

FAKULTNÍ NEMOCNICE BRNO
A LÉKAŘSKÁ FAKULTA
MASARYKOVY UNIVERZITY



**KLINIKA DĚTSKÉ
ANESTEZILOGIE
A RESUSCITACE**

Ketamin – návrat ztraceného syna

Ivo Křikava

KDAR & OLB FN Brno, LF MU



XXVI. kongres ČSARIM
Brno 2019

M U N I
M E D

INVITED COMMENTARY

Ketamine stakes in 2018

Right doses, good choices

Georges Mion

Eur J Anaesthesiol 2019; **36**:8–15

Low-dose ketamine infusion reduces postoperative hydromorphone requirements in opioid-tolerant patients following spinal fusion

A randomised controlled trial

Kirsten Boenigk, Ghislaine C. Echevarria, Emmanuel Nisimov, Annelise E. von Bergen Granell, Germaine E. Cuff, Jing Wang and Arthur Atchabahian

Eur J Anaesthesiol 2019; **36**:16–24

Effects of a single subanaesthetic dose of ketamine on pain and mood after laparoscopic bariatric surgery

A randomised double-blind placebo controlled study

Jing Wang, Ghislaine C. Echevarria, Lisa Doan, Nydia Ekasumara, Steven Calvino, Floria Chae, Erik Martinez, Eric Robinson, Germaine Cuff, Lola Franco, Igor Muntyan, Marina Kurian, Bradley F. Schwack, Andrea S. Bedrosian, George A. Fielding and Christine J. Ren-Fielding

Postavení ketaminu v průběhu let napříč obory

anestetikum

delirogen?

„psychedelický heroin“ - psychonauti

antikonvulzivum, neuroprotektivum

rychle účinkující antidepresivum

pouliční droga – „super K, vitamin K, látka“

„ko-anxiolytikum“ ? (premedikace)

analgetikum

imunomodulans

Anestetikum

EDITORIAL

History of anaesthesia

The ketamine story – past, present and future

Georges Mion

1962 – Calvin Stevens – CL 369

Parke – Davis Co. > Warner – Lambert > Pfizer



Historie - CI-581

Pharmacologic effects of CI-581, a new dissociative anesthetic, in man

*Clinical Pharmacology
and Therapeutics*

Edward F. Domino, M.D., Peter Chodoff, M.D., and Guenter Corssen, M.D.

Ann Arbor, Mich.

Departments of Pharmacology and Anesthesiology, The University of Michigan Medical Center

1965 – Corssen, Domino
odpojení thalamokortikálního
a limbického systému
disociativní anestetikum

- účinky „hypnotické“
- analgetické, amnestické

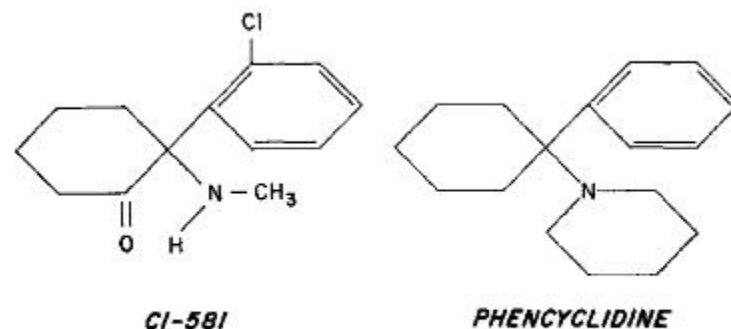
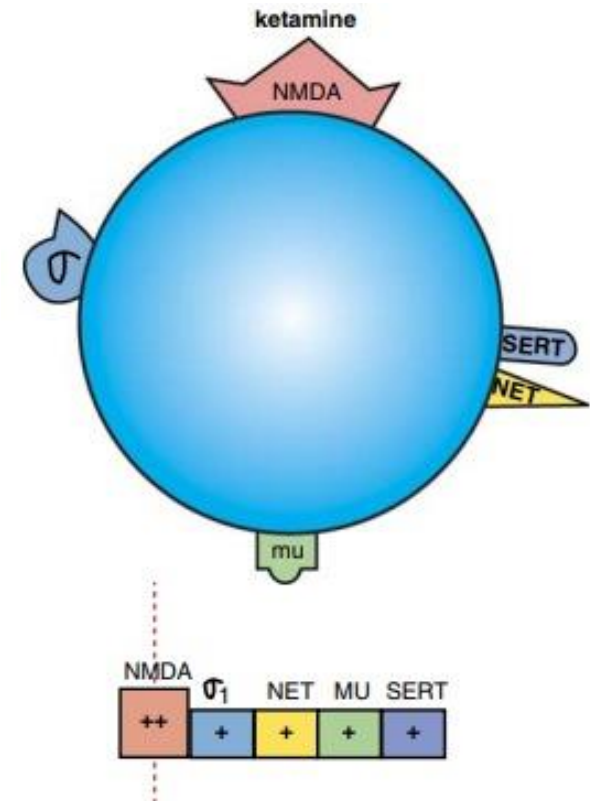
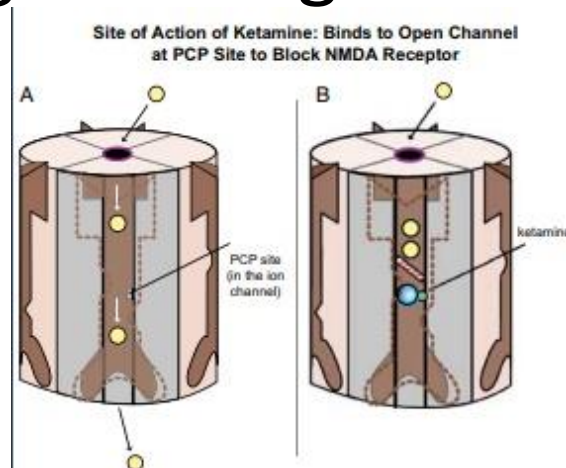


Fig. 1. Chemical structures of CI-581 and phencyclidine.

Mechanismus účinku

- nekompetitivní blokáda NMDA receptorů
 - otázka blokády NMDA receptorů, rychlosti nástupu a obsazenosti receptoru (rychlý nástup , vysoká obsazenost – stav „high“, závislostní potenciál, opak – pomalý nástup, pomalé odeznění – antidepressivní účinek, bez psychomimetických a delirantních stavů – Stahl 2013)
 - vápníkový kanál, ketamin blokuje v otevřeném stavu na „PCP site“
- AMPA receptory – stimulace?
- agonista sigma 1 receptorů



Ketamin jako anestetikum (i mimo operační sály)

- udržení oběhové stability
 - šokový pacient, podpora sympatické aktivity
- zachování respiračních reflexů
- vynikající analgezie – srovnatelná s morfinem a fentanylem
 - popáleniny, zlomeniny, mnohočetná poranění
- procedurální analgezie na urg.příjmu
- výhodná kombinace s propofolem – „ketofol“

delirogen
„psychedelický heroin“
psychonauti

Karl Jansen M.D., Ph.D.

Ketamine: Dreams and Realities

Karl Jansen M.D., Ph.D.



Ketamine: Dreams and Realities

With a new preface by the author.

Introduction by
Emanuel Sferios, Founder of *DanceSafe*

MAPS

- John Lilly (1915-2001)



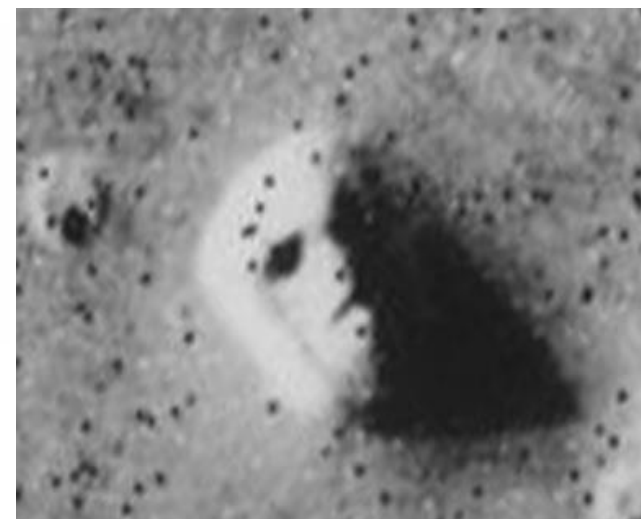
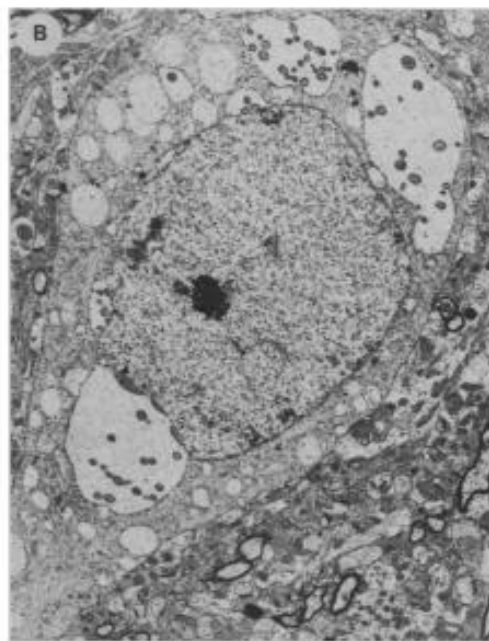
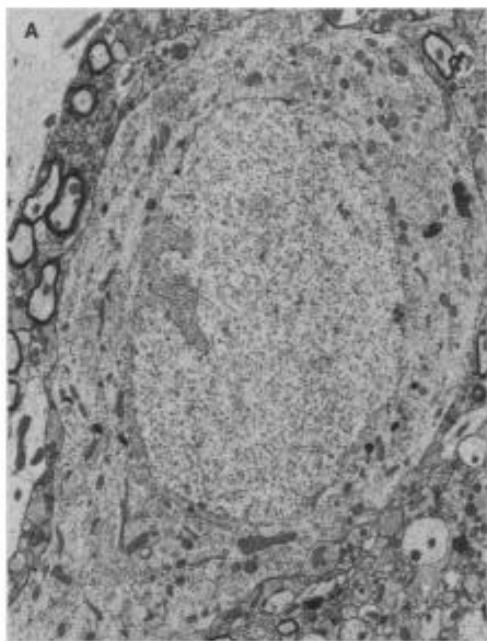
antikonvulzivum
neuroprotektivum

Neurotoxicita ?

Pathological Changes Induced in Cerebrocortical Neurons by Phencyclidine and Related Drugs

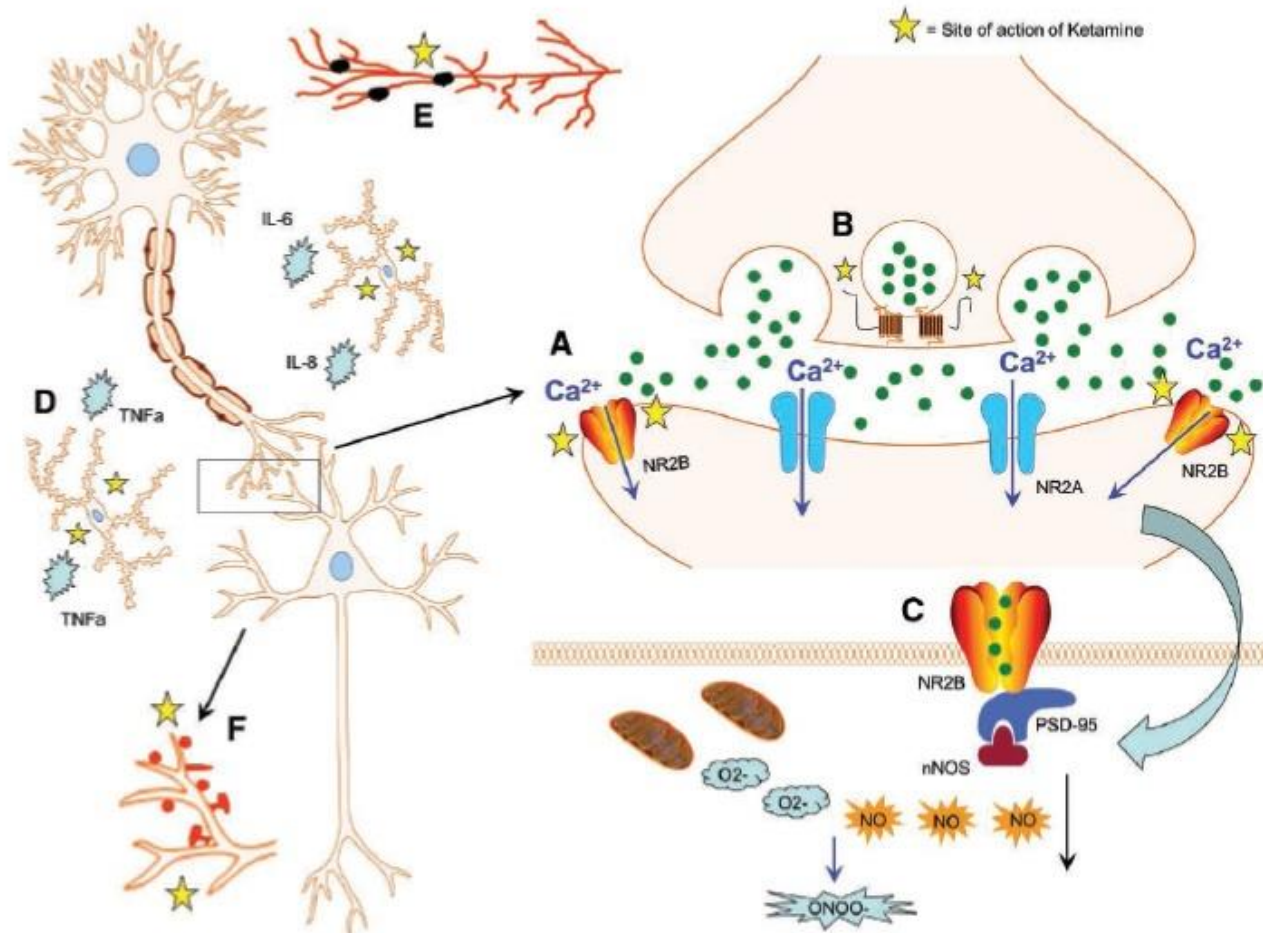
JOHN W. OLNEY, JOANN LABRUYERE, MADELON T. PRICE

Phencyclidine (PCP), a dissociative anesthetic and widely abused psychotomimetic



In Vogue: Ketamine for Neuroprotection in Acute Neurologic Injury

Josh D. Bell, MD, PhD



PAIN MANAGEMENT AND SEDATION/EDITORIAL

Ketamine and Intracranial Pressure: No Contraindication Except Hydrocephalus

Steven M. Green, MD*; Gary Andolfatto, MD; Baruch S. Krauss, MD, EdM

*Corresponding Author. E-mail: steve@stevegreenmd.com.

- | | |
|----------------------------|---|
| 1969 Tjaden ¹ | Fifty children underwent ketamine-assisted pneumoencephalography with "consistent" but unreported elevations of ICP; none had sequelae. |
| 1971 Evans ² | Four children undergoing ketamine-assisted neurodiagnostic procedures were noted to have ICPs of 210 to 300 mm H ₂ O; none had sequelae. |
| 1971 Gardner ³ | Eleven healthy adults had ICP increases with ketamine, averaging 253 mm H ₂ O and ranging up to 433 mm H ₂ O; none had sequelae. |
| 1972 Gibbs ⁴ | Six of 9 adults with intractant space-occupying lesions had an average of 12 mm Hg ICP increases after ketamine; none had sequelae. |
| 1972 List ⁵ | An infant with hydrocephalus and a "flat" fontanelle was given ketamine; shortly thereafter, apnea ensued, with a "tense and bulging" fontanelle. Treatment included ventricular puncture and drainage of cerebrospinal fluid. Seven subsequent children with hydrocephalus had ICP measured before and after ketamine; the increases averaged 247 mm H ₂ O and ranged up to 550 mm H ₂ O; none had sequelae. |
| 1972 Lockhart ⁶ | Two infants with symptomatic hydrocephalus developed apnea and bradycardia shortly after intramuscular ketamine and required intubation. |
| 1972 Shapiro ⁷ | Five children with ventriculostomies were noted to have ICPs increase by an average of 42 mm Hg after ketamine was administered, with increases ranging up to 60 mm Hg. They were treated with mask hyperventilation and thiopental. |
| 1972 Wyte ⁸ | One child with obstructive hydrocephalus had an ICP increase from 8 to 72 mm Hg after ketamine; he was treated with thiopental. |
| 1975 Crumrine ⁹ | Twenty-six children underwent ventriculostomy revision; 25 were noted to have ICP elevations ranging from 2 to 8 times baseline (highest increase 1,600 mm H ₂ O), peaking a mean of 4 minutes after ketamine. Several were treated with CSF removal, but no other treatment or sequelae are described. |

Revising a Dogma: Ketamine for Patients with Neurological Injury?

Anesth Analg 2005;101:524-34

Sabine Himmelseher, MD*, and Marcel E. Durieux, MD, PhD†

doi: 10.1111/j.1742-6723.2006.00802.x

Emergency Medicine Australasia (2006) 18, 37-44

EMA

ORIGINAL RESEARCH

Ketamine for rapid sequence induction in patients with head injury in the emergency department

Rajesh S Sehdev, David AD Symmons and Korana Kindl
Emergency Department, The Townsville Hospital, Townsville, Queensland, Australia

ICP, TBI

studie KIND
NCT02636218
February 2019 -
-> March 2020
SAK

Neuroprotection by Ketamine: A Review of the Experimental and Clinical Evidence

Judith A. Hudetz, PhD, and Paul S. Pagel, MD, PhD

Journal of Cardiothoracic and Vascular Anesthesia, Vol 24, No 1 (February), 2010: pp 131-142

PAIN MANAGEMENT AND SEDATION/SYSTEMATIC REVIEW-META-ANALYSIS

The Effect of Ketamine on Intracranial and Cerebral Perfusion Pressure and Health Outcomes: A Systematic Review

Lindsay Cohen, MD; Valerie Athaide, MD, FRCP(C); Maeve E. Wickham, MSc; Mary M. Doyle-Waters, MA, MLT
Nicholas G. W. Rose, MD, FRCP(C); Corinne M. Hohl, MD, FRCP(C)*

Volume 65, NO. 1 : January 2015
Annals of Emergency Medicine 43

„ko-anxiolytikum“ (premedikace)

Pooperační neklid

Research Report



Journal of
**INTERNATIONAL
MEDICAL RESEARCH**

Journal of International Medical Research
2014, Vol. 44(2) 258–266
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DOI: 10.1177/0300060515621639


Effect of ketamine versus alfentanil following midazolam in preventing emergence agitation in children after sevoflurane anaesthesia: A prospective randomized clinical trial

Sevgi Bilgen¹, Özge Köner¹, Safak Karacay²,
Nurcan Kizilcik Sancar¹, Elif Cigdem Kaspar³
and Selami Sözübir²

Research Report



Journal of
**INTERNATIONAL
MEDICAL RESEARCH**

Journal of International Medical Research
2016, Vol. 44(2) 258–266
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DOI: 10.1177/0300060515621639
imr.sagepub.com


Comparison of effects of intravenous midazolam and ketamine on emergence agitation in children: Randomized controlled trial

Kyung Mi Kim^{1,2}, Ki Hwa Lee³, Yong Han Kim³,
Myoung Jin Ko³, Jae-Wook Jung³
and Eunsu Kang³

Society for Pediatric Anesthesia

Section Editor: James DiNardo

A Comparative Evaluation of Nebulized Dexmedetomidine, Nebulized Ketamine, and Their Combination as Premedication for Outpatient Pediatric Dental Surgery

Ola M. Zanaty, MD, PhD, and Shahira Ahmed El Metainy, PhD

Pooperační neklid

British Journal of Anaesthesia 104 (2): 216–23 (2010)
 doi:10.1093/bja/aep376 Advance Access publication January 3, 2010

BJA

PAEDIATRICS

CME **Pharmacological prevention of sevoflurane- and desflurane-related emergence agitation in children: a meta-analysis of published studies**

S. Dahmani^{1*}, I. Stany¹, C. Brasher¹, C. Lejeune¹, B. Bruneau¹, C. Wood¹, Y. Nivoche¹,
 I. Constant² and I. Murat²



Emergence delirium in children: an update

Souhayl Dahmani^{a,b,c}, Honorine Delivet^{d,e}, and Julie Hilly^{a,b}

Ketamine	IV, preoperative	Yes	0.25 mg/kg
	IV, end of surgery	Yes	0.25 mg/kg
	OR, preoperative	Yes	6 mg/kg

antidepressivum

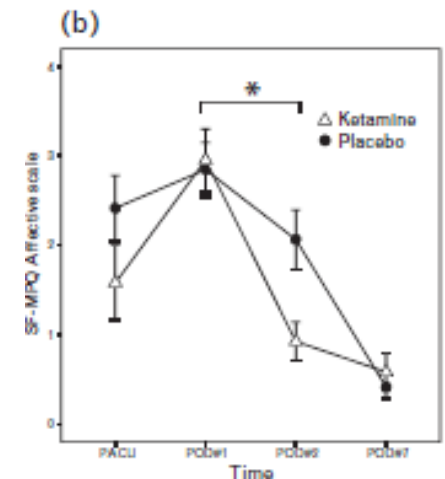
INVITED COMMENTARY

Targeting the affective component of pain with ketamine*A tool to improve the postoperative experience?*

Bianca Robu and Patricia Lavand'homme

Effects of a single subanaesthetic dose of ketamine on pain and mood after laparoscopic bariatric surgery*A randomised double-blind placebo controlled study*

Jing Wang, Ghislaine C. Echevarria, Lisa Doan, Nydia Ekasumara, Steven Calvino, Floria Chae, Erik Martinez, Eric Robinson, Germaine Cuff, Lola Franco, Igor Muntyan, Marina Kurian, Bradley F. Schwack, Andrea S. Bedrosian, George A. Fielding and Christine J. Ren-Fielding



- antidepressivní účinek nefunguje u memantinu (NMDA antagonisty)
- platí jen pro racemický ketamin, (R)-ketamin zprostředkovává antidepressivní účinek

5. březen 2019 - Spravato®



BODY & BRAIN

FDA approves ketamine-based drug for severe depression

Doctors have a new weapon in the fight against particularly hard-to-treat depression: a drug based on the powerful anesthetic ketamine.

The drug – called Spravato and developed by Janssen Pharmaceuticals – was approved March 5 by the U.S. Food and Drug Administration as a treatment for severely depressed people who have tried at least two other treatments without success. Spravato is a nasal spray that must be delivered in a doctor's office and is intended to be used in addition to an oral antidepressant.

pouliční droga
„super K, vitamin K, látka“



ELSEVIER

Contents lists available at ScienceDirect

Brain Research Bulletin

journal homepage: www.elsevier.com/locate/brainresbull


KДАР
 FN BRNO a LF MU

Review

Ketamine abuse potential and use disorder

Yu Liu^a, Deyong Lin^a, Boliang Wu^a, Wenhua Zhou^{a,b,*}


- 2,3 milionu adolescentů a dospělých užilo ketamin někdy v životě v UK 2006 (Administration, S.A.M.H.S, 2008)
- úmrtí po užití ketaminu se v UK zvýšilo 10x v letech 1999-2008 (Morgan et al., 2012)
- 40 % uživatelů párty drog přiznalo užití ketaminu (Breen et al., 2008)
- 4-násobné zvýšení uživatelů ketaminu v Malajsii 2006-2012 (Singh et al., 2013)
- zvýšení z 21,5 % na 40 % (2001-2009) u reg. uživatelů drog v Číně (Jia et al., 2015)
- 3. nejčastěji detekovaná droga u řidičů s pozitivním testem na psychoaktivní látky v Šanghaji (Zhuo et al., 2010)
- 9 % řidičů s fatální autonehodou bylo pozitivních na ketamin v Hong Kongu (Cheng et al., 2005)


 VOL. 3, NO. 8, AUGUST 2019

 6001604 

Sensor applications

An Electronic Nose System for Rapid Detection of Ketamine Smoke

Cheng-Chun Wu, Shih-Wen Chiu, and Kea-Tiong Tang* 

#ketamineismedicine



WFSA
WORLD FEDERATION OF SOCIETIES OF
ANAESTHESIOLOGISTS

FACT SHEET KETAMINE

Ketamine is an essential medicine

It is the only anaesthetic that does not require oxygen, electricity, anaesthetic equipment, or trained anaesthesia providers, all of which remain limited in low and middle income countries.



work in LMICs. This huge shortage means nurses & clinical assistants give the most anaesthetics



people in rural areas in LMICs already lack access to essential medicines



of medical facilities in 22 LMICs recently surveyed had ketamine available. Oxygen was consistently available only 46% of the time

(přece jen)
Anestetikum



Contents lists available at ScienceDirect

Journal of Clinical Anesthesia

journal homepage: www.elsevier.com/locate/jclinane



Editorial

The role of ketamine in addressing the anesthesia gap in low-resource settings

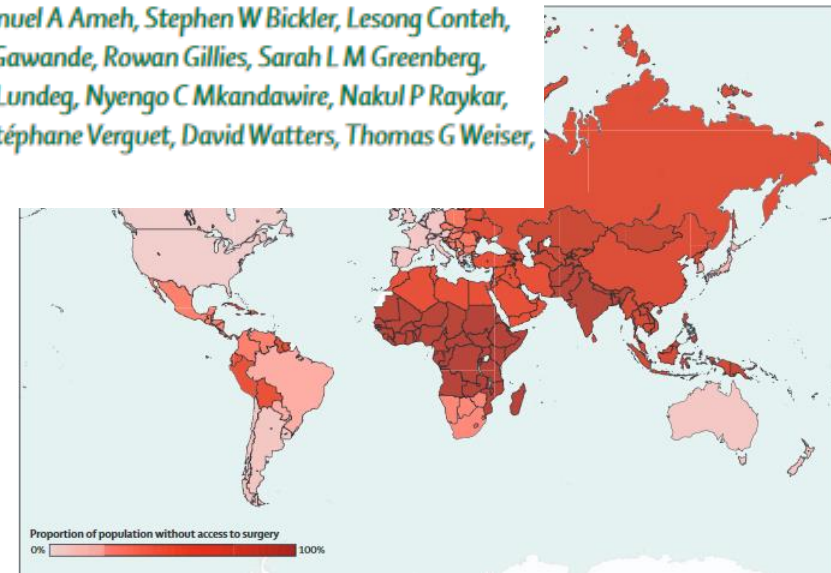


Global Surgery 2030: evidence and solutions for achieving health, welfare, and economic development

John G Meara^{}, Andrew J M Leather^{*}, Lars Hagander^{*}, Blake C Alkire, Nivaldo Alonso, Emmanuel A Arneh, Stephen W Bickler, Lesong Conteh, Anna J Dare, Justine Davies, Eunice Déruvois Mérisier, Shenaaz El-Halabi, Paul E Farmer, Atul Gawande, Rowan Gillies, Sarah L M Greenberg, Caris E Grimes, Russell L Gruen, Edna Adan Ismail, Thaim Buya Kamara, Chris Lavy, Ganbold Lundeg, Nyengo C Mkandawire, Nakul P Raykar, Johanna N Riesel, Edgar Rodas[†], John Rose, Nobhojit Roy, Mark G Shrimme, Richard Sullivan, Stéphane Verguet, David Watters, Thomas G Weiser, Iain H Wilson, Gavin Yamey, Winnie Yip*

Lancet 2015; 386: 569–624

- 5 miliard lidí nemá včas přístup k akutnímu nebo nezbytnému chirurgickému výkonu
- v Africe jsou celé země, ve kterých se měsíčně provede méně zákroků než na Cleveland Clinic za den



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

DOI: 10.29063/ajrh2019/v23i1.4

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}

African Journal of Reproductive Health March 2019; 23 (1): 39

ESM – KETAMINE™ SAFETY CHECKLIST

For emergency/essential surgery and procedural sedation

- Complete ESM-Ketamine Clinical Record
- Confirm ketamine concentration
- Confirm equipment function
 - Pulse Oximeter
 - Blood Pressure Device
 - Oxygen Source/Facemask
 - Suction
 - Bag Valve Mask
- Place IV of normal saline
- Place pulse oximeter onto the same side as the IV
- Place blood pressure cuff on arm opposite the pulse oximeter and IV
- Place oxygen on patient
- Titrate appropriate IV ketamine dosing:
 - 1) Emergency/Essential surgery:
 - 2 mg/kg initially over 30-60 seconds
 - 1-2 mg/kg every 10-15 minutes
 - 2) Procedural Sedation:
 - 1 mg/kg initially over 30-60 seconds
 - 0.25-1 mg/kg additionally as needed
- Complete ESM-Ketamine Clinical Record

Additional Potentially Useful Medications in Adults Undergoing ESM – Ketamine

- Diazepam 5 MG IM (discourage IV use! If IV, give 2.5 mg over 60 seconds x 1 only) for agitation and/or hallucinations. May repeat IM x 1
- Promethazine 25 mg IM (do not give IV!) or prochlorperazine 10 mg IV for nausea and/or vomiting, every 2 hours as needed
- Atropine 0.5 mg IV for hypersalivation x 1
- Hydralazine 5mg IV given slowly over one minute for a pregnant patient who has severe preeclampsia or eclampsia and who has high blood pressure. Dose may be repeated every 20 minutes up to 4 doses.

PLEASE NOTE:

No medications other than as stated on this card are allowed in the ESM - Ketamine clinical pathway

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)

#ketamineismedicine

Ketamine does not cause significant social harm

Although chronic and heavy abuse can cause limited harmful effects, in the vast majority of countries the medical benefits of ketamine vastly outweigh potential harm.

16th

Ketamine is **not** widely abused globally. The drug ranked 16th in popularity in Global Drug Survey's 2014 findings, often not appearing in the 'Top 20' list in individual countries



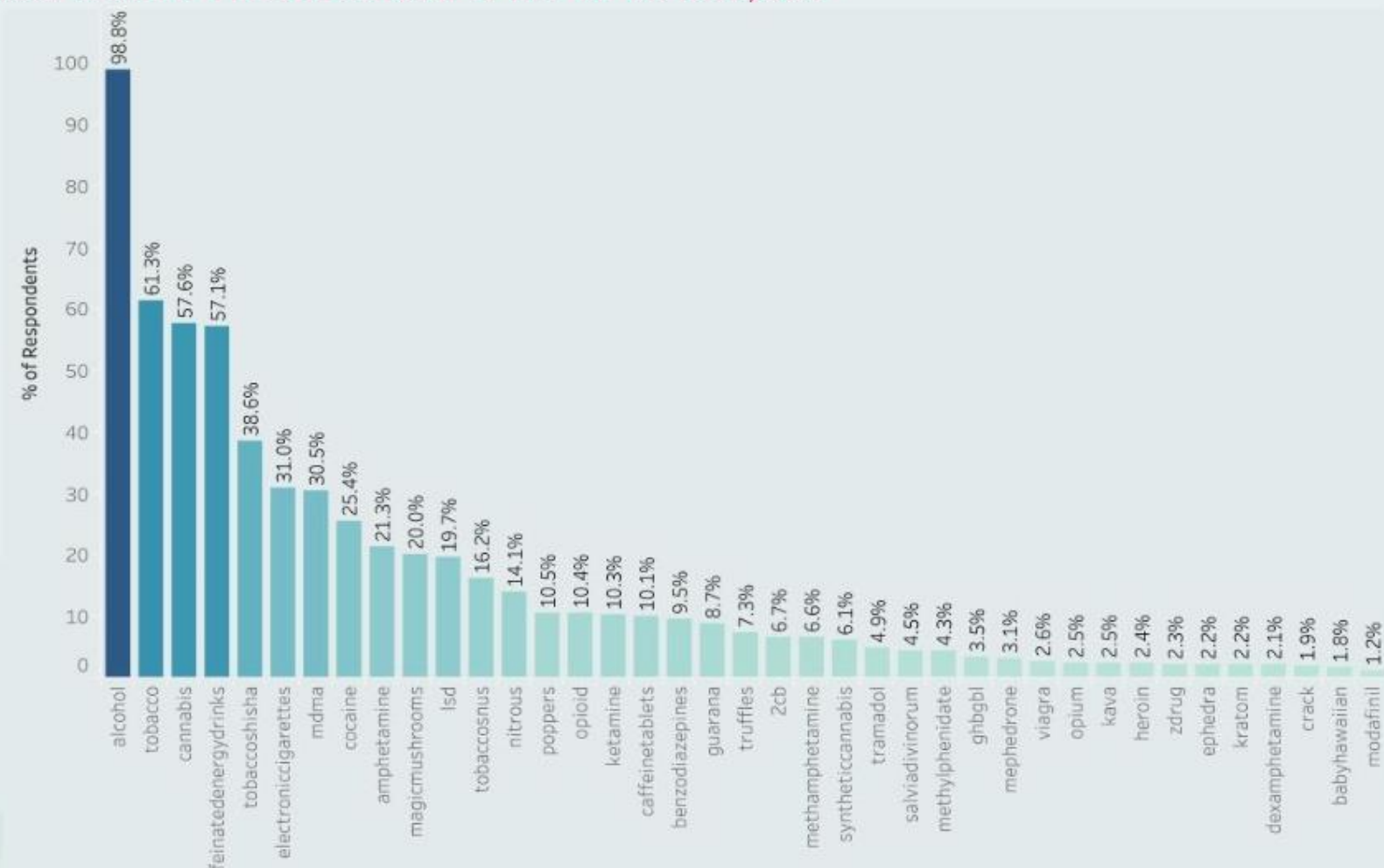
In the USA and Europe, Ketamine is used to manage pain in cancer patients, to treat depression and other mental illnesses, and is used on an ad-hoc basis in hospitals

While a number of countries control ketamine domestically, the World Health Organisation Expert Committee on Drug Dependence (ECDD) has critically evaluated ketamine 3 times (2006, 2012 and 2014) and advised against placing ketamine under international control because:

“Ketamine abuse does not appear to pose a sufficient public health risk of global scale to warrant scheduling.”

The Committee recognized that in countries where such abuse is a problem, putting ketamine under national control may be considered.

LIFETIME DRUG USE IN THE GDS2018 SAMPLE N>130,000



Analgetikum

(u nás v Brně 😊)

KDAR FN Brno

- Calypsol 500 mg/ 10 ml 5 amp.
- 2015 – 9 balení
- 2016 – 15 balení
- 2017 – 23 balení
- 2018 – 29 balení
- 2019 - ??



Postavení ketaminu v průběhu let napříč obory

anestetikum

delirogen?

„psychedelický heroin“ - psychonauti

antikonvulzivum, neuroprotektivum

rychle účinkující antidepresivum

pouliční droga – „super K, vitamin K, látka“

„ko-anxiolytikum“ ? (premedikace)

analgetikum

imunomodulans

Take home message

- ketamin podávejte pacientovi (ne sobě) v malých (analgetických) dávkách
- a když není zbytků, tak v ketaminu můžete relativně bezpečně vést celkovou anestezii



Děkuji za pozornost

