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Congreso Internacional de Cuidados Paliativos

*"Cuidado paliativo integrativo
e innovador"*

Octubre 4, 5 y 6 de 2018
Plaza Mayor - Palacio de Exposiciones
Medellín - Colombia

5º Encuentro de Residentes Medicina
del Dolor y Cuidado Paliativo



ACC Paliativos
Asociación Colombiana
de Cuidados Paliativos



**Javier Esteban
Toro López**

Médico Anestesiólogo

Fellow Dolor y Cuidados
Paliativos Universidad CES

Uso de Ketamina en dolor agudo

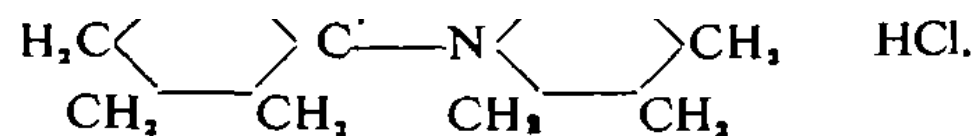
Argumentos a favor

Conflicto de intereses



Declaro no tener conflicto de intereses

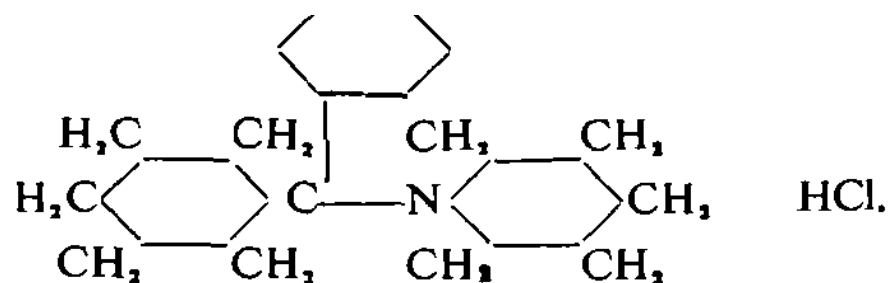
Historia



Comprehensive investigation of its effects in several animal species revealed potent analgesic activity without evidence of cellular toxicity. The intravenous administration of 0.3–0.6 mg/kg to monkeys induced a cataleptoid state which lasted up to 1 hour during which time major surgery could be performed without difficulty whilst the animals appeared to be awake and alert. The oral administration of somewhat larger doses to cats and dogs produced similar results. Doses in excess of those required for “surgical anaesthesia” tended to cause excitation and convulsions in these animals. These studies which included tests in

pulse rates were increased in some patients and slightly decreased in others. Electrocardiography revealed no evidence of arrhythmia. Moderate changes were observed in the electroencephalographic patterns unlike those associated with natural or barbiturate-induced sleep. Reflex activity was unimpaired by moderate doses. Vertical nystagmus appeared in all patients and sometimes persisted for 24 to 36 hours postoperatively, associated with diplopia and vertigo.

When the drug was made available to us, along with the pharmacological and initial clinical reports, it was decided to investigate its use in the three phases of surgical treatment: pre-operative sedation, surgical anaesthesia and postoperative



Comprehensive investigation of its effects in

Historia

without any reaction in the limbs. When the testis was handled he suddenly opened his eyes and made
may persist for 12 hours after a single dose. The
excitation has a disturbing resemblance to the
acute toxic psychoses and is often associated with
delirium
usually of
times rat
psychotic r
in young
patient immediately
widely open and
infinity. The blo

HISTORY OF PCP



Synthesized
in 1926



Developed and sold
as Sernyl by Parke,
Davis and Company



PCP became an
illegal substance in
the United States

1926

1950

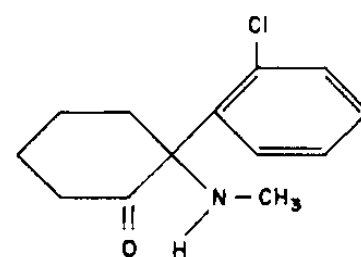
1978

**GUENTER CORSEN, M.D.
EDWARD F. DOMINO, M.D.
Ann Arbor, Michigan***

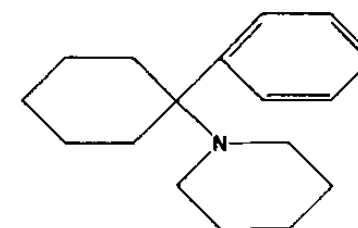
DISOCIATIVO ANESTHESIA: Further Pharmacologic Studies and First Clinical Experience with the Phencyclidine Derivative CI-581

THERE IS A definite need for safe and potent intravenously administered anesthetics of short duration which combine analgesic and sleep-producing effects without significant cardiovascular and respiratory depression. Recently, a number of compounds related to phenylcyclohexylamine have aroused clinical interest because they appear to approach such requirements. Phencyclidine hydrochloride was the prototype of this group of agents. After preliminary laboratory studies¹ its clinical usefulness as an anesthetic was investigated by Greifenstein and associates.²

The intravenously administered drug was



CI-581



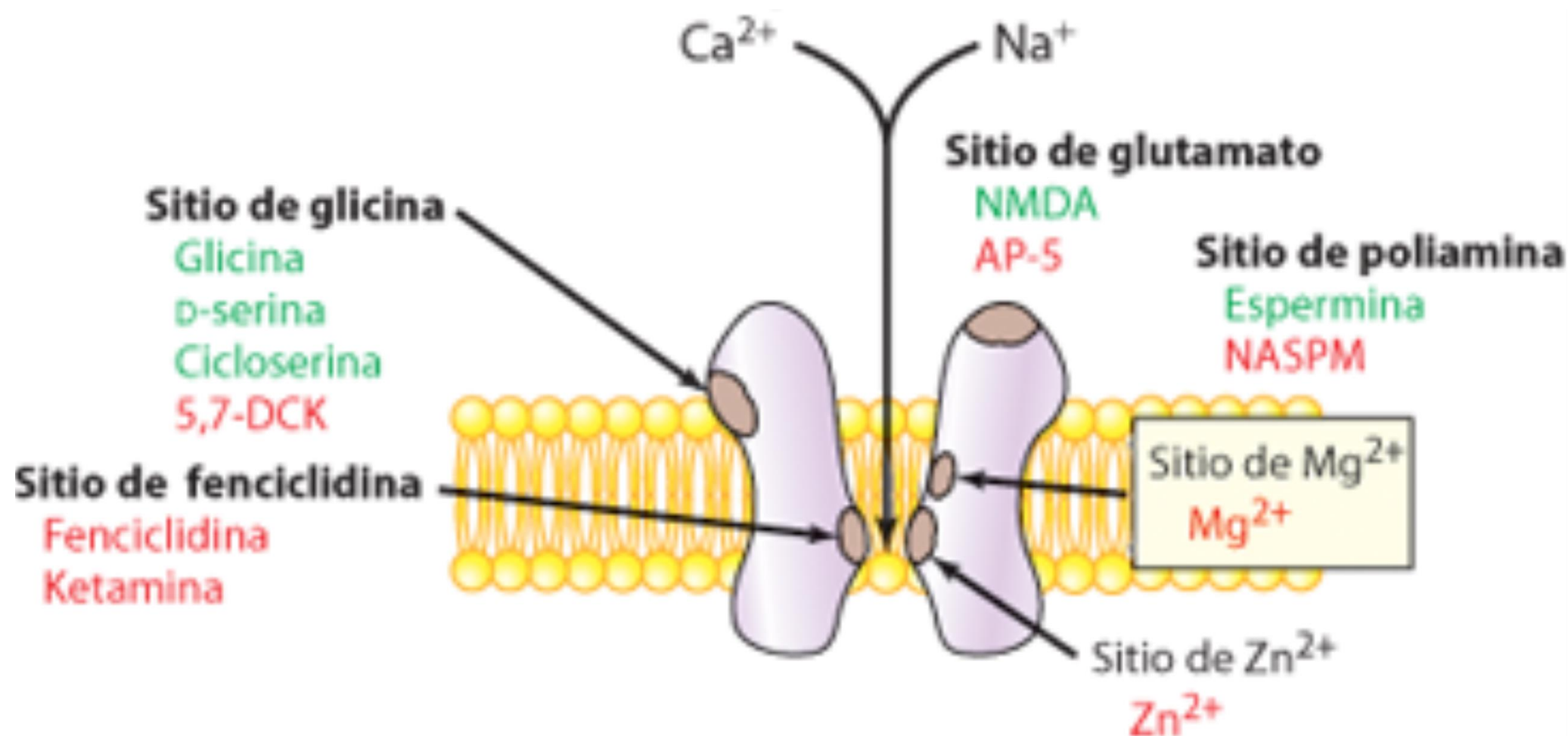
PHENCYCLIDINE

FIG. 1. Structural formulae of CI-581 and phencyclidine.

CI-581 is a white crystalline substance with a melting point of 259° C. It is soluble in water to 20 per cent as a clear, colorless solution. A 10 per cent aqueous solution has a pH of 3.5. In animals the agent was found

* Hospital in Chicago, Illinois.

Mecanismo de acción



Fuente: Eric J. Nestler, Steven E. Hyman, David M. Holtzman, Robert C. Malenka: *Neurofarmacología Molecular. Fundamentos de neurociencia clínica*, 3e
www.accessmedicina.com
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Anesthesiology 2001; 95:1406-1413

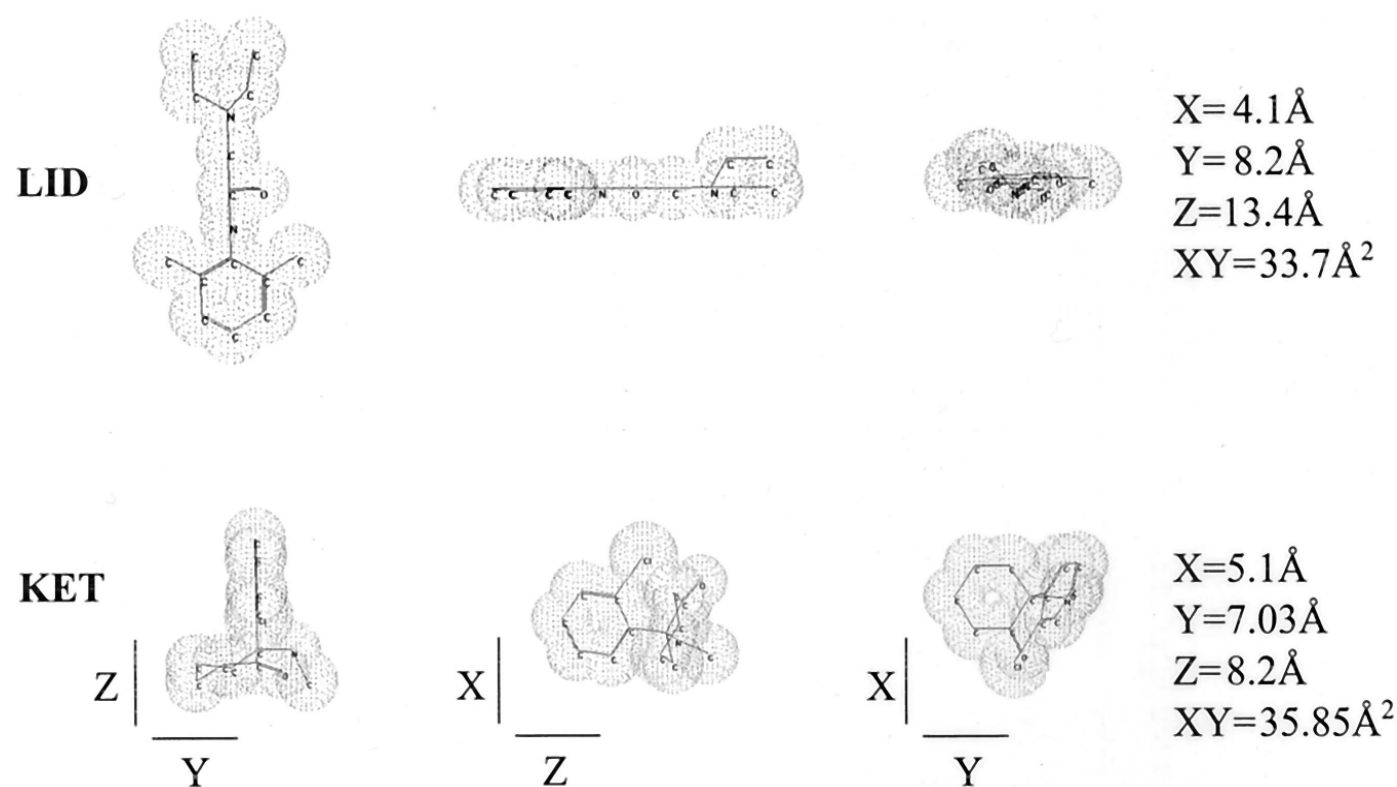
© 2001 American Society of Anesthesiologists, Inc. Lippincott Williams & Wilkins, Inc.

Ketamine Blockade of Voltage-gated Sodium Channels

Evidence for a Shared Receptor Site with Local Anesthetics

Larry E. Wagner II, B.S.,* Kevin J. Gingrich, M.D.,† John C. Kulli, M.D.,‡ Jay Yang, Ph.D., M.D.§

Fig. 5. Three-dimensional molecular modeling of ketamine (KET) and lidocaine (LID). Structures for the drugs were modeled using HyperChem (see Materials and Methods). The energetically optimized molecular conformation in an aqueous environment was rotated in space to align the two molecules along the indicated axes. For visual clarity, hydrogen atoms are not shown. Bars = 3.4 Å.



Mecanismo de acción

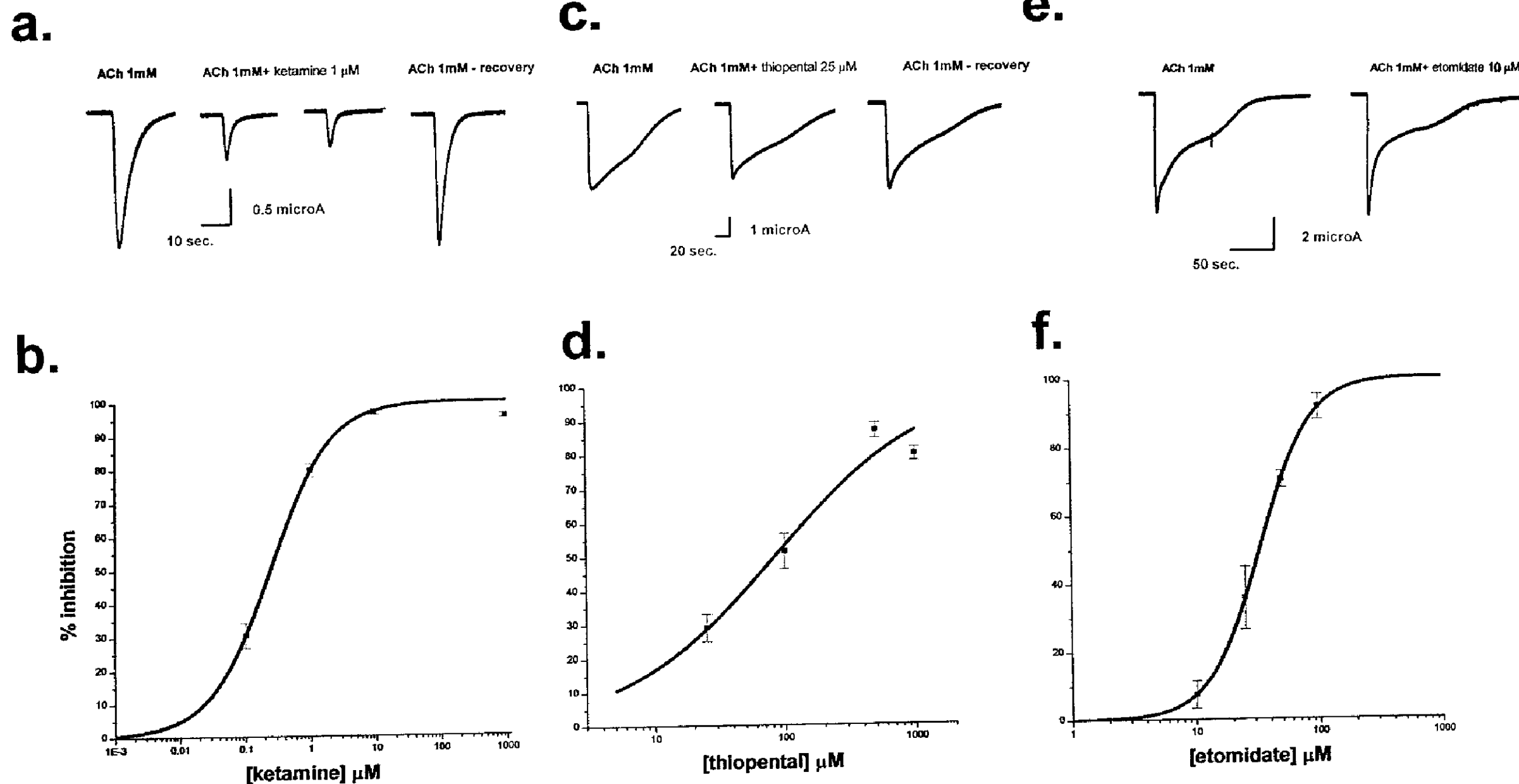


humans, S-ketamine is 3–4 times as potent as R-ketamine as an analgesic (Klepstad *et al.* 1990) and as an anaesthetic agent (White *et al.* 1980). The analgesic effect can not be antagonized by naloxone in doses sufficient to antagonize the effect of the opioid μ agonist, pethidine (Maurset *et al.* 1989). In some animal studies, the analgesic effect was antagonized by naloxone (Ryder *et al.* 1978; Pekoe & Smith 1982; Smith *et al.* 1990; Crisp *et al.* 1991), while the anaesthetic effect was not (Smith *et al.* 1985). On the other hand, Fratta *et al.* (1980) and Takahashi *et al.* (1987) found no effect of naloxone on the antinociceptive effect of ketamine. In the guinea-pig ileum preparation, ketamine depresses the electrically induced contractions. This effect is only partly reversible with naloxone (Smith *et al.* 1982; Finck & Ngai

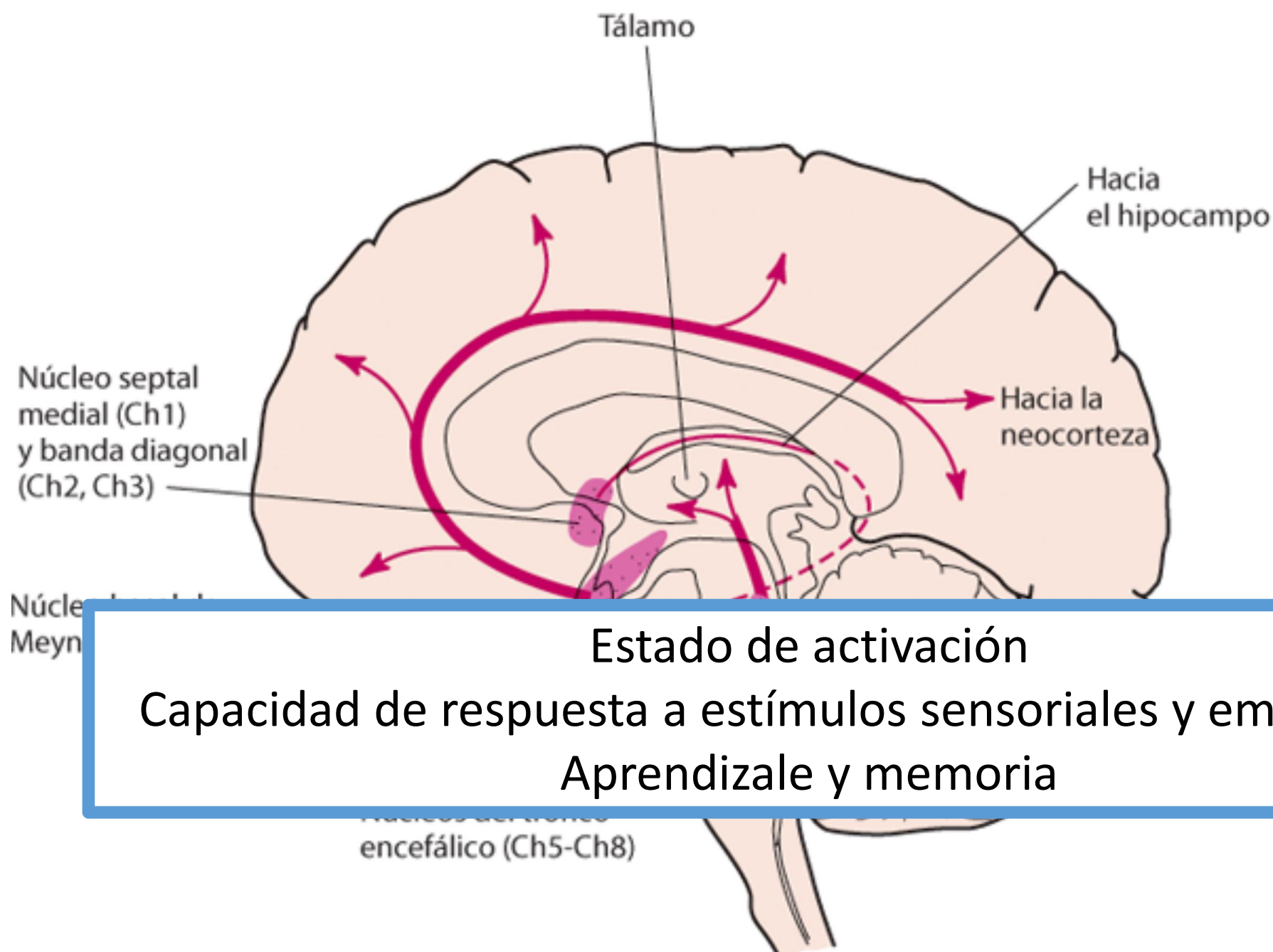
The guinea-pig ileum assay. Male Dunkin-Hartley guinea pigs weighing 250–300 g were killed with a blow on the head and exsanguinated. A segment of ileum was isolated and gently flushed with bath fluid. The 15 cm nearest to the colon were discarded. Fifteen mm sections of ileum were mounted in an organ bath at 37° with 30 ml modified Ringer-solution with pH 7.4 (composition in mM: Na⁺ 137, K⁺ 5.9, Mg²⁺ 1.2, Ca²⁺ 2.5, Cl⁻ 134, HPO₄ 1.2, HCO₃ 15.5, glucose 11.5). The bath fluid was bubbled with 5% CO₂ in 95% O₂. The preparations were allowed to equilibrate at 37° for at least 1 hr and were field-stimulated via platinum electrodes on each side 6 mm apart (single pulses, pulse duration 1 msec. frequency 0.1 Hz and just supramaximal voltage). Resting tension was adjusted to achieve optimal contractions (about 0.3 g). The contractions were recorded isometrically with a Grass force displacement transducer (type FT03C) connected to a Grass model 7 polygraph.

Concentration-response experiments were performed by adding

Mecanismo de acción

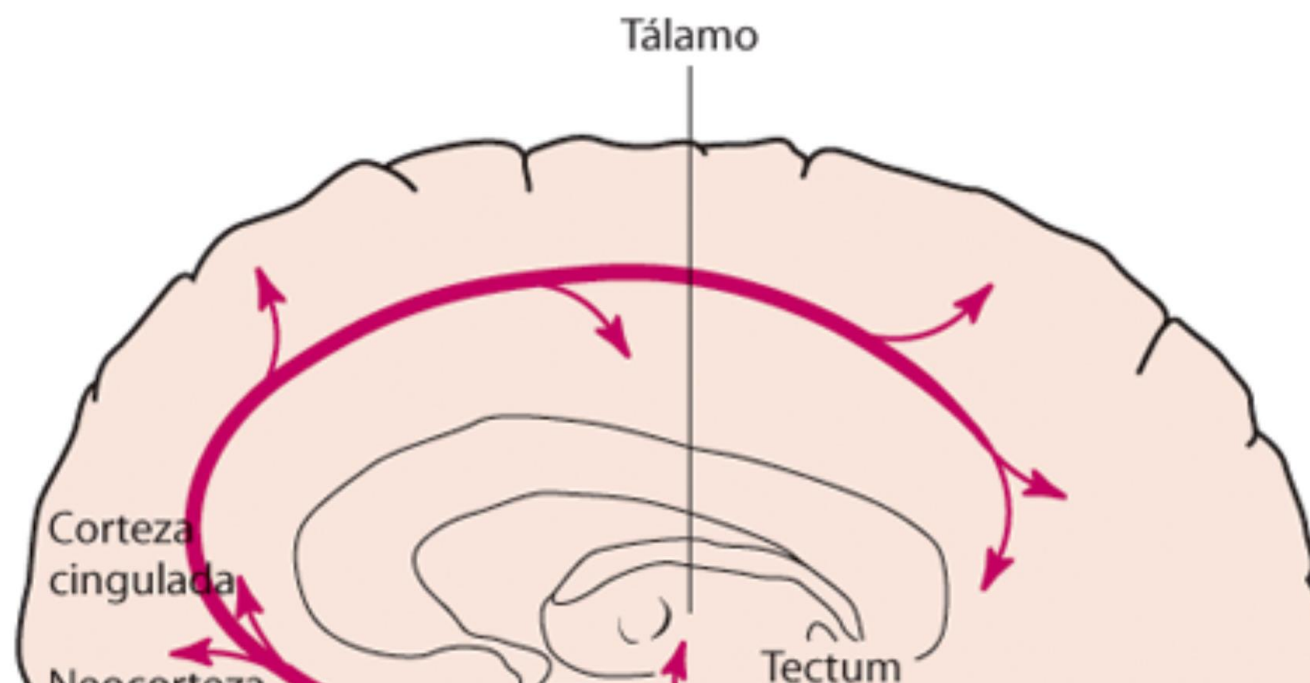


Mecanismo de acción

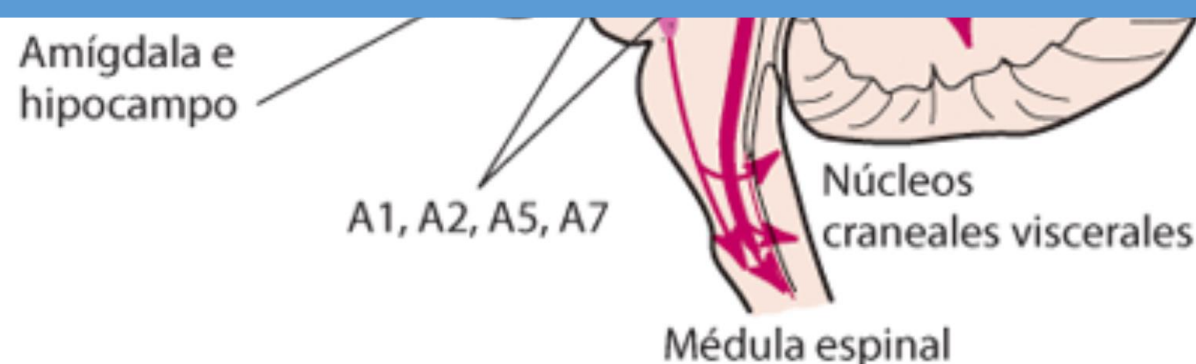


Fuente: Eric J. Nestler, Steven E. Hyman, David M. Holtzman, Robert C. Malenka: *Neurofarmacología Molecular. Fundamentos de neurociencia clínica*, 3e : www.accessmedicina.com
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Mecanismo de acción



Control cognitivo del comportamiento
Memoria de trabajo
Control de la atención



Fuente: Eric J. Nestler, Steven E. Hyman, David M. Holtzman, Robert C. Malenka:
Neurofarmacología Molecular. Fundamentos de neurociencia clínica, 3e
www.accessmedicina.com Derechos reservados© McGraw-Hill Education.

Perspective

APRIL 21, 2016

Reducing the Risks of Relief — The CDC Opioid-Prescribing Guideline

Thomas R. Frieden, M.D., M.P.H., and Debra Houry, M.D., M.P.H.

JAMA Internal Medicine | [Original Investigation](#)

Incidence of and Risk Factors for Chronic Opioid Use Among Opioid-Naive Patients in the Postoperative Period

Eric C. Sun, MD, PhD; Beth D. Darnall, PhD; Laurence C. Baker, PhD; Sean Mackey, MD, PhD

N ENGL J MED 374;16 NEJM.ORG APRIL 21, 2016

JAMA Internal Medicine September 2016 Volume 176, Number 9

Table 2. Risk Factors for Chronic Opioid Use Following Surgery^a

Risk Factor	Odds Ratio (SE) ^a	P Value
Demographics		
Male	1.34 (0.0648)	<.001
Age >50 y	1.74 (0.0942)	<.001
Preoperative drug use		
Benzodiazepines	1.82 (0.1049)	<.001
Antidepressants	1.65 (0.0928)	<.001
Antipsychotics	1.14 (0.1330)	.28
Medical comorbidities		
Depression	1.15 (0.0717)	.03
Psychosis	1.03 (0.2094)	.89
Alcohol abuse	1.83 (0.2834)	<.001
Drug abuse	3.15 (0.5385)	<.001

Figure 2. Risk of Chroni

Simple m
Transurethral prostate
Functional endoscopic sinu
Cesarea
Open appe
Laparoscopic appe
Open cholecy
Laparoscopic cholecy
Total hip art
Total knee art

^a Table lists the results of a multivariable logistic regression in which the dependent variable was chronic opioid use and the independent variables were preoperative use of benzodiazepines, antidepressants, or antipsychotics; reported odds ratios are for chronic use associated with each risk factor, with robust standard errors (SEs) reported in parentheses. Not shown are controls for the remaining medical variables listed in Table 1 or controls for year of surgery.

ed are the adjusted odds
r chronic opioid use within 1
er surgery for each study
procedure. Error bars
95% CIs, which were
ed using robust standard
ur regression model included
for age, sex, year of surgery,
rall health care utilization. In
, the model also included
for preoperative use of
azepines, antidepressants,
psychotics, and controls for
ical comorbidities listed in

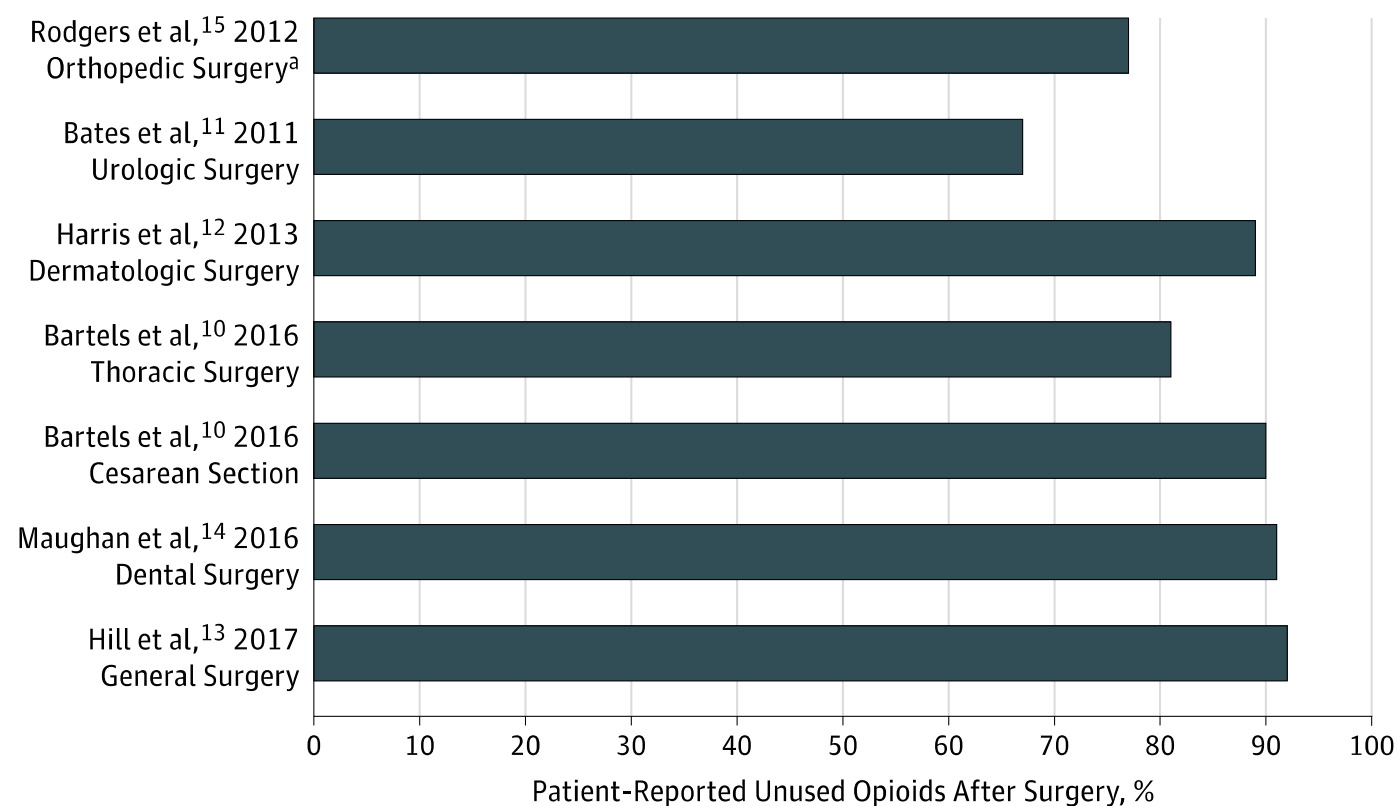
Clinical Review & Education

JAMA Surgery | Review

Prescription Opioid Analgesics Commonly Unused After Surgery A Systematic Review

Mark C. Bicket, MD; Jane J. Long, BS; Peter J. Pronovost, MD, PhD;
G. Caleb Alexander, MD, MS; Christopher L. Wu, MD

Figure. Prevalence of Unused Opioids Prescribed After Surgery



JAMA Surgery November 2017 Volume 152, Number 11

Principios claves en el manejo del dolor postoperatorio:

- Minimizar el uso de opioides sistémicos
- Utilizar técnicas analgésicas regionales siempre que sea posible
- Maximizar el uso de NO opioides sistémicos y adyuvantes

Postoperative pain: mechanisms, treatment, and organizational aspects. Chapter 14.
In Pain 2018: refresher courses 17th world congress on pain. Gold, M. Pogatzki-Zahn,
E. Wallace, M. Boston, USA, September 2018.

Pacientes en quienes se espere dolor POP grave

Can J Anesth/J Can Anesth (2011) 58:911–923

DOI 10.1007/s12630-011-9560-0

REPORTS OF ORIGINAL INVESTIGATIONS

A systematic review of intravenous ketamine for postoperative analgesia

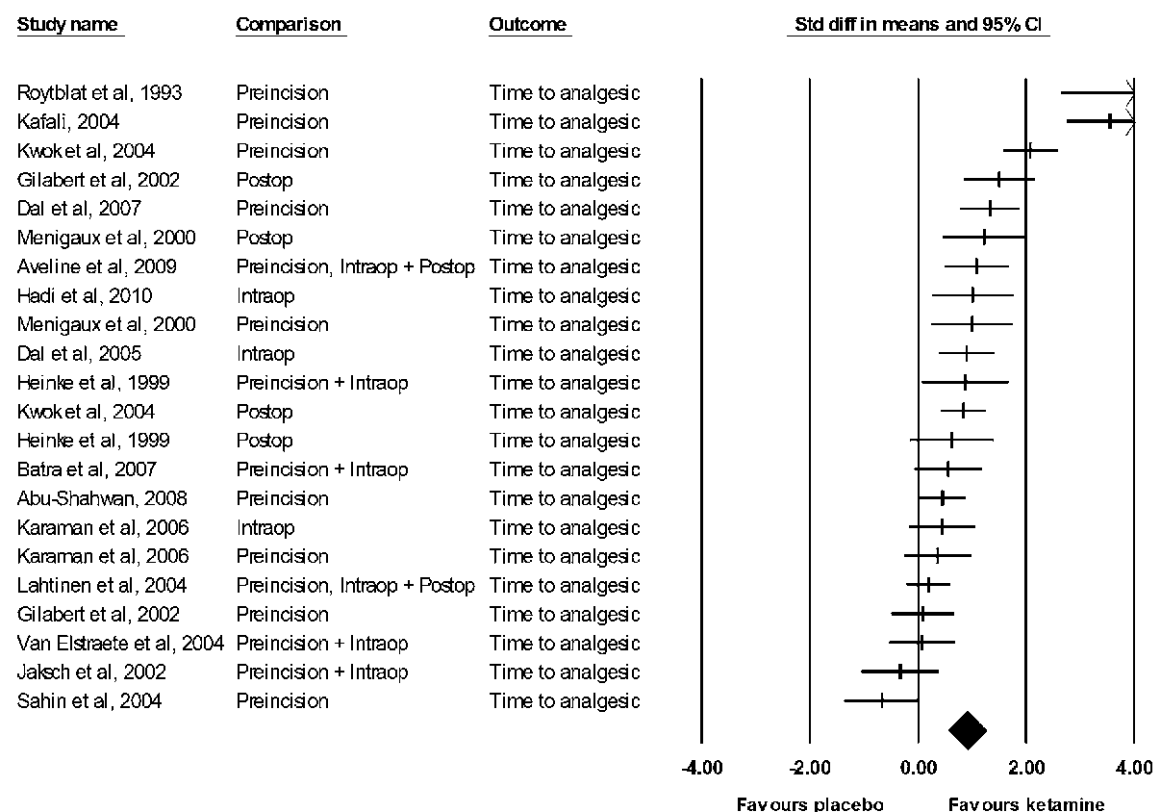
Revue méthodique de l'utilisation de la kétamine intraveineuse pour l'analgésie postopératoire

**Kevin Laskowski, MD • Alena Stirling, MD •
William P. McKay, MD • Hyun J. Lim, MD**

Received: 9 November 2010 / Accepted: 8 July 2011 / Published online: 20 July 2011

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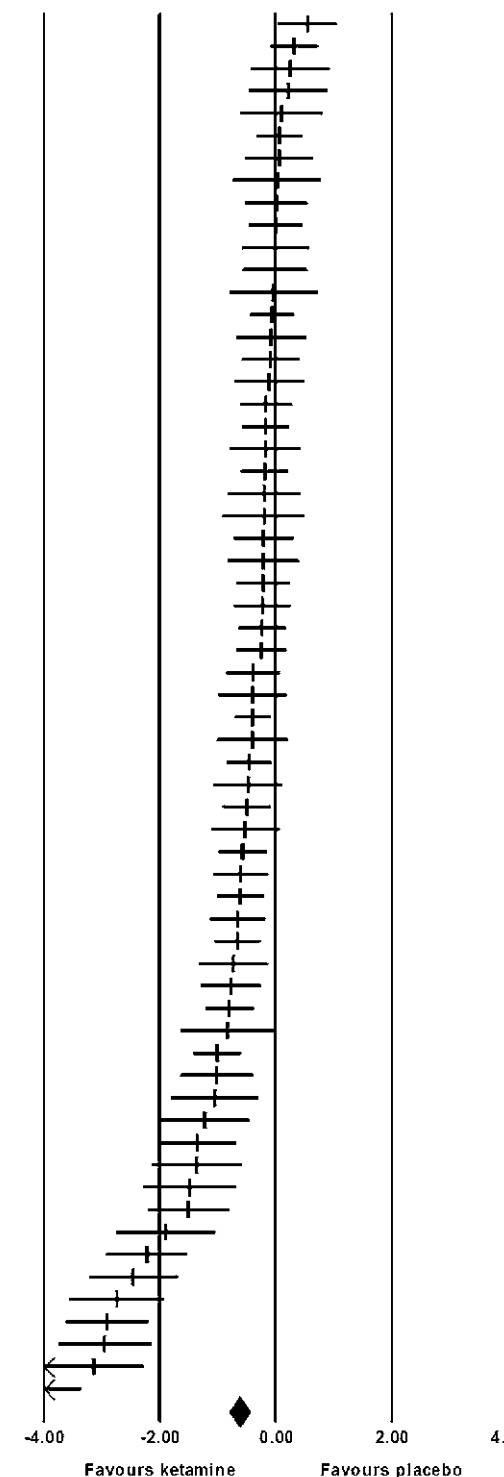
A favor del uso de ketamina



Forest plot of core meta-analysis (time to first analgesic).

Study name Comparison Outcome Std diff in means and 95% CI

Lebrun et al, 2006	Preincision	Total opioid
Aubrun et al, 2006	Preincision + PCA	Total opioid
Sahin et al, 2004	Preincision	Total opioid
Engelhardt et al, 2008	Preincision + Intraop	Total opioid
Jalsch et al, 2002	Preincision + Intraop	Total opioid
Katz et al, 2004	Intraop	Total opioid
Murdoch et al, 2002	Intraop + PCA	Total opioid
Heinke et al, 1999	Postop	Total opioid
Lebrun et al, 2006	Postop	Total opioid
Reeves et al, 2001	PCA	Total opioid
Jensen et al, 2006	Preincision + PCA	Total opioid
Hercock et al, 1999	Preincision + PCA	Total opioid
Heinke et al, 1999	Preincision + Intraop	Total opioid
Deng et al, 2009 (3)	Preincision, Intraop + Postop	Total opioid
Van Elstraete et al, 2004	Preincision + Intraop	Total opioid
Ganne et al, 2005	Preincision + Intraop	Total opioid
McKay et al, 2007	Preincision, Intraop + Postop	Total opioid
Dullenkopf et al, 2009 (2)	Preincision	Total opioid
Kwok et al, 2004	Postop	Total opioid
Batra et al, 2007	Preincision + Intraop	Total opioid
Yamauchi et al, 2008 (L2)	Preincision, Intraop + Postop	Total opioid
Karaman et al, 2006	Preincision	Total opioid
Yentur et al, 2004	Postop	Total opioid
Dahl et al, 2000	Postop	Total opioid
Karaman et al, 2006	Intraop	Total opioid
Dullenkopf et al, 2009 (1)	Preincision	Total opioid
Dahl et al, 2000	Preincision	Total opioid
Katz et al, 2004	Preincision + Intraop	Total opioid
Lehmann et al, 2001	Preincision	Total opioid
Suzuki et al, 1999 (1)	Intraop	Total opioid
Yamauchi et al, 2008 (C1)	Preincision, Intraop + Postop	Total opioid
Rembrandt et al, 2009	Preincision, Intraop + Postop	Total opioid
Gillies et al, 2007	Postop	Total opioid
Loftus et al, 2010	Preincision + Intraop	Total opioid
Gilbert et al, 2002	Preincision	Total opioid
Lahtinen et al, 2004	Preincision, Intraop + Postop	Total opioid
Gilbert et al, 2002	Postop	Total opioid
Yamauchi et al, 2008 (L1)	Preincision, Intraop + Postop	Total opioid
Suzuki et al, 1999 (2)	Intraop	Total opioid
Guillou et al, 2003	Preincision, Intraop + Postop	Total opioid
Suzuki et al, 1999 (3)	Intraop	Total opioid
Deng et al, 2009 (2)	Preincision, Intraop + Postop	Total opioid
Chazan et al, 2010	PCA	Total opioid
Reza et al, 2010	Preincision	Total opioid
Kwok et al, 2004	Preincision	Total opioid
Srijdelaar et al, 2004	Preincision, Intraop + PCA	Total opioid
Deng et al, 2009 (1)	Preincision, Intraop + Postop	Total opioid
Kapfer et al, 2006	Postop	Total opioid
Menigaux et al, 2000	Preincision	Total opioid
Menigaux et al, 2000	Postop	Total opioid
Javery et al, 1996	PCA	Total opioid
Ogun et al, 2001	Preincision and intraop	Total opioid
Adriaenssens et al, 1999	Postop	Total opioid
Sen et al, 2009	Preincision + Intraop	Total opioid
Hadi et al, 2010	Intraop	Total opioid
Lak et al, 2010	Postop	Total opioid
Primer et al, 2006	Postop	Total opioid
Unlugenc et al, 2002	Postop + PCA	Total opioid
Kafali, 2004	Preincision	Total opioid
Aveline et al, 2009	Preincision, Intraop + Postop	Total opioid
Yamauchi et al, 2008 (C2)	Preincision, Intraop + Postop	Total opioid
Roytblat et al, 1993	Preincision	Total opioid



Can J Anesth/J Can Anesth (2011) 58:911–923
DOI 10.1007/s12630-011-9560-0

A favor del uso de ketamina



- Pacientes tolerantes o dependientes a opiodes y aquellos con exacerbación de enfermedad crónica

■ PAIN MEDICINE

Anesthesiology 2010; 113:639 – 46

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Intraoperative Ketamine Reduces Perioperative Opiate Consumption in Opiate-dependent Patients with Chronic Back Pain Undergoing Back Surgery

Randy W. Loftus, M.D.,* Mark P. Yeager, M.D.,† Jeffrey A. Clark, M.D.,*
Jeremiah R. Brown, M.S., Ph.D.,‡ William A. Abdu, M.S., M.D.,§ Dilip K. Sengupta, M.D., Ph.D.,||
Michael L. Beach, M.D., Ph.D.†

A favor del uso de ketamina



Table 4. Outcomes

	Placebo	Ketamine	<i>P</i> Value
24 hr ME, total mg/24 hr	202 (176)	142 (82)	0.032
48 hr ME, total mg/48 hr	309 (341)	195 (111)	0.029
48 hr ME Adjusted, mg*	323 (347)	203 (109)	0.045
PACU VAS, cm	5.6 (3.0)	4.1 (3.1)	0.033
PACU ME, mg total	22 (20)	18 (14)	0.218
Ward VAS 24-hr, cm	4.8 (2.4)	4.7 (2.7)	0.902
Ward VAS 48-hr, cm	5.3 (2.2)	5.4 (2.1)	0.838
6-wk ME, mg/hr intravenous morphine	2.8 (6.9)	0.8 (1.1)	0.041
6-wk VAS, cm	4.2 (2.4)	3.1 (2.4)	0.026
PACU Discharge Time, min	160 (77)	174 (62)	0.321
Hospital Discharge Time, min	4,571 (4,099)	4,364 (2,296)	0.728

Data are presented as mean (SD).

* Analysis of patients who did not receive intraoperative nonsteroidal medications (ketorolac).

ME = morphine equivalent; PACU = postanesthesia care unit; VAS = visual analog scale.

Table 5. Adverse Events

	Placebo	Ketamine	<i>P</i> Value	RR (95% CI)
48 hr				
Nausea	22.5	26.9	0.603	1.20 (0.60, 2.38)
Vomiting	12.2	15.4	0.648	1.26 (0.47, 3.36)
Hallucinations	2.0	1.9	0.737	0.94 (0.06, 14.65)
Urinary Retention	2.0	7.7	0.200	3.77 (0.44, 32.56)
6 wk				
Nausea	17.0	11.8	0.458	0.69 (0.26, 1.84)
Vomiting	8.5	9.8	0.552	1.15 (0.33, 4.04)
Hallucinations	23.4	11.8	0.128	0.50 (0.20, 1.25)
Constipation	57.5	45.1	0.222	0.79 (0.53, 1.16)

CI = confidence interval; RR = risk ratio.

Anesthesiology 2010; 113:639 – 46

Clinical Note

The Role of a Low-Dose Ketamine-Midazolam Regimen in the Management of Severe Painful Crisis in Patients With Sickle Cell Disease

Qutaiba A. Tawfic, MBChB, FIBMS, Ali S. Faris, MBChB, FIBMS, and
Rajini Kausalya, MD

Department of Anesthesiology (Q.A.T., A.S.F.), The Ottawa Hospital, University of Ottawa, Ottawa, Ontario, Canada; and Department of Anesthesia (R.K.), Sultan Qaboos University Hospital, Muscat, Oman

Reduction of central neuropathic pain with ketamine infusion in a patient with Ehlers–Danlos syndrome: a case report

This article was published in the following Dove Press journal:

Journal of Pain Research

15 September 2016

Number of times this article has been viewed



Perioperative opioids aggravate obstructive breathing in sleep apnea syndrome: mechanisms and alternative anesthesia strategies

Jan P. Mulier

Curr Opin Anesthesiol 2016, 29:129–133

A favor de ketamina



Systematic Review and Meta-Analysis

PAIN[®]

Benefit and harm of adding ketamine to an opioid in a patient-controlled analgesia device for the control of postoperative pain: systematic review and meta-analyses of randomized controlled trials with trial sequential analyses

Benjamin Assouline^{a,*}, Martin R Tramèr^{a,b}, Lukas Kreienbühl^a, Nadia Elia^{a,c}

- Intensidad del dolor en 24 horas <32%
- Consumo acumulado de morfina <28%
- Náusea y vómito <44%
- No diferencia en eventos respiratorios adversos

B. Assouline et al. • 157 (2016) 2854–2864

A favor de ketamina



- Medicamento económico y ampliamente disponible
- Diferentes rutas de administración: oral, nasal, tópica, intravenosa, intramuscular, transrectal
- Múltiples mecanismos de acción
- Estabilizador de la emoción y el afecto
- Diferentes escenarios clínicos en los cuales puede ser útil
- Efecto ahorrador de opiodes
- Útil en dolor somático y neuropático

A favor de ketamina



Javier Esteban Toro López
Médico Anestesiólogo
Fellow Dolor y Cuidados Paliativos
Universidad CES – Medellín

javieretoro@gmail.com

CH