Available online on 15.05.2025 at http://jddtonline.info

Journal of Drug Delivery and Therapeutics

Open Access to Pharmaceutical and Medical Research

Open Access Full Text Article

Research Article

Pharmacological Requirements For Intravenous Sedation in Oncological Patients Undergoing Chronic Opioid Analgesic Treatment During Percutaneous Interventional Procedures

Ana Karen Castillo-Desaida [1], María del Rocio Guillén-Nuñez [2*], Ángel Juárez-Lemus [3], Berenice Carolina Hernández Porras [4], Grezzia Isareyda Avellaneda-Peralta [5], Hectór Alberto Arámbula-Morones [6]

1. Pain Management, Instituto Nacional de Cancerología, México;

2. Interventional Pain Management and Palliative Care, Instituto Nacional de Cancerología, México;

3. Interventional Pain Management and Palliative Care, Instituto Nacional de Cancerología, México;

4. Interventional Pain Management and Palliative Care, Instituto Nacional de Cancerología, México;

5. Pain Management, Instituto Nacional de Cancerología, México;

6. Pain Management, Instituto Nacional de Cancerología, México;

Article Info:

Article History:

Received 20 Feb 2025
Reviewed 04 April 2025
Accepted 27 April 2025
Published 15 May 2025

Cite this article as:

Castillo-Desaida AK, Guillén-Nuñez MR, Juárez-Lemus A, Hernández Porras BC, Avellaneda-Peralta GI, Arámbula-Morones HA, Pharmacological Requirements For Intravenous Sedation in Oncological Patients Undergoing Chronic Opioid Analgesic Treatment During Percutaneous Interventional Procedures, Journal of Drug Delivery and Therapeutics. 2025; 15(5):71-77
DOI:
http://dx.doi.org/10.22270/jddt.v15i5.7146

*Address for Correspondence:

María del Rocío Guillen-Nunez, Interventional Pain Management and Palliative Care, Instituto Nacional de Cancerología, Mexico;

Abstract

Objective: To describe the pharmacological requirements of the doses used for fentanyl, propofol and midazolam, during intravenous sedation in oncology patients with chronic opioid analgesic treatment undergoing percutaneous interventional procedures.

Materials and methods: An observational, retrospective, cross-sectional, and descriptive study was conducted after obtaining approval from the Research and Ethics Committee. Information was obtained through the review of clinical records of patients undergoing interventional procedures for oncological pain at the Pain Clinic of the National Cancer Institute between March 1st, 2020, and February 29th, 2024. A descriptive statistical analysis was performed, followed by a bivariate analysis using Chi-square and ANOVA tests to identify the association between chronic opioid analgesic treatment and pharmacological requirements in our population.

Results: A total of 494 patients were studied, of whom 68.6% were female (n = 339) and 31.4% were male (n = 155). 99% of the patients were between 45 and 70 years of age, with a mean age of 57.66 years. The most frequently identified oncological diagnoses in our population were: breast cancer (20.4% of cases) (n = 101), multiple myeloma (14.2% of cases) (n = 70), and cervical cancer (12.6%) (n = 62).

Regarding opioid analgesic treatment for pain control prior to the interventional procedure (n=494), 438 patients (88.6%) were identified as receiving opioid treatment (average Morphine Equianalgesic Daily Dose:56 mg), while only 56 patients (11.3%) were not. We found a trend toward greater use of fentanyl during intravenous sedation in patients without chronic opioid use compared to the group of patients with chronic opioid use. With respect to midazolam and propofol, similar requirements were found between the groups. No significant correlation was identified between the dose of intravenous sedation drugs and chronic drug use.

Conclusions: There was no correlation on the average doses of midazolam, fentanyl and propofol in patients with chronic pain treatment who underwent percutaneous interventional procedures, regardless of whether they were on analgesic treatment or not. Prospective studies are required to corroborate these results.

Keywords: Opioids, percutaneous interventional procedures, cancer pain, intravenous sedation.

INTRODUCTION

In 2015, there were 17.5 million new cases of cancer and 8.7 million related deaths. In these patients, the prevalence of pain (33–64%) is closely related to the clinical stage of the cancer, affecting their quality of life. [1]

Pain represents a health problem; in its acute form, it functions as a natural protective signal from the body; however, when it becomes chronic, it can become a health condition in itself. [2,3]

In oncological settings, pain is one of the most frequently reported symptoms, and its prevalence increases in advanced or metastatic disease and often persists despite curative treatment. It is estimated that approximately half of cancer patients may experience pain, of which 38% classify it as moderate to severe, with

an average intensity of 6.4 on the NRS (Numeric Rating Scale). The World Health Organization (WHO) pain management ladder is one of the main elements for the treatment of cancer pain, providing relief to up to 75–90% of patients. Opioid analgesics are considered the cornerstone of treatment for moderate to severe pain. [4,5]

However for patients with pain refractory to conventional therapy or intolerable side effects, interventional strategies are available, providing an option for achieving pain control. Patients undergoing this type of approach generally receive drugs for mild to moderate intravenous sedation, which provides a better experience during the procedure. [6,7] However, transanesthetic requirements may be higher in patients receiving chronic opioid treatment, which could be attributed to the clinical stage of the disease or to analgesic tolerance effects, which may contribute to increased drug consumption during intravenous sedation. [8,9]

Describing the drug requirements during intravenous sedation in patients with pain and prior analgesic treatment will provide a guideline for understanding their average requirements compared to those without pre-procedural analgesic treatment for pain, allowing us to regulate therapeutic management in this healthcare setting.

MATERIALS AND METHODS

An observational, retrospective, cross-sectional, and descriptive study was conducted with information obtained through a review of medical records of patients with cancer pain who underwent percutaneous interventional pain relief procedures at the Pain Clinic of the National Cancer Institute from March 1, 2020 to February 29, 2024.

Data Analysis

After obtaining approval from the Research Ethics Committee, the medical records were reviewed, obtaining the required information and recording it in an Excel database. For the statistical analysis, we used IBM SPSS Statistics 25.0, performing a descriptive statistical analysis, identifying the characteristics of the study population, obtaining frequencies, means, medians, and percentages. We performed a bivariate analysis using chi-square tests and ANOVA to identify the association between chronic opioid analgesic treatment and pharmacological requirements during intravenous sedation in patients undergoing percutaneous interventional pain relief procedures.

Inclusion Criteria

-Patients with pain who received care at the INCan Pain Clinic between March 1, 2020, and February 29, 2024 and who underwent a percutaneous interventional procedure for pain control.

Exclusion Criteria

- Patient undergoing interventional procedures for pain management without sedation.

-Patient's records lack all required information.

Elimination Criteria

-Not applicable.

RESULTS

A total of 494 patients were studied, of whom 68.6% were female (n = 339) and 31.4% were male (n = 155).

Ninety-five percent of the patients were between 45 and 70 years of age, with a mean age of 57.66 years.

The most frequently identified oncological diagnoses in our population were: breast cancer (20.4% of cases) (n = 101), multiple myeloma (14.2% of cases) (n = 70), and cervical cancer (12.6%) (n = 62). (Table 1)

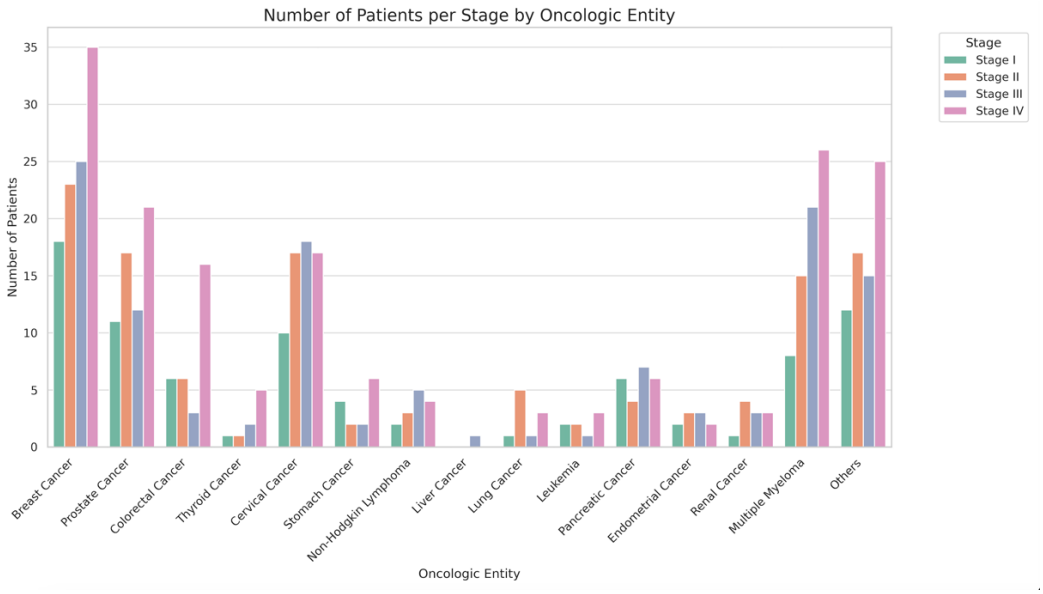
Table 1: Oncologic Pathology

ONCOLOGIC PATHOLOGY	n	%
Breast cancer	101	20.4
Prostate cancer	61	12.3
Colorectal cancer	31	6.3
Thyroid cancer	9	1.8
Cervical cancer	62	12.6
Stomach cancer	14	2.8
Non-Hodgkin lymphoma	14	2.8
Liver cancer	1	0.2
Lung cancer	10	2.0
Leukemia	8	1.6
Pancreatic cancer	23	4.7
Endometrial cancer	10	2.0
Renal cancer	11	2.2
Multiple myeloma	70	14.2
Others	69	14.0
TOTAL	494	100

Source: Prepared by the author, Dr. Ana Karen Castillo Desaida, Algology, INCAN.

Regarding oncological entities by clinical stage, we found that the largest proportion of patients undergoing interventional procedures are in advanced clinical stages. (Graph number 1)

Graph number 1



Source: Prepared by the author, Dr. Ana Karen Castillo Desaida, Algology, INCAN

The most prevalent oncological pathologies in our population were also more frequently associated with mixed-type pain and/or pain with a bone component. (Table 2)

Table 2: Cross-tabulation: Pathology and type of pain

Pathology	Somatic nociceptive	Visceral nociceptive	Peripheral neuropathic	Central neuropathic	Bone pain	Mixed (Somatic + Neuropathic)	Mixed (Visceral + Neuropathic)	Mixed (Neuropathic + Bone pain)
Breast cancer	7	3	8	9	0	47	0	27
Prostate cancer	0	4	0	0	12	20	0	25
Colorectal cancer	1	8	0	0	1	2	0	0
Thyroid cancer	2	0	1	0	1	4	0	0
Cervical cancer	5	27	0	0	0	4	0	0
Stomach cancer	0	12	0	0	0	2	0	0
Non-Hodgkin lymphoma	0	0	0	0	0	3	0	0
Liver cancer	0	1	0	0	0	0	0	0
Lung cancer	1	0	0	0	2	4	0	3
Leukemia	0	0	0	0	0	0	0	0
Pancreatic cancer	2	0	0	0	3	2	0	2
Endometrial cancer	0	4	1	0	0	1	0	0
Kidney cancer	1	1	0	0	0	3	0	1
Multiple myeloma	1	0	2	0	43	9	1	5
Others	7	23	7	2	1	21	1	5

Pearson's Chi-Squared Test (p 0.000) *Source: Prepared by the author, Dr. Ana Karen Castillo Desaida, Algology, INCAN.*

Regarding the opioid analgesic treatment patients received for pain control prior to the interventional procedure (n = 494), 438 patients (88.6%) were receiving opioid treatment, and only 56 patients (11.3%) were not taking an opioid analgesic as part of their analgesic management.

We found that 53% (n = 262) of the study population used gabapentinoids, and 47.2% (n = 233) used paracetamol. About the duration of pharmacological treatment, the average was 18 months (Table 3).

Table 3. Type of chronic pain treatment

Total sample		N=494	100%
		n	%
Type of drugs	Opioids	438	88.6
	NSAIDs	82	16.6
	COX-2 inhibitors	33	6.7
	Gabapentinoids	262	53
	Tricyclic antidepressants	50	10.1
	SSRIs	22	4.4
	Simple analgesics	233	47.2
	Topical therapy	11	2.2
	Anticonvulsants	7	1.4
	Antispasmodics	9	1.8
		Values	
Pain therapy (months)	Minimum	1	
	Maximum	144	
	Average	18.05	
	SD	21.61	

Source: Prepared by the author, Dr. Ana Karen Castillo Desaida, Algology, INCAN.

The most frequent interventional procedures were epidural steroid depot + local anesthetic (ESD+ LA) in 58.4% (n = 271) and autonomic nervous system (ANS) block in 24.8% (n = 123). (Table 4).

Table 4: Therapies and guides

Total sample		N=494	100%
		n	%
Number of interventional techniques per patient	One	394	79.8
	Two	96	19.4
	Three	4	0.8
Types of Interventional Approaches	Radiofrequency	72	14.6
	ESD + LA	271	58.4
	Prolotherapy	3	0.6
	Neurolytic	33	6.7
	Cementation	96	19.4
	ANS blockade	123	24.8
Number of guides	One	475	96.2
	Two	19	3.8
Types of guides	Fluoroscopy	378	76.5
	CT	110	22.3
	USG	25	5

Source: Prepared by the author, Dr. Ana Karen Castillo Desaida, Algology, INCAN.

The most commonly used drug for intravenous sedation was fentanyl, in 99.4% (n = 491) of patients with a mean dose of 166.79 mcg; the second most commonly used was propofol, in 88.1% (n = 435) of cases with a mean dose of 99.61 mg/l; and finally, midazolam, in 68% of patients undergoing interventional procedures (n = 336), for which the mean dose was 1.31 mg. The mean sedation time was 58 minutes.

Table 5: Drugs and time during sedation

Total sample		N=494	100%
		N	%
Drugs per patient	One	12	2.4
	Two	196	39.7
	Three	286	57.9
Type of drug	Midazolam	336	68
	Fentanyl	491	99.4
	Propofol	435	88.1
		Value	
Midazolam (mg)	Minimum	0.5	
	Maximum	5	
	Average	1.31	
	SD	0.78	
Fentanyl (mcg)	Minimum	25	
	Maximum	525	
	Average	166.79	
	SD	77.63	
Propofol (mcg)	Minimum	10	
	Maximum	500	
	Average	99.61	
	SD	76.58	
Sedation time (min)	Minimum	2	
	Maximum	180	
	Average	58.07	
	SD	24.24	

Source: Prepared by the author, Dr. Ana Karen Castillo Desaida, Algology, INCAN.

The average MEDD (Morphine Equianalgesic Daily Dose) in patients with chronic opioid use was 56 mg.

When comparing patients with chronic opioid use with those without, a trend toward higher fentanyl requirements during intravenous sedation was observed in the group without chronic opioid use. However, midazolam and propofol requirements were similar in both groups.

No statistically significant differences were found that would allow establishing a correlation between chronic opioid use and the required doses of drugs used for intravenous sedation during percutaneous interventional analgesic procedures.

On the other hand, the baseline NRS (Numeric Rating Scale) was higher in patients with chronic opioid use, which may be related to several factors. First, the proposal for an interventional procedure is carried out most of the time in the subpopulation of patients with pain that is difficult to control or refractory to conventional treatments. Second, as we observed in this study, 59% of patients (n=292) were in an advanced clinical stage of the disease (Stage III = 120 and Stage IV = 172), which, according to various publications, generates a greater likelihood of experiencing pain

Table 6: T Comparison of opioid consumption prior to interventional procedure by patient group

	OPIOIDS	N	Average	SD	Significance
MIDAZOLAM REQUIREMENT	Chronic Use	287	1.29	0.77	0.183
	No prior opioid use	48	1.45	0.86	
FENTANYL REQUIREMENT	Chronic Use	436	164.97	76.74	0.129
	No prior opioid use	55	181.82	83.54	
PROPOFOL REQUIREMENT	Chronic Use	393	99.90	76.69	0.932
	No prior opioid use	43	98.84	79.71	
SEDATION TIME (MINUTES)	Chronic Use	438	58.14	24.36	0.518
	No prior opioid use	56	60.36	22.50	
PREVIOUS NRS	Chronic Use	438	5.61	2.08	0.003*
	No prior opioid use	56	4.73	2.15	
NRS POSTPROCEDURE	Chronic Use	438	2.46	2.06	0.105
	No prior opioid use	56	1.98	2.05	
MEDD	Chronic Use	438	56.64	37.86	0.000*
	No prior opioid use	56	0	0	
CHRONIC PAIN TREATMENT TIME (MONTHS)	Chronic Use	438	18.8	22.6	0.000*
	No prior opioid use	56	11.9	8.8	

The average requirements for midazolam and propofol are expressed in milligrams and for fentanyl in micrograms.

Source: Prepared by the author, Dr. Ana Karen Castillo Desaida, Algology, INCAN.

DISCUSSION:

The present study focused on describing and quantifying the pharmacological requirements for intravenous sedation in cancer patients undergoing percutaneous interventional procedures for pain control. Our findings provide relevant data on the doses used and their possible relationship with chronic opioid use.

A study conducted in Amsterdam compared different sedation regimens applicable to fluoroscopy-guided percutaneous ablation procedures.[10] This study used a dual regimen with midazolam and fentanyl, with mean doses of 4.5 ± 2.1 mg and 205 ± 102 mcg, respectively. Similarly, Simopoulos et al., in Massachusetts, reported the average use of 2.4 mg of midazolam and 125 mcg of fentanyl. [11]

In our study, the average doses administered were lower: 1.31 ± 0.71 mg for midazolam, 166.79 ± 77.63 mcg for fentanyl, and 99.61 ± 76.58 mg for propofol. It is important to note that three-drug were used in 57.9% of cases, which may influence the reduction in individual doses of each drug when compared with previously mentioned literature.

The average sedation time in our study was 58.07 ± 24.24 minutes, lower than that reported in the Amsterdam study (101 ± 50 minutes). This may be related to the technical knowledge and skill of the interventional physicians who performed these procedures or the anatomical difficulty of the approaches included in the studies described. A finding of great interest was that patients without chronic opioid use had higher fentanyl requirements during sedation. Pre- and post-procedure pain scores assessed by the Numeric Rating Scale (NRS) were higher in patients with chronic opioid use, this phenomenon could be explained by central sensitization mechanisms, a pathophysiological process that increases the reactivity of the central nervous system to painful stimuli, even in the presence of treatment with multiple analgesic drugs. [12,13]

Patients with chronic opioid use often present refractory pain, which motivates the consideration of interventional procedures to optimize the control of these pain syndromes. In addition, these may be less effective due to the distorted anatomy derived from the progression of the oncological disease or from the treatments implemented to combat the neoplasia. [14]

Besides, advanced stages of cancer could affect the patient's general condition, including their ability to metabolize drugs and contribute to lower requirements. [15]

According to the results obtained, we interestingly observed that the pharmacological requirements for intravenous sedation for a percutaneous interventional analgesic approach do not vary independently of prior opioid analgesic use. This is completely different from

what has been published by different authors, as points to consider for the transanesthetic management of cancer patients receiving chronic analgesic treatment. [16]

CONCLUSIONS

In our patient sample, no direct association was found between chronic opioid use and increased pharmacological requirements during the transanesthetic period. There was no correlation on the average doses of midazolam, fentanyl and propofol in patients with chronic pain treatment who underwent percutaneous interventional procedures, regardless of whether they were on analgesic treatment or not. These findings underscore the importance of individualizing anesthetic management, considering multiple factors that may influence drug requirements beyond a history of chronic opioid use.

In this context, prospective studies are essential to further understand relevant variables, such as the impact of anxiety during the transanesthetic period to optimize therapeutic strategies.

Conflicts of interest: All of the authors have stated that no organization provided financial support for the work they submitted

Author Contributions: All authors have equal contribution in the preparation of manuscript and compilation.

Source of Support: Nil

Funding: The authors declared that this study has received no financial support.

Data Availability Statement: The data presented in this study are available on request from the corresponding author.

Ethical approval: Not applicable

REFERENCES

1. Magee D, Bachtold S, Brown M, Farquhar-Smith P. Cancer pain: Where are we now? Pain Manag. 2018 Jan 1;9(1):63-79. https://doi.org/10.2217/pmt-2018-0031 PMid:30516438

2. (PDF) Consenso Mexicano de Manejo de Dolor por Cáncer. Available from: https://www.researchgate.net/publication/303874243_Consenso_Mexicano_de_Manejo_de_Dolor_por_Cancer

3. Van Den Beuken-Van Everdingen MHJ, Hochstenbach LMJ, Joosten EAJ, Tjan-Heijnen VCG, Janssen DJA. Update on Prevalence of Pain in Patients With Cancer: Systematic Review and Meta-Analysis. J Pain Symptom Manage. 2016;51(6):1070-1090.e9. https://doi.org/10.1016/j.jpainsymman.2015.12.340 PMid:27112310

4. George B, Minello C, Allano G, Maindet C, Burnod A, Lemaire A. Opioids in cancer-related pain: current situation and outlook. Supportive Care in Cancer 2019 27:8 [Internet]. 2019;27(8):3105-18. https://doi.org/10.1007/s00520-019-04828-8 PMid:31127436

5. Russo MM, Sundaramurthi T. An Overview of Cancer Pain: Epidemiology and Pathophysiology. Semin Oncol Nurs [Internet]. 2019 ;35(3):223-8. https://doi.org/10.1016/j.soncn.2019.04.002 PMid:31085106

6. Kaye AD, Jones MR, Viswanath O, Candido KD, Boswell M V, Soin A, et al. Guidelines ASIPP Guidelines for Sedation and Fasting Status of Patients Undergoing Interventional Pain Management Procedures. 2019; Available from: www.painphysicianjournal.com

7. Practice guidelines for sedation and analgesia by non-anesthesiologists: An updated report by the American Society of Anesthesiologists task force on sedation and analgesia by non-anesthesiologists. Anesthesiology 2002;96(4):1004-17. https://doi.org/10.1097/00000542-200204000-00031 PMid:11964611

8. Dsouza RS, Warner MA, Olatoye OO, Langford BJ, Bruns DL, Schroeder DR, et al. Perioperative Opioid Consumption and Clinical Outcomes in Surgical Patients with a Pre-Existing Opioid-Based Intrathecal Drug Delivery System. Anesth Analg. 2022;134(1):35. https://doi.org/10.1213/ANE.0000000000005662 PMid:34260427 PMCid:PMC8678135

9. Silverman JE, Gulati A. An overview of interventional strategies for the management of oncologic pain. Pain Manag. 2018;8(5):389-403. https://doi.org/10.2217/pmt-2018-0022 PMid:30320541

10. Puijk RS, Ziedses Des Plantes V, Nieuwenhuizen S, Ruarus AH, Laurien, Vroomen GPH, et al. Propofol Compared to Midazolam Sedation and to General Anesthesia for Percutaneous Microwave Ablation in Patients with Hepatic Malignancies: A Single-Center Comparative Analysis of Three Historical Cohorts. Cardiovasc Intervent Radiol. 2019;42:1597-608. https://doi.org/10.1007/s00270-019-02273-y PMid:31243542 PMCid:PMC6775535

11. Simopoulos T, Leffler D, Barnett S, Campbell D, Lian SJ, Gill JS. Prospective Assessment of Pain and Comfort in Chronic Pain Patients Undergoing Interventional Pain Management Procedures. Pain Medicine. 2018;19(2):336-47. https://doi.org/10.1093/pm/pnx064 PMid:28431040

12. French R, Fellow P, Mchugh MD, Lake E, Scott JM, Margo J, et al. A Systematic Review of Care Needs for Surgical Patients with Chronic Opioid Use Chair for Nursing Education, Professor of Nursing Term Chair in Nursing and Health Policy, Professor of Nursing and Sociology HHS Public Access. Vol. 29, Medsurg Nurs. 2020.

13. Ji RR, Nackley A, Huh Y, Terrando N, Maixner W. Neuroinflammation and central sensitization in chronic and widespread pain. Anesthesiology. 2018;129(2):343. https://doi.org/10.1097/ALN.0000000000002130 PMid:29462012 PMCid:PMC6051899

14. Poço Gonçalves J, Veiga D, Araújo A. Chronic pain, functionality and quality of life in cancer survivors. Br J Pain. 2020;15(4):401. https://doi.org/10.1177/2049463720972730 PMid:34840788 PMCid:PMC8611292

15. Aboel Dahab A, El-Hag D, Moutamed GM, Aboel Dahab S, Abuknesha R, Smith NW. Pharmacokinetic variations in cancer patients with liver dysfunction: applications and challenges of pharmacometabolomics. Cancer Chemother Pharmacol. 2016;78(3):465-89. https://doi.org/10.1007/s00280-016-3028-4 PMid:27061417

16. Burns SL, Majdak P, Urman RD. Perioperative and Periprocedural anesthetic management of opioid tolerant patients and patients with active and medically treated opioid use disorder. Vol. 35, Current Opinion in Anaesthesiology. Lippincott Williams and Wilkins; 2022. p. 514-20. https://doi.org/10.1097/ACO.0000000000001157 PMid:35788122 PMCid:PMC9308736