

#8_Postoperative naloxone administration after perioperative methadone: A retrospective analysis

Presenting Author: Vijay K Ramaiah MD

Co-Author: Evan D. Kharasch MD PhD

Department of Anesthesiology, Duke University School of Medicine, Durham NC 27710

Background:

Intravenous (IV) methadone is commonly used perioperatively due to excellent intraoperative antinociception and superior postoperative analgesia with significant opioid sparing up to 72 hr postoperatively. Some practitioners may have concerns of potential postoperative respiratory depression due to the long methadone half-life of 1-2 days. The goal was to evaluate postoperative naloxone administration as a surrogate for respiratory depression after intraoperative methadone.

Methods:

We conducted a retrospective review of postoperative naloxone administration in adults ≥ 18 yr receiving perioperative opioids from January 2022 to February 2025. Any patients receiving the opioids methadone, fentanyl, hydromorphone, morphine, sufentanil or remifentanil any time between anesthesia start and stop; or receiving naloxone 0-48 hours after anesthesia stop were included. Excluded were cases with another surgery within 24 hours before or after the index case.

Results:

208,198 adult non-cardiac surgical patients were included in our analysis. There was no significant difference between naloxone administration in patients who received methadone (11/1154, 0.95%) and those who did not receive methadone (1384/207044, 0.67%); $P=0.237$. Methadone use was uncommon (1154; 0.55% of cases). Methadone dose was 20 mg (median), range 1-100 mg. Methadone and non-methadone groups were similar in size, age, weight, and sex. Methadone administration was more common in neurosurgery, ENT, urology and pediatric surgery. Methadone dose was not different between patients who did or did not receive naloxone ($P=0.227$). Naloxone administration occurred more commonly after thoracic and general surgery. The large majority of naloxone administration was by infusion (78%), and most naloxone (99%) was administered to patients who had not received methadone. Naloxone infusions were most common in thoracic, general surgery, and gynecology cases. Most adults (90%) went to post anesthesia care unit (PACU) postoperatively. The majority (89%) of naloxone administration occurred outside of the PACU, and only 11% occurred in the PACU. Only 1 patient who received perioperative methadone also received naloxone in the PACU. In patients receiving naloxone post-PACU, the average time to administration was 18 hour after anesthesia stop (12 hr in those who received methadone and 18 hr in those who had not received methadone). In neurosurgery, naloxone use was 1.26% in patients receiving methadone and 0.22% in patients not receiving methadone. Methadone use in craniotomy and spine was not a risk factor for naloxone administration. In patients receiving methadone, naloxone administration was not more frequent in patients receiving PACU methadone. In patients receiving methadone, naloxone administration was not associated with administration of PACU analgesics. No intraoperative pharmacologic risk factor, alone or in combination with methadone, for the administration of

postoperative naloxone, was identified. Anesthesia duration was substantially longer in patients receiving methadone. PACU LOS adjusted for duration of surgery was not longer in patients receiving methadone.

Conclusions:

Analysis of data from 208,198 patients does not suggest a statistically significant or clinically meaningful association between perioperative methadone administration and postoperative naloxone administration. Methadone, compared with other opioids, or no opioids, does not appear as a risk factor for respiratory depression, as assessed by naloxone administration.

Table 1. Adult patient cohort demographics

	<u>Methadone</u>	<u>SD</u>	<u>No Methadone</u>	<u>SD</u>	<u>Total</u>	<u>SD</u>
No of patients	1154		207044		208197	
Age (yr)	54	16	58	17	58	17
Weight (kg)	85	22	84	31	84	22
Male	545		86091		86636	
Female	609		120941		121550	
Anesthesia Duration (median)	4.8		1.9			
PACU LOS hr (median)	2.4		1.3		1.3	
PACU LOS hr (relative) median	0.57		0.83		0.83	

SD: Standard deviation

Table 2. Naloxone administration, location, type and methadone administration in adults

Total Patients 208198		<u>Any Methadone</u>			<u>Naloxone %</u>	
		<u>Yes</u>	<u>No</u>	<u>Total</u>	<u>Methadone Y</u>	<u>Methadone N</u>
Any naloxone	Yes	11	1384	1395	0.95%	0.67%
	No	1143	205660	206803		
	Total	1154	207044	208198		
a. Naloxone given in PACU	Yes	1	179	180		
	No	4	214	218		
	Total	11	1384	1395		
a.1.PACU naloxone by injection	Yes	1	73	74		
a.2 PACU naloxone by infusion	Yes	0	106	106		
b. Naloxone given post-PACU	Yes	4	214	218		
b.1 Post-PACU naloxone injection	Yes	2	54	56		
3.b.2. Post-PACU naloxone infusion	Yes	2	160	162		

Table 3. Methadone and naloxone administration in neurosurgery patients, and craniotomy and spine surgery

		<u>Methadone Yes</u>			<u>Methadone No</u>		
		<u>Naloxone Yes</u>		<u>Naloxone No</u>	<u>Naloxone Yes</u>		<u>Naloxone No</u>
		<u>Injection</u>	<u>Infusion</u>		<u>Injection</u>	<u>Infusion</u>	
Neurosurgery	N 12684	3	2	392	26	1	12260
Craniotomy	4060	1	1	91	5	0	3962
No craniotomy	8624	2	1	301	21	1	8298
Spine Surgery	180	0	0	16	5	0	163

