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Implementation of a perioperative ketamine shortage mitigation strategy

Julie Dibridge[1], Jennifer Holder-Murray[2], Susan Skledar[3], Kathirvel Subramaniam[4], Stephen A Esper[4]

[1]Department of Pharmacy, University of Pittsburgh Medical Center, [2]Department of Pharmacy and Therapeutics, University of Pittsburgh School of Pharmacy, [3]Department of Surgery, University of Pittsburgh School of Medicine, [4]Department of Anesthesiology and Perioperative Medicine, University of Pittsburgh School of Medicine, Pittsburgh, PA, USA

Letter to the Editor

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Corresponding author:
Stephen A. Esper, M.D., M.B.A.
Department of Anesthesiology and Perioperative Medicine, University of Pittsburgh School of Medicine, 200 Lothrop Street, Pittsburgh, PA 15213, USA
Tel: +1-4126476644
Fax: +1-4126476290
Email: espersa@upmc.edu
ORCID: https://orcid.org/0000-0003-4839-8030

Medication shortages are an ongoing obstacle for clinicians in the United States [1]. The American Society of Health-System Pharmacists has established guidelines on managing drug product shortages and recommends healthcare worker education to mitigate and prevent drug shortages [1]. In the face of drug shortages, inventory control personnel and multidisciplinary healthcare teams should consider therapeutic equivalents and alternatives to critical medications to avoid inadvertent harm to or inferior treatment for patients [1,2].

The role of ketamine in Enhanced Recovery Protocols (ERP) has been well described in the literature [3]. There is evidence that ketamine helps to attenuate central sensitization and hyperalgesia, thus reducing opioid tolerance [4] and making it effective in reducing postoperative pain. To minimize opioid use, surgeons and anesthesiologists aim to provide multimodal analgesia through parenteral and enteral pharmacologic adjuncts and alternatives to opioids. The purpose of this study was to evaluate the intravenous ketamine waste associated with two different ketamine dosage preparation methods.

The project was approved by the Quality and Safety Committee (#869) at the University of Pittsburgh Medical Center. This is a retrospective analysis of the wasted drug amounts of ketamine for patients undergoing complex abdominal surgery (such as colectomy, pancreas resection, liver resection, or laparotomy) via an ERP from January 2017 to March 2018 at a single university medical center. Patients were excluded if the patient had more than one surgery within 24 h, did not receive intraoperative ketamine, or received a formulation of ketamine intraoperatively that deviated from the standard medication supply with concentration of 10 mg/ml for induction and 2 mg/ml for infusion.

Retrospective chart review was used to gather data on bolus dose upon induction of anesthesia (0.75 mg/kg), infusion dose (0.4 mg/kg/h), and total intraoperative dose of ketamine. Standard ketamine concentration supplied for all induction doses were 200 mg/20 ml vials (10 mg/ml), of which the calculated dose was administered while the remaining amount was wasted. Standard ketamine concentration supplied for maintenance intraoperative infusion was 200 mg in 100 ml (2 mg/ml) normal saline solution (NSS). Based on the standard ketamine formulations supplied and the actual patient consumption, drug waste was calculated. Data are presented as mean ± SD.

During the 14 month period, 988 surgeries utilizing ERPs occurred, of which 318 were excluded. For the remaining 670 surgeries done with ERPs, a total of 95,140 mg of intraoperative ketamine was consumed during the induction and maintenance infusions for all 670 patients (Table 1). The mean bolus dose on induction, taken from a 200 mg vial of ketamine, was 46 ± 18 mg. The mean intraoperative infusion total dose administered from a 200 mg in 100 ml NSS bag of ketamine was 96 ± 58 mg.

Table 1. Ketamine Waste Analysis

(n = 670)	Former state	Current state	Difference between former and current
Total intraoperative dose per patient (mg)*	142		
Induction, mean dose	46 ± 18		
Infusion, mean dose	96 ± 58		
Induction, mean waste	153 ± 18	55 ± 17	98 ± 17.5
Infusion, mean waste	115 ± 48	51 ± 28	64 ± 38
Total ketamine induction waste	101,582 (508 vials)	36,642 (184 vials)	65,660 (328 vials)
Total ketamine infusion waste	76,969 (385 vials)	34,269 (172 vials)	42,880 (214 vials)
Total ketamine waste†	178,551 (893 vials)	70,911 (356 vials)	108,540 (542 vials)
Total cost waste	$11,609	$4,628	$7,046

*Total intraoperative dose includes bolus dose upon induction of anesthesia (0.75 mg/kg), infusion dose (0.4 mg/kg/h), and total intraoperative dose of ketamine. †The standard ketamine formulations supplied and the actual patient consumption.

Medication waste was estimated to total 178,551 mg (266 mg/patient). Induction dose waste alone was estimated to exceed 101,582 mg of ketamine or 153 mg ± 18 mg per patient. Infusion waste was estimated to exceed 76,969 mg or 115 mg ± 48 mg per patient.

After identifying an alternative suited our institutional needs, ketamine 100 mg in 10 ml (10 mg/ml) syringes were procured to be utilized for both induction and maintenance intraoperative infusion. The medication waste was estimated to be 268 mg/patient but decreased the mean total ketamine consumption to 106 mg/patient. The mean ketamine waste avoidance per patient was calculated as 162 mg/patient, resulting in 108,540 mg of potential ketamine waste avoidance in our patient cohort of 670 patients. This is a 61% reduction in waste when compared to the estimated medication waste of 178,551 mg, resulting in an estimated cost savings of $7,046.

Based on the results of this analysis, our institution standardized dispensing practices to include 100 mg of ketamine hydrochloride in 10 ml (10 mg/ml) for induction bolus and maintenance infusion with an electronic syringe smart pump. Amidst the national shortage, we identified two 503B compounders to supply us with ketamine in the form of a 100 mg (10 mg/ml) syringe. 503B compounders are drug compounding facilities established by the federal Drug Quality and Security Act in the United States. These facilities prepare personalized compounded medications for patients and for use by physicians. When pre-filled ketamine syringes are not available, ketamine is compounded pursuant to patient specific order under sterile conditions in our operating room satellite pharmacy's Contained Aseptic Isolator.

The surgical protocol at our university hospital includes an induction dose of 0.75 mg/kg followed by an infusion ranging between 0.4 and 0.6 mg/kg depending on the type of ERPs ordered [5]. There is also an agreement among our experts that low dose or sub-anesthetic doses of ketamine, when added as an adjunct to general anesthesia reduces postoperative pain and opioid requirements [4]. Opioid sparing effects of ketamine may be masked when the drug is used in small doses (0.15 mg/kg) against the background of multimodal or epidural analgesia [5]. It is known that nociceptive and inflammatory signals are generated throughout surgery and after the procedure, to prevent pathologic pain, in an attempt to reduce sensitization of central and peripheral pain pathways [5]. Ketamine administration can also lead to a longer time spent in the post anesthesia care unit, longer time to patient discharge secondary to less controlled pain, and increased opioid requirements.

The primary limitation of the study was that potential medication waste avoidance was calculated and did not consider actual medication savings as we utilized a retrospective comparative analysis method that did not include patients who received the alternative preparation of ketamine. Lastly, we only predicted the amount of ketamine saved using the current institutional supplier, due to the use of our 503B compounder and the intermittent availability of ketamine syringes nationally.

Clinicians continue to experience supply challenges for numerous medications. We conclude that the utilization of alternative concentration ketamine 10 mg/ml 10 ml syringes could reduce both overall and average ketamine waste per case. Our study shows that a multidisciplinary approach to analyze institutional best practices assisted in the standardization of shortage mitigation approaches related to ketamine without restricting patient access to this drug.

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Conflicts of Interest

No potential conflict of interest relevant to this article was reported.

Author Contributions

Julie Dibridge (Conceptualization; Data curation; Formal analysis; Writing – original draft; Writing – review & editing)
Jennifer Holder-Murray (Writing – review & editing)
Susan Skledar (Investigation; Supervision; Writing – review & editing)
Kathirvel Subramaniam (Supervision; Writing – review & editing)
Stephen A Esper (Conceptualization; Supervision; Writing – original draft; Writing – review & editing)

ORCID

Julie Dibridge, https://orcid.org/0000-0002-7132-2475
Jennifer Holder-Murray, https://orcid.org/0000-0003-0030-9297
Susan Skledar, https://orcid.org/0000-0002-3961-2624
Kathirvel Subramaniam, https://orcid.org/0000-0002-4647-1372
Stephen A Esper, https://orcid.org/0000-0003-4839-8030

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