

#5291 “Effects of Perioperative Dronabinol Use in Total Knee Arthroplasty”

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ASRA PAIN MEDICINE

INTRODUCTION

- CC1=C(C(=C(C=C1)O)C2=CC=CC=C2)C3=CC=CC=C3
C₂₁H₃₀O₂ (molecular weight = 314.47)
- ★ Dronabinol is a synthetic tetrahydrocannabinol (Δ9-THC) agent FDA approved for chemotherapy-induced nausea and vomiting, and as an appetite stimulant for patients suffering from HIV or AIDS. Studies suggest that cannabinoids may have analgesic properties, making them potential alternatives for managing chronic pain conditions, such as neuropathic pain.
 - ★ Retrospective research on perioperative dronabinol indicated it may reduce opioid intake and shorten hospital stays for joint arthroplasty patients. In addition to alleviating acute pain, Δ 9-THC may also enhance respiration and impact the apnea-hypopnea index.
 - ★ Post-operative pain management following TKA can be effectively managed on the first day after surgery with a multimodal pain regimen including regional anesthesia techniques. Patients often experience a resurgence of pain the day following surgery, especially as nerve blocks wear off and they engage in activities and ambulation.



METHODS

- ★ A double-blind, placebo-controlled trial (IRB#2019-1416, NCT#04734080) assessed the possible opioid-sparing effect of perioperative dronabinol in TKA patients.
- ★ The **primary outcome** was opioid consumption (in oral morphine equivalents) 24-48 hours after surgery (powered to detect a 30% decrease). Additional **secondary outcomes** included cumulative opioid requirements through POD 2, pain during ambulation on POD 2, number of oxygen desaturation events, and sleep quality.



- ★ Eligible TKA patients were enrolled between March 8th, 2021, and October 4th, 2023. A total of 114 participants were recruited and randomized to either the placebo group (sesame oil capsules), or dronabinol group.
- ★ The dronabinol group received 5mg active capsules twice per day for a total of five doses, beginning in the preoperative period and concluding on POD 2. The placebo group received same-sized and colored capsules in the same dosing regimen.
- ★ Categorical variables reported as frequencies and percentages and compared using chi-square tests. Continuous variables reported as mean and standard deviation or median and interquartile range and compared using t-test or Mann-Whitney U tests. P-values less than 0.05 were statistically significant.

Table 1. Patient and Surgical Characteristics

	Dronabinol (n=51)		Placebo (n=51)		P-Value
	N	%	N	%	
Age, median [IQR]	62 [58-66]		63 [57-66]		0.599
BMI, median [IQR]	31.0 [28.2-34.3]		29.8 [27.9-34.1]		0.433
Gender					0.196
Male	20	39.2	27	52.9	
Female	31	60.8	24	47.1	
Comorbidities					0.458
Pulmonary Hypertension	4	8.0	0	0.0	
Hyperlipidemia	6	12.0	6	11.8	
Hypothyroidism	3	6.0	5	9.8	
Asthma	4	8.0	3	5.9	
Anemia	1	2.0	1	2.0	
None	31	62.0	33	64.7	
Other/Decline to Answer	1	2.0	3	5.9	
Total time in operating room (minutes), median [IQR]	139.0 [128.0-157.0]		144.5 [126.0-158.0]		0.852
Length of stay (hours), median [IQR]	24.3 [22.3-29.6]		23.4 [21.6-27.5]		0.665
Readiness for discharge (hours), median [IQR]	18.9 [17.5-23.1]		20.6 [17.5-23.8]		0.360

“Perioperative dronabinol administration (5mg, BID) **did not reduce opioid consumption** 24 - 48 hours post-TKA compared to placebo.”

Table 2. Cumulative Opioid Intake, NRS Pain

		Dronabinol (n=51)		Placebo (n=51)		P-value
Opioid Consumption						
	POD 1 (0-24 hrs), median [IQR]	15 [7.5-30]		23.3 [7.5-33.8]		0.320
	POD 2 (24-48 hrs), median [IQR]	15 [7.5-30]		15 [7.5-30]		0.136
	Cumulative (PACU-POD 2), median [IQR]	60.0 [37.5-82.5]		75.0 [45.0-120.0]		0.154
NRS Pain (PACU)	at rest, median [IQR]	0 [0-5]		0 [0-4]		0.547
	at rest, median [IQR]	0 [0-2]		0 [0-4]		0.795
NRS Pain (POD 1)	with movement, median [IQR]	3 [2-5]		4 [2-6]		0.588
	at rest, median [IQR]	2 [0-3]		2 [0-3]		0.834
NRS Pain (POD2)	with movement, median [IQR]	6 [4-8]		7 [4-9]		0.177
	at rest, median [IQR]	0 [0-3]		1 [0-2]		0.889
NRS Pain (POD7)	with movement, median [IQR]	4 [2-7]		5 [3-7]		0.481

References, additional figures, & sources of support



RESULTS

- Both groups reported equal OME opioid use (median=15) at POD2. There was a trend of lower cumulative opioid consumption, but no statistical significance (Table 2).
- Baseline and surgical characteristics were evenly distributed between the two groups (Table 1).
- There was a trend of lower overall pain ratings both at rest and with activity during the 7-day postoperative period in the dronabinol group but no statistical significance.
- There was no statistically significant difference (p=0.582) in desaturation events (Fig. 2) between the two groups, and the ActiLife activity monitor showed that the dronabinol group had higher sleep efficiency and lower instances of wake after sleep onset (WASO).

Figure 2 .Oxygen desaturation events within the first 24 hours

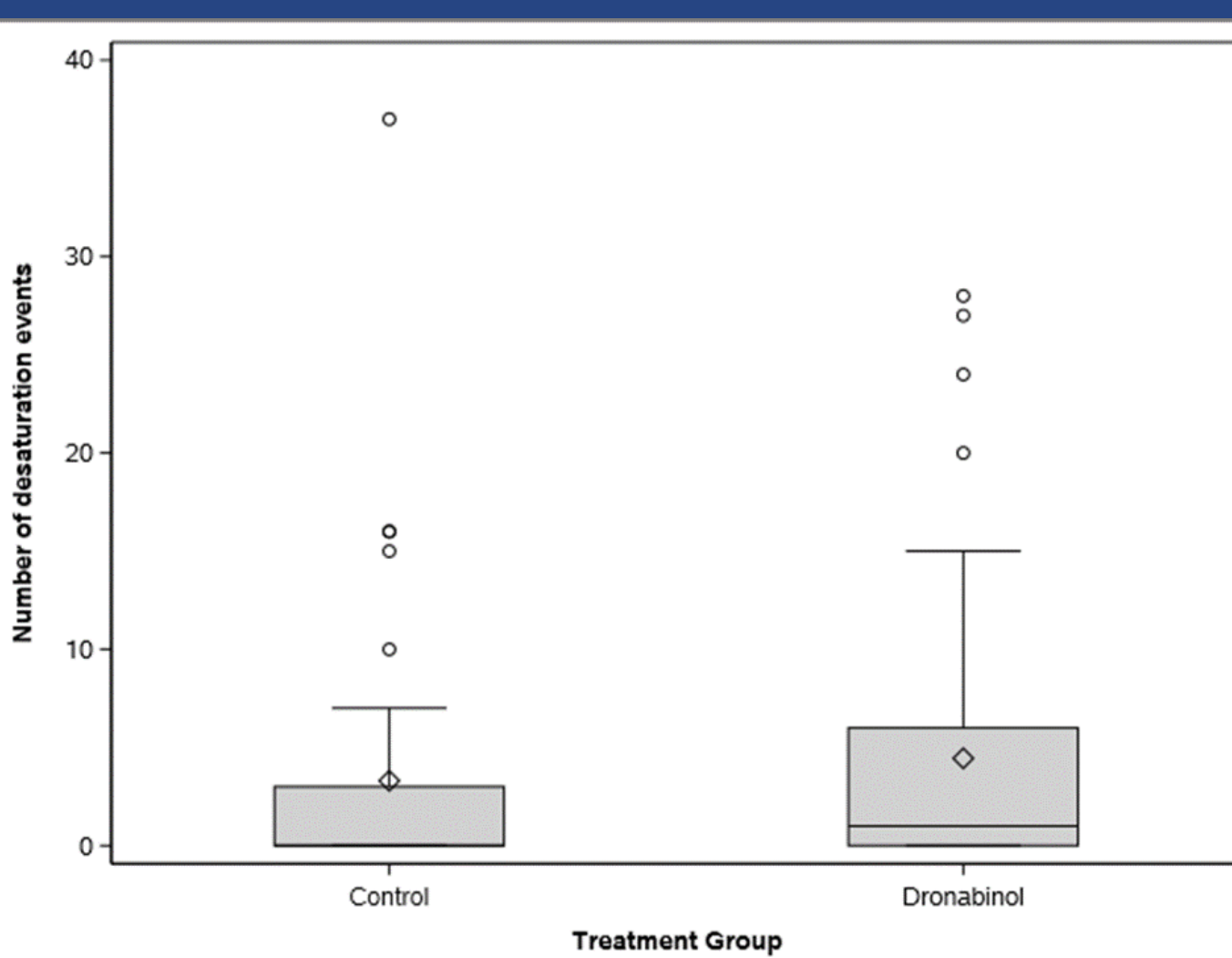


Table 3. Masimo & Actigraphy

Masimo Pulse Oximetry	Dronabinol (n=49)	Placebo (n=45)	P-value
Desaturation events, mean (SD)	4.4 (7.3)	3.3 (6.6)	0.433
Actigraphy*	Dronabinol (n=48)	Placebo (n=48)	
Total sleep time (TST), mean (SD)	562.0 (215.4)	519.6 (211.2)	0.333
Sleep Efficiency**, mean (SD)	88.4 (5.5)	87.1 (6.5)	0.283
Wake after sleep onset (WASO), mean (SD)	69.0 (31.4)	72.2 (42.3)	0.672

*Data average across patients' hospital stay

**>85% signifies having a normal sleep period

DISCUSSION

- ★ Compared to placebo, at the doses administered, no serious side effects were observed and dronabinol did not reduced 24-48 hours opioid requirements after TKA. The quantity and quality of desaturation events during sleep were comparable (Table 3).
- ★ We present prospective data on dronabinol's perioperative effects due to our study's rigorous criteria for sample selection, uniformity of protocols, and controlled settings. Notably, prior to the surgery, the trial included TKA patients who were not currently taking opioids or cannabis.
- ★ More patients with a history of cannabis use or chronic opioid use should be included in future trials, as should examining different doses and dosing regimens of dronabinol.

