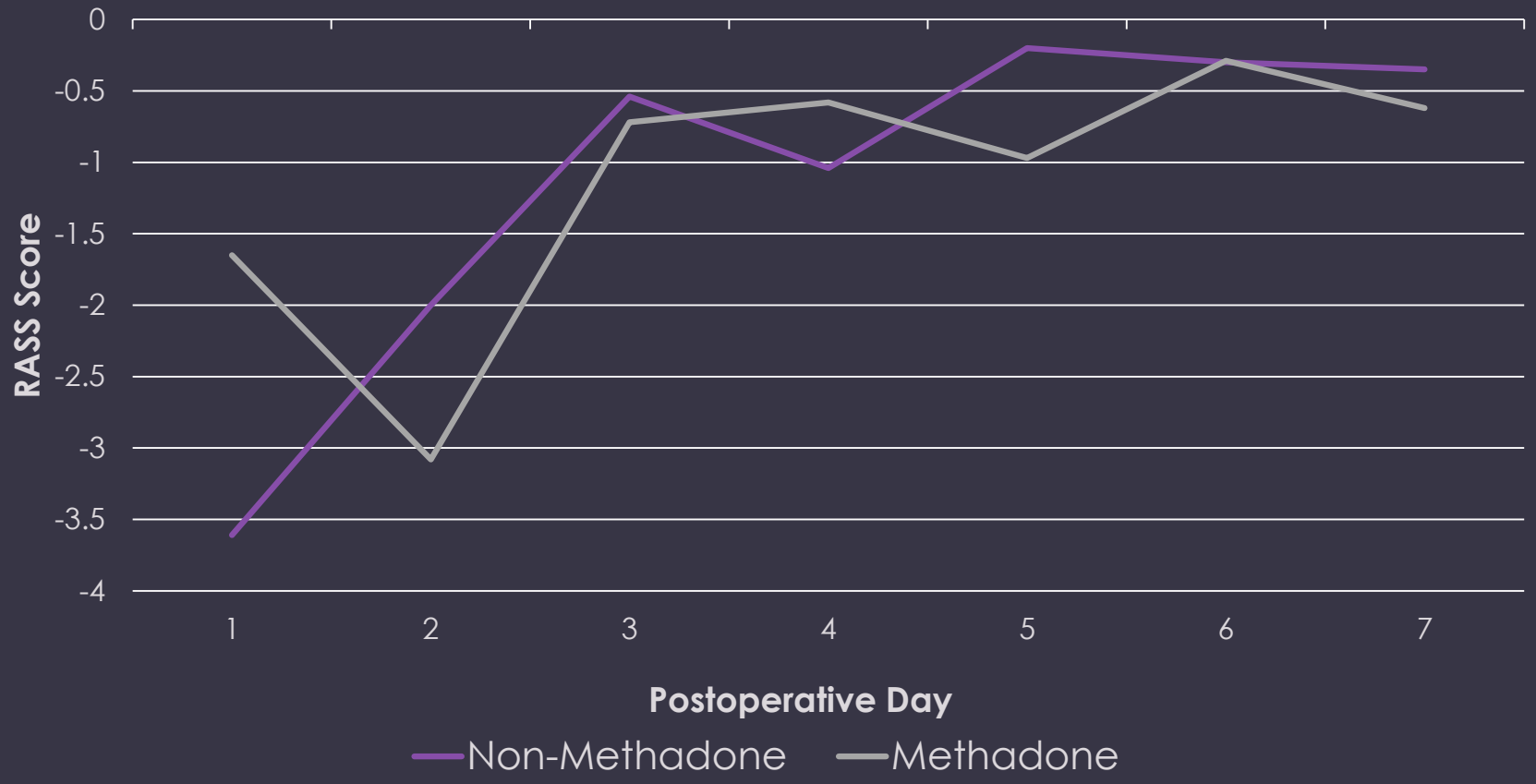
Additional Secondary Outcomes in Neonatal Patients

	Pre	Post	p-value
Naloxone Used	1 (4.76%)	0 (0%)	0.4773[2]
Oxycodone Used	6 (28.57%)	4 (17.39%)	0.4805[2]
Time to First Oxycodone dose (hrs)	127.37 (29.00)	129.15 (34.07)	0.9313[3]
Extubation in OR	1 (4.76%)	1 (4.35%)	1[2]

Average NPASS Scores



Average RASS Score



Non-neonatal Group

- Patients age >30 days
- 154 total patients
  - 69 patient pre-Methadone, 85 patients post-Methadone intervention

Intraoperative Medication

	Pre	Post	P-value
Opioids (MME/kg)	1.82 (1.08)*	0.94 (0.80)*	<0.001[1]
Midazolam (mg/kg)	0.19 (0.24)*	0.10 (0.15)*	0.003[3]
Ketamine (mg/kg)	0.82 (1.01)	0.55 (0.88)	0.482[1]
Acetaminophen (mg/kg)	11.60 (6.00)	11.64 (6.34)	0.3251[1]
Dexmedetomidine (mcg/kg)	3.39 (1.57)*	1.91 (1.52)*	<0.001[1]

First 24-hour Postoperative Medication Use

	Pre	Post	P-value
Opioids (MME/kg)	2.18(2.70)*	1.42(1.92)*	0.0193[1]
Midazolam (mg/kg)	0.22(1.59)	0.01(0.07)	0.5[1]
Ketamine (mg/kg)	0.42(1.24)	0.44(1.31)	0.8694[1]
Acetaminophen (mg/kg)	54.41(10.59)	55.40(9.53)	0.2054[1]
Dexmedetomidine (mcg/kg)	8.42 (10.00)*	5.11 (7.04)*	0.0109
Lorazepam (mg/kg)	0.08(0.14)*	0.02(0.07)*	0.0005[1]

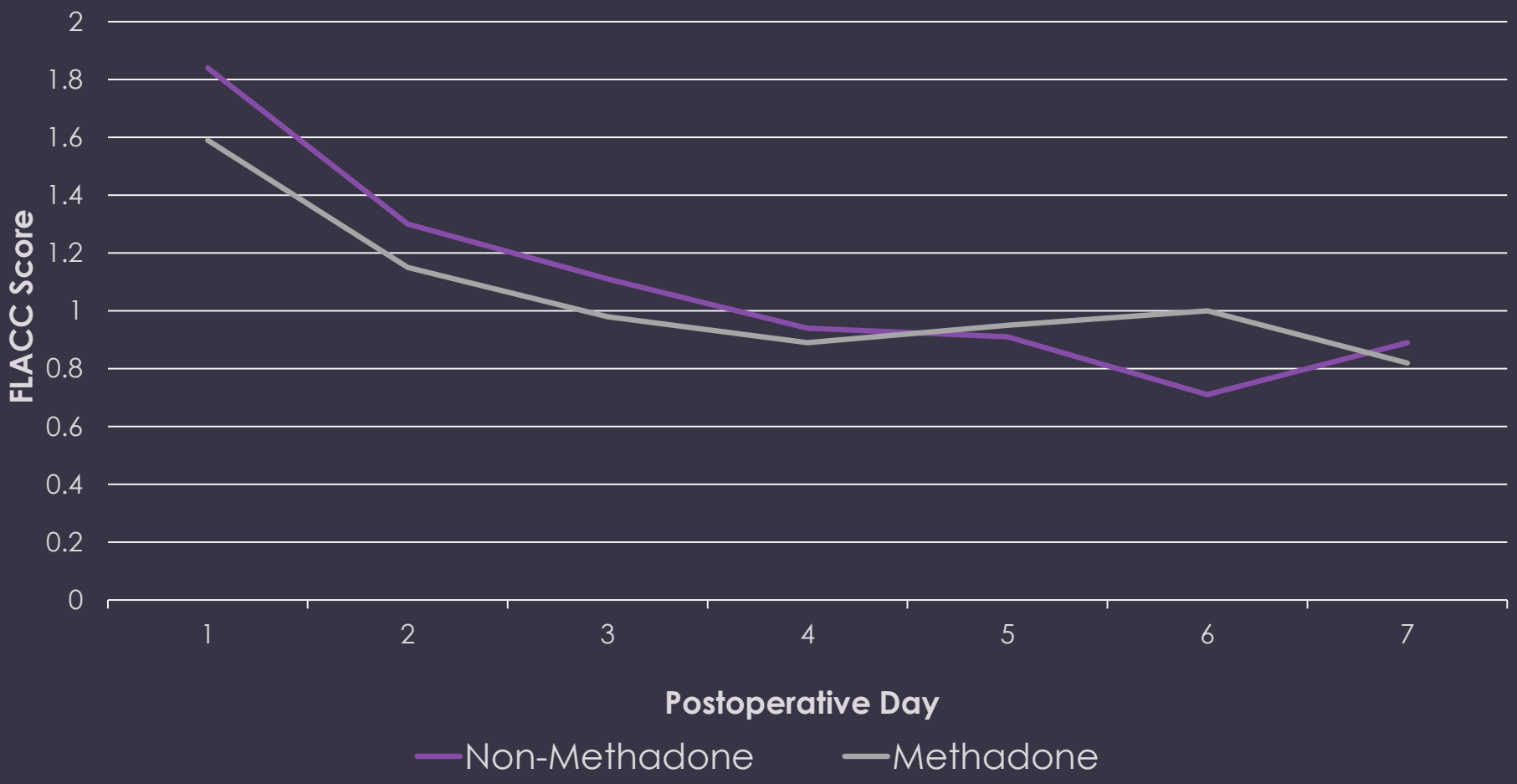
First 7-days Postoperative Medication Use

	Pre	Post	P-value
Opioids (MME/kg)	51.12 (82.98)	36.78 (65.48)	0.0932[1]
Midazolam (mg/kg)	0.01 (0.04)	0.05 (0.29)	0.7812[1]
Ketamine (mg/kg)	3.79 (12.54)	1.62 (4.02)	0.6471[1]
Acetaminophen (mg/kg)	198.27 (88.57)	179.86 (88.46)	0.2087[1]
Dexmedetomidine (mcg/kg)	64.73 (114.41)*	23.06 (45.95)*	0.0043[1]
Lorazepam (mg/kg)	0.25 (0.55)*	0.06 (0.17)*	<0.001[1]

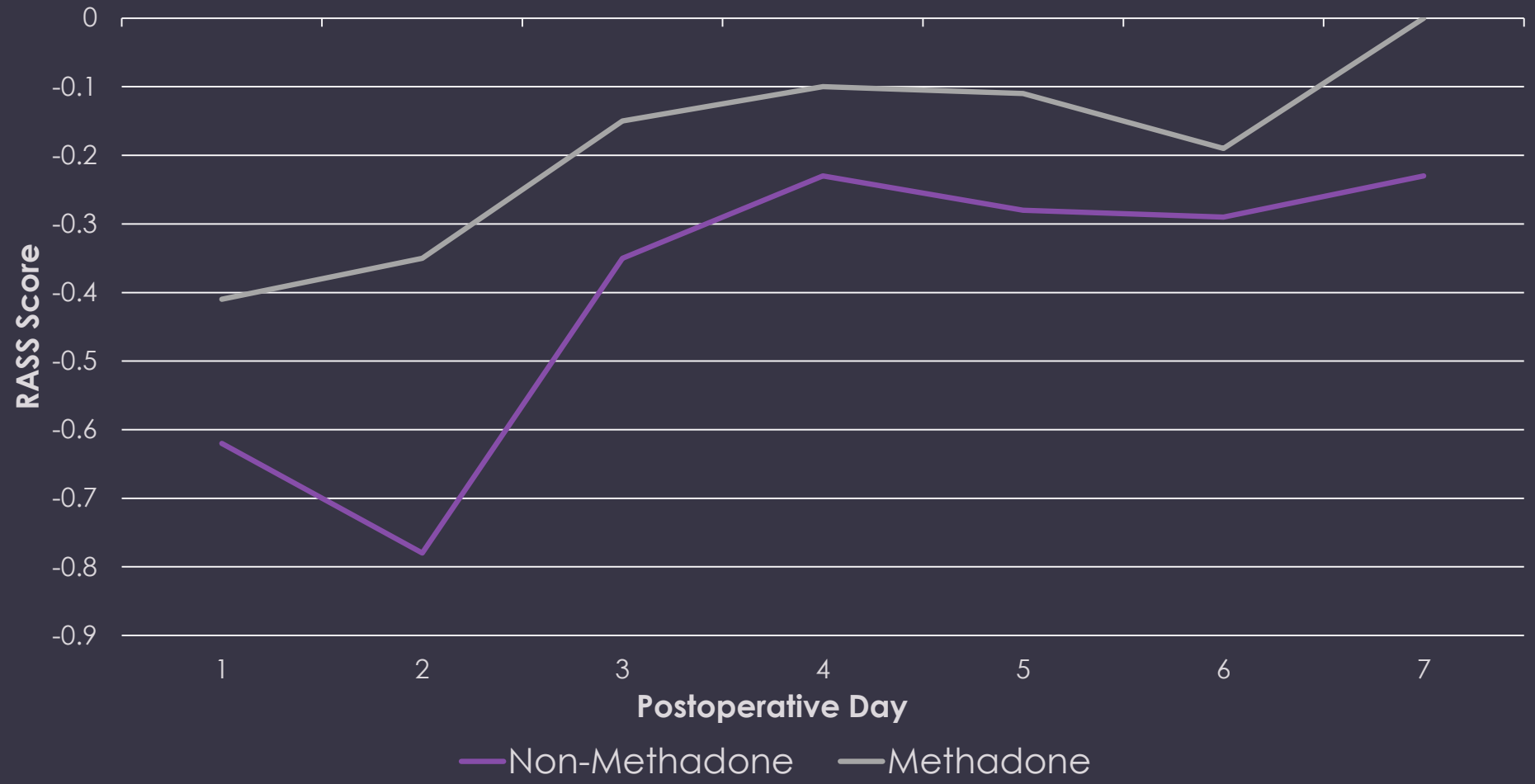
Additional Secondary Outcomes

	Pre	Post	P-value
Naloxone Used	0 (0%)	3 (3.53%)	0.2532[2]
Time to 1st Oxycodone dose (hrs)	45.36 (31.79)	41.53 (28.23)	0.5711[1]
Extubation in OR	43 (62.32%)	49 (57.65%)	0.6213[2]

Average FLACC Scores



Average RASS Score



Discussion

- Less intraoperative opioids and dexmedetomidine requirements in all patients
- Less differences seen in the neonatal group compared to non-neonatal group
- Decreased postoperative opioid requirements in non-neonatal group
- Decreased need for sedation in non-neonatal group along with higher sedation scores
- No difference in pain scores
- Limitations:
  - Retrospective study
  - ICU did not change practice
- Future studies will look at differences up to 30 days postoperatively

Conclusion

Methadone is an efficacious alternative to Fentanyl for intraoperative pain control in this patient population and may facilitate decrease postoperative opioid and sedation medication requirements

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Questions or Comments