

ORIGINAL RESEARCH ARTICLE

Feasibility of a Ketamine Anesthesia Package in Support of Obstetric and Gynecologic Procedures in Kenya When No Anesthetist is Available

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Charles O. Masaki^{1,2}, Jennifer Makin^{1,3}, Sebastian Suarez^{1*}, Gabriella Wuyke^{1,4}, Ayla N. Senay^{1,5}, Daniela Suarez-Rebling¹, Javan Imbamba⁴, Jackton Juma⁴, Moytrayee Guha^{1,4} and Thomas F. Burke^{1,2,4,6}

Division of Global Health and Human Rights, Department of Emergency Medicine, Massachusetts General Hospital, Boston, MA, USA¹; Harvard T.H. Chan School of Public Health, Boston, MA, USA²; SUNY Upstate Medical School, Department of Obstetrics and Gynecology, Syracuse, NY³; African Institute for Health Transformation at Sagam Community Hospital, Luanda, Kenya⁴; Albany Medical College, Albany, NY, USA⁵; Harvard Medical School, Boston, MA, USA⁶

*For Correspondence: Email: ssuarezarate@mgh.harvard.edu; Phone: +1 857-294-3848

Abstract

The objective was to assess the feasibility and safety of the ‘Every Second Matters for Emergency and Essential Surgery – Ketamine’ (ESM-Ketamine) package in support of obstetric and gynecologic emergency and essential surgery when no anesthetist is available. A consecutive case series was conducted in twelve hospitals across five severely resource-limited counties in Kenya. 530 women underwent obstetric or gynecological operative procedures supported by non-anesthetist clinicians using the ESM-Ketamine package between November 1, 2013 and September 30, 2017. Main outcomes included reasons for ESM-Ketamine activations and ketamine-related adverse events. There were two (0.4%) prolonged (>30 seconds) oxygen desaturations below 92%. Brief oxygen desaturations (<30 seconds) below 92% occurred in 15 (2.8%) cases and 113 (21.3%) were administered diazepam to treat hallucinations or agitation. There were no ketamine-related deaths or injuries. The ESM-Ketamine package appears feasible and safe for use in support of obstetric and gynecologic surgeries when no anesthetist is available. (*Afr J Reprod Health* 2019; 23[1]: 37-45).

Keywords: Obstetrics, Gynecology, Anesthesia, Ketamine, low-resource settings

Résumé

L’objectif était d’évaluer la faisabilité et la sécurité du paquet «Chaque seconde compte pour la chirurgie urgente et essentielle – L’ensemble Kétamine» (CSC-Kétamine) à l’appui de l’urgence obstétricale et gynécologique et de la chirurgie essentielle en l’absence de l’anesthésiste. Une série de cas consécutifs a été menée dans douze hôpitaux du Kenya, dans cinq comtés aux ressources limitées. Entre le 1er novembre 2013 et le 30 septembre 2017, 530 femmes ont subi une intervention chirurgicale gynécologique ou obstétricale soutenue par des cliniciens non anesthésistes, à l’aide du progiciel CSC-Kétamine. Les principaux résultats comprenaient les raisons des activations de la Kétamine et des événements indésirables liés à la kétamine. Deux (0,4%) désaturations prolongées en oxygène (> 30 secondes) étaient inférieures à 92%. Des désaturations brèves en oxygène (<30 secondes) inférieures à 92% sont survenues dans 15 cas (2,8%) et 113 (21,3%) ont reçu du diazépam pour traiter des hallucinations ou une agitation. Il n’y a eu aucun décès ou blessure lié à la kétamine. Le progiciel CSC-Kétamine semble utilisable et sans danger pour les chirurgies obstétricales et gynécologiques lorsqu’aucun anesthésiste n’est disponible. (*Afr J Reprod Health* 2019; 23[1]: 37-45).

Mots-clés: Obstétrique, gynécologie, anesthésie, kétamine, paramètres à faibles ressources

Introduction

Approximately five billion people world-wide do not have access to emergency and essential surgery in a timely fashion¹⁻³. Lack of safe and affordable anesthesia services is a primary barrier¹. In resource scarce settings, anesthesia services are often unavailable despite functional operating theatres, adequate surgical equipment and staff capable of performing and supporting surgical procedures^{4,5}.

Kenya's northern and eastern counties are chronically severely stressed due to poverty, drought, food insecurity, violence and large populations of Somali and South Sudanese refugees⁶. In these settings, lack of anesthesia services is often a critical barrier to life-saving and life-improving surgical procedures^{7,8}. In 2017, the World Federation of Societies of Anaesthesiologists (WFSA) reported that Kenya has 0.44 anesthetists per 100,000 population overall⁹. However, since anesthetists are unevenly distributed throughout the country, large regions have poor or no coverage of anesthesia services¹⁰. Most hospitals in the northern and eastern regions do not have adequate access to anesthesia services.

Lack of access to obstetric and gynecologic operative procedures, especially cesarean sections, is associated with adverse maternal and newborn health^{7,11,12}. While the World Health Organization (WHO) recommends that optimal cesarean section rates should be about 19%, the rates are less than 1% across several regions of Kenya^{4,13}. For example, the scarcity of anesthesia services in Mandera County, located in northern Kenya, contributes to a cesarean section rate near zero percent and a maternal mortality ratio (3,795 maternal deaths per 100,000 live births) among the worst in the world¹⁴. This statistic demonstrates the disproportionate impact across the country, where the average maternal mortality is estimated as 488 maternal deaths per 100,000 live births⁴.

To address the anesthesia gap within these low resource regions of Kenya, our team previously designed the 'Every Second Matters for Emergency and Essential Surgery – Ketamine'

(ESM-Ketamine) package¹⁵. The ESM-Ketamine package is an evidence-based protocol on which non-anesthetist providers are trained to support emergency and essential operative procedures when no anesthetist is available. Ketamine is an ultra-low-cost analgesic, amnesic, and anesthetic dissociative drug that has been used safely worldwide for more than 50 years¹⁶. Ketamine is especially attractive for use in resource-scarce settings because it is inexpensive, readily available, preserves cardiorespiratory functions, has a wide safety margin, and does not require anesthesia machines¹⁶⁻¹⁸. However, the use of ketamine in resource-limited settings has not been integrated into health systems in an organized fashion¹⁵. The objective of this study was to assess the feasibility and safety of the ESM-Ketamine package in support of obstetric and gynecologic operative procedures in severely resource-scarce settings in Kenya, when no anesthetist was available.

Methods

Health Directors from five severely resource-limited counties in Kenya (Siaya, Homa Bay, Garissa, Mandera, and Wajir) were invited to participate in implementation of the ESM-Ketamine package. The five counties included in this study are home to approximately 5 million people. In these regions, poor access to basic healthcare, including anesthesia services, means that women's reproductive health needs are often not met^{14,19}.

Participating County Health Directors and their Health Management Teams selected county and sub-county hospitals that were designated to provide operative care but had limited access to anesthesia services. Requirements for facility selection included: a functional operating theatre with continuous oxygen supply, adequate surgical equipment, peri-operative services, and doctors capable of performing emergency cesarean sections and other common emergency surgical procedures. The Managing Director of each participating hospital selected two or more mid-level or higher-level practitioners for ESM-

Ketamine training, including clinical officers, medical officers (doctors), and nurses.

ESM-Ketamine training took place at the African Institute for Health Transformation (AIHT) at Sagam Community Hospital, Luanda, Kenya. The ESM-Ketamine package consists of an intensive competency-based 5-day training program, a defined ESM-Ketamine kit, wall charts and pocket checklists¹⁵. Training on ESM-Ketamine was led by Kenyan master trainer anesthetists and clinical officers. The training included hands-on participation during obstetric and gynecological surgical cases performed in the operating theatre, as well as didactics on ketamine pharmacology, patient monitoring, documentation, and basic adult and newborn airway management. The American Academy of Pediatrics' Helping Babies Breathe program was also included.

After the ESM-Ketamine providers transitioned to their home facility, one of them was selected ESM-Ketamine Champion. ESM-Ketamine Champions oversaw other ESM-Ketamine providers and record keeping for each ESM-Ketamine case at their facility. ESM-Ketamine champions provided weekly reports on cases completed. Adverse events triggered immediate reporting to the AIHT research team and the principal investigator. The AIHT-based research team conducted unannounced monthly visits at each facility to collect data cards and compare them with medical records.

The ESM-Ketamine clinical pathway was activated in support of emergency or essential operative procedures in four circumstances: if an anesthetist was unavailable; if patient transfer would potentially have resulted in untoward consequences; if an anesthetist would previously not have been called; or if the patient refused care because they could not afford an anesthetist. Once activated, ESM-Ketamine providers performed a standardized pre-operative evaluation as well as defined pre-induction tasks. These included vital signs assessment, initiation of intravenous access, pre-oxygenation, and placement of pulse oximetry and blood pressure monitoring devices. Induction of anesthesia was performed with racemic

ketamine administered over 30-60 seconds (Figure 1). Hallucinations and/or agitation were managed with diazepam, nausea with promethazine, hypersalivation with atropine, and hypertension in pregnant women with hydralazine. Patients were recovered until their mental status was back to baseline.

All women who underwent obstetric or gynecological procedures supported by ESM-Ketamine between November 1, 2013 and September 30, 2017 were enrolled. Training and non-training cases were included in the analysis. No cases were excluded. Data were collected prospectively using program-specific data collection cards for every operative procedure supported by ESM-Ketamine (Figure 2). Safety was determined by monitoring adverse events, and closely following outcomes through the time of hospitalization and post-operative visits. Adverse events (AEs) were defined as hallucinations and/or agitation treated with diazepam and brief periods (less than 30 seconds) of oxygen desaturation below 92%. Serious adverse events (serious AEs) were defined as deaths or injuries potentially related to ESM-Ketamine and any prolonged periods (more than 30 seconds) of oxygen desaturation below 92%. Data collected included reasons for ESM-Ketamine activation, patient demographics, medical history, pre-operative diagnoses, procedure(s) performed, medications administered, oxygen saturation levels, AEs, and intra- and post-operative complications.

The database was constructed using Excel 2015 (Microsoft, Redmond, WA, USA). Standard descriptive statistical analyses were conducted using RStudio version 1.0.153 (RStudio, Inc, Boston, MA, USA). Normality was assessed using the Shapiro-Wilk test. Ethical approval was obtained from the Partners Healthcare Institutional Review Board (Boston, MA, USA) (Ref: 2014P002197) and the Maseno University School of Medicine Ethical Review Committee (Maseno, Kenya) (Ref: MUERC/00101/14). Informed consent was not required from patients beyond their usual operative and anesthesia consents.

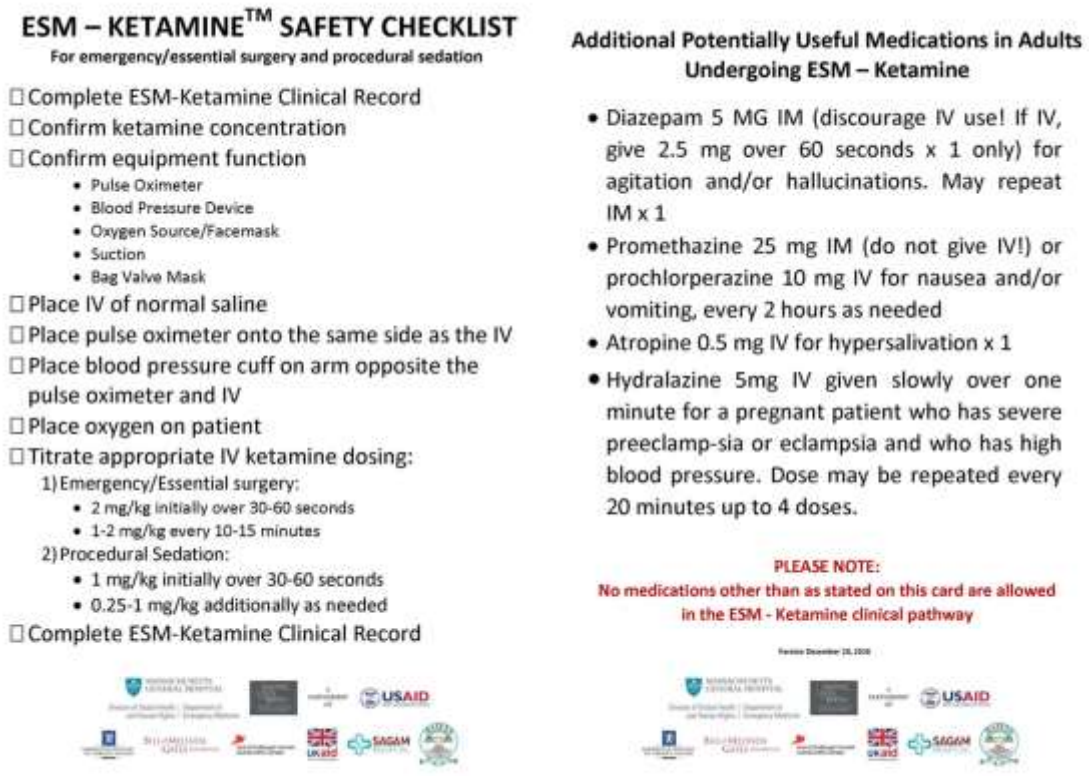


Figure 1: ESM- Ketamine Pocket Checklist (front and back)

Results

County Health Directors from Siaya, Homa Bay, Garissa, Mandera, and Wajir Counties in Kenya selected twelve facilities in which to implement the ESM-Ketamine package. Forty-three providers were trained on the ESM-Ketamine Package between November 4, 2013 and September 30, 2017, the ESM-Ketamine package was used to support 1 244 emergency and essential operative procedures, of which 530 (42.6%) were obstetric or gynecologic in nature.

The median age and weight were 29 years (IQR 22-30 years) and 63 kg (IQR 56 - 71.12 kg) respectively. Among the 530 operative procedures, 141 (26.6%) were training cases while the remaining 389 (72.3%) were operative procedures supported by an ESM-Ketamine provider without

the presence of an anesthetist or ESM-Ketamine instructor (Table 1).

Among the 389 non-training reproductive health operative cases, the ESM-Ketamine pathway was activated in support of 246 (63.2%) emergency procedures when no anesthetist was available, 189 (48.6%) of which were emergency cesarean sections and laparotomies. Fifty-seven (14.7%) of the 389 were non-emergent yet essential or life-improving surgeries. The ESM-Ketamine pathway was activated in these cases because an anesthetist was not available in a timely fashion and, in the judgment of the operative providers, delay would have potentially resulted in harm or long-term disability. Sixty-four (16.5%) cases were minor cases where an anesthetist would previously not have been called or was called but then instructed the ESM-

Figure 2: ESM-Ketamine data collection card

Table 1: Non-training operative procedures supported by the ESM- Ketamine package

Procedure	n (%)	Ketamine dose (mg/kg) (median, IQR)
Cesarean section	151 (38.8)	6.0 (4.0-7.0)
Obstetric laceration repair	70 (18.0)	3.0 (2.0-4.0)
Manual vacuum extraction	44 (11.3)	2.0 (2.0-3.0)
Bilateral tubal ligation	28 (7.2)	4.0 (3.0-5.0)
Dilation and curettage	17 (4.4)	3.0 (2.0-3.9)
Manual removal of placenta	17 (4.4)	2.0 (2.0-2.0)
EUA and cervical cancer biopsy	14 (3.6)	2.0 (1.8-2.0)
LEEP	13 (3.3)	2.0 (2.0-2.1)
Incision and drainage	8 (2.1)	2.0 (2.0-2.0)
EUA	5 (1.3)	2.0 (2.0-2.0)
Hysterectomy	5 (1.3)	14.0(11.0-17.6)
Adnexal surgery	4 (1.0)	6.2 (4.8-7.7)
Vulvar surgery	4 (1.0)	3.5 (2.8-6.0)
Contraceptive management	3 (0.8)	4.0 (3.0-5.0)
Dilation and evacuation	2 (0.5)	3.0 (2.5-3.5)
Other minor gynecologic procedures*	4 (1.0)	2.3 (2.2-2.5)
Total	389 (100)	3.9 (2.0-6.0)

EUA Examination under Anesthesia, LEEP Loop Electrosurgical Excision Procedure

* Procedures include EUA following defilement, hymen cruciate incision, and LEEP complication

Ketamine provider to proceed without an anesthesiologist. Twenty (5.1%) women refused surgery due to anesthesiologist charges, and only consented when support from ESM-Ketamine was offered. The reason for activating the ESM-Ketamine pathway was not documented in two (0.4%) cases. Among the 530 obstetric and gynecologic operative cases supported by ESM-Ketamine there were two (0.4%) serious AEs and 128 (24.2%) AEs. Two (0.4%) women had prolonged periods (>30 seconds) of oxygen saturation levels below 92% (Table 2). One prolonged desaturation (>30 seconds) event occurred during an ovarian cystectomy due to rapid administration of ketamine at induction. The other case of potential prolonged desaturation occurred during an emergency cesarean section where there were no palpable peripheral pulses from hypotension due to severe maternal hemorrhage. Both women recovered uneventfully. Brief periods (<30 seconds) of oxygen saturation levels below 92% were recorded in 15 (2.8%) cases. Diazepam was administered for hallucinations and/or agitation in

Table 2: Adverse events among training and non-training obstetric and gynecologic cases

	Non-training n (%)	Training n (%)	Total n (%)	Ketamine dose (mg/kg) (median, IQR)
Prolonged periods (more than 30 seconds) of SaO ₂ < 92%	1 (0.3)	1 (0.6)	2 (0.4)	7.0 (6.5-7.5)
Brief periods (less than 30 seconds) of SaO ₂ < 92%	12 (3.1)	3 (1.7)	15 (2.8)	6.0 (5.4-10.1)
Hallucinations and/or agitation treated with diazepam	66 (17.0)	47 (26.0)	113 (21.3)	4.0 (2.0-7.6)
Total operative procedures	389 (100)	141 (100)	530 (100)	

SaO₂ Oxygen saturation

113 (21.3%). Additional administered medications included atropine (n=68, 12.8%), promethazine (n=10, 1.9%), and hydralazine (n=7, 1.3%). Of the 530 cases, three (0.6%) women died from causes unrelated to ketamine. Two died from advanced cervical cancer within 30 days of ESM-Ketamine supported biopsies, and one woman died six hours after ESM-Ketamine supported surgery for a ruptured uterus, after late referral from another facility that could not access an anesthetist.

Discussion

This series of surgical cases supported by the ESM-Ketamine package adds to the mounting evidence that trained ESM-Ketamine providers may safely support emergency and essential obstetric and gynecologic operative procedures in severely resource-limited settings when no anesthetist is available. Although ketamine has been used as a general anesthetic worldwide for over 50 years^{16,20-22}, its use in support of operations by non-anesthetists in severely resource limited settings is not well reported. The low incidence of serious AEs suggests that ESM-Ketamine may serve as an alternative to no care when anesthetists are not available in severely resource-constrained settings.

The incidence of AEs in this series was like other reports of ketamine use^{16,18,21,23,24}. Among the 530 women that underwent obstetric and gynecologic operative procedures supported by ESM-Ketamine, only two (0.4%) experienced a serious AE. The ESM-Ketamine providers were able to readily address the AEs and serious AEs and all women recovered uneventfully. No women

died or were injured from the use of ESM-Ketamine. Therefore, the ESM-Ketamine package may serve as a safe alternative to support emergency and essential surgeries in the absence of anesthesia services. Given that standard anesthesia services are scarce in many severely low resource settings; this study suggests that the benefit of the ESM-Ketamine package – saving and improving the lives of women and pregnant mothers – may at times outweigh the potential for harm.

The ESM-Ketamine package provided a life-saving alternative for pregnant women when no anesthetist was available. This package allowed surgeons to perform 151 (38.8%) cesarean sections in regions where they would not have been able to do so previously. Therefore, this package may help decrease maternal and infant mortality in resource limited settings, where women and children die from lack of access to anesthesia services^{7,8}. Among this case series, two (cesarean sections and laparotomy) of the three Bellwether Procedures described by the 2015 Lancet Commission on Global Surgery¹ were supported by ESM-Ketamine. The Bellwether Procedures are considered a proxy for surgical systems that can provide a broad range of necessary emergency and essential surgeries in surrounding communities¹. It therefore follows that the ESM-Ketamine package may be helpful in support of a wide range of surgical procedures in severely resource-constrained settings.

ESM-Ketamine providers spontaneously began using the package for procedural sedation in support of minor procedures where previously an anesthetist would not have been called. This

unexpected use of the ESM-Ketamine pathway emerged in an entirely organic fashion, led by the ESM-Ketamine providers themselves. This use subsequently allowed for improved compassionate and quality care and led the authors to revise the clinical pathway and allow for more modest dosing (see procedural sedation section in Figure 1) in support of painful yet minor operative procedures. The use of the ESM-Ketamine package in support of minor painful procedures may provide an opportunity to increase access to compassionate care across a wide range of cases. More evidence is needed to better understand the benefit-harm ratio regarding use of the ESM-Ketamine package in support of minor procedures.

Twenty (5.1%) women that were deemed to need life-improving surgery refused the procedure due to the required up-front charges of the anesthetist. These women only consented to surgery when support from ESM-Ketamine was offered. The ESM-Ketamine package provided an alternative for women willing to suffer the consequences of no care due to cost. The authors are aware that the option of ESM-Ketamine for the extreme poor is potentially a slippery slope and may have unintended consequences. Further studies should seek to define the patient populations and clinical conditions where the harm-benefit equations are favorable.

The main strength of this study is the moderate size of the data set of 530 cases. Since the distribution half-life of ketamine is short (10 minutes in adults)²⁵, follow-up through the first postoperative visit should have captured most adverse events. Nonetheless, the authors recognize that 530 operative cases may have been too few to capture rare events. Moreover, since the ESM-Ketamine program is intensively monitored, quality of care may be higher than usual due to careful oversight.

The ESM-Ketamine package is in no way designed to replace anesthetists. Every person deserves the basic right of access to high quality surgical care when needed. This absolutely means a fully trained surgical team, including a well-trained anesthetist. However, anesthetists are often not available in the most severely resource-

constrained settings world-wide. Across many poor regions, in the absence of anesthesia services, unnecessary death and disability is the only recourse for so very many. To only allow quality anesthesia services in these settings when no anesthetist is available is sentencing people to unnecessary deaths and disability. With the emergence of ESM-Ketamine, women no longer need to lose their lives or become permanently disabled across large stretches of our planet, when no reasonable alternatives are available. In addition, to promote the responsible and diligent use of ketamine, national guidelines could be created to regulate its use only to healthcare facilities that have the necessary infrastructure and capacity, such as the availability of oxygen and oxygen saturation monitoring devices. The ESM-Ketamine training is constantly improving to ensure provider competency and promote safe implementation of the ESM-Ketamine package, which includes consistent data collection and monitoring of adverse events.

Conclusion

The ESM-Ketamine package appears feasible and safe for use in support of emergency and essential obstetric and gynecologic operative procedures in extremely resource-limited settings when no anesthetist is available. Future studies will need to further evaluate the safety profile of the ESM-Ketamine package while additionally exploring domains such as policy, liability, political will, integration into health systems, and potential roles in compassionate and quality care.

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Contribution of Authors

As principal investigator, TFB made substantial contributions to the concept development, study design, and interpretation of data. COM, JM, and SS contributed to data analysis interpretation of data. COM, JM, SS, and TFB drafted the initial version of this manuscript and revised it based on input from other co-authors. GW, ANS, DSR, JI, JJ, and MG contributed to data acquisition and manuscript editing. All authors approved the final version of this manuscript and agree to be accountable for all aspects of the work.

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