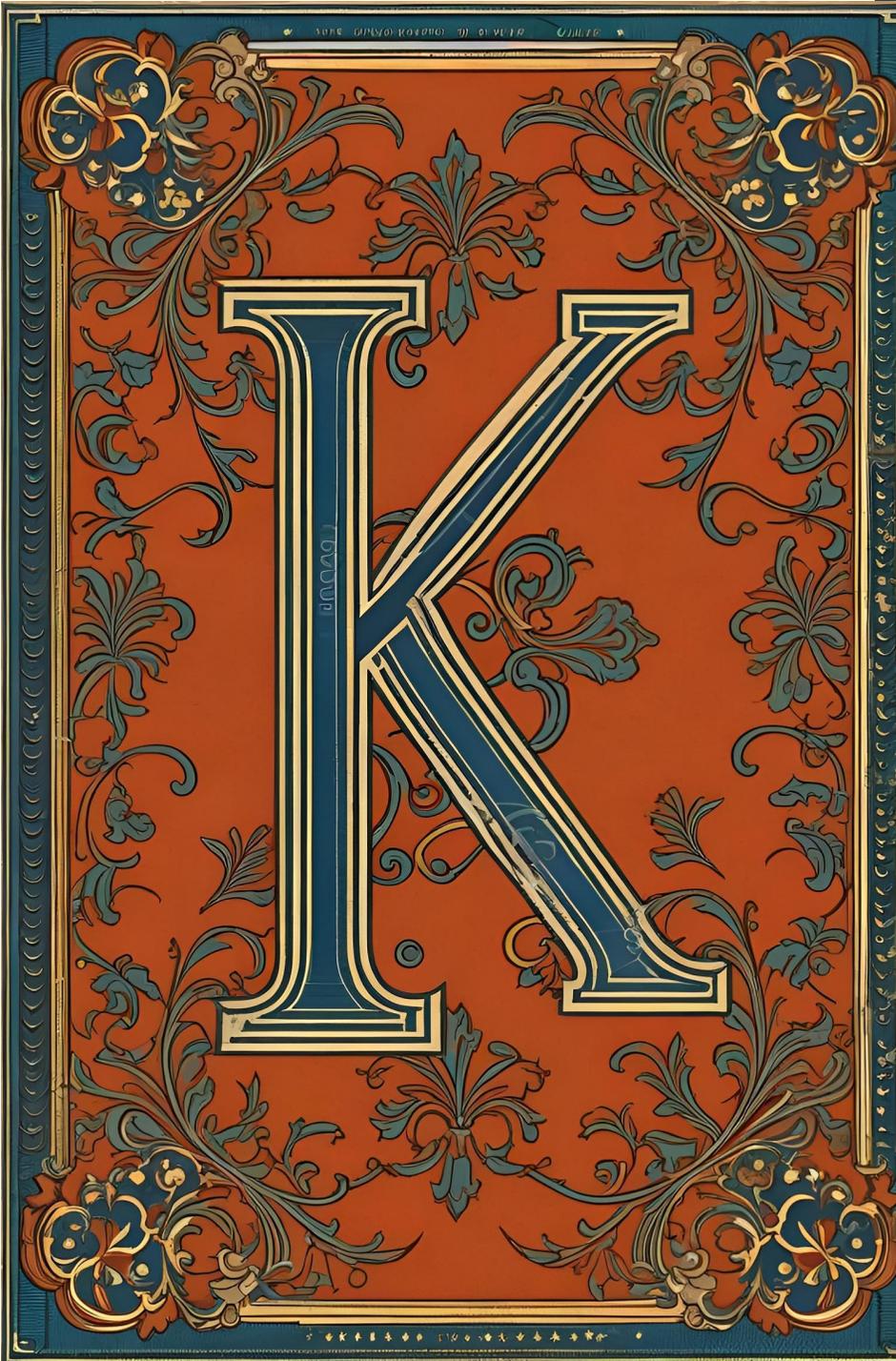


Alessandro Riccardi

Direttore Pronto Soccorso e Medicina d'Urgenza
Ospedale Santa Corona, Pietra Ligure
Faculty SIMEU Sedazione e Analgesia in Urgenza (SAU)
Responsabile Formazione SIMEU

KETAMINA

NON SOLO SEDAZIONE



Sedazione
Analgesia
Urgenza

Woody Allen



**“Tutto quello che
avreste voluto sapere
sulla ketamina ✿**

✿ Ma non avete mai osato chiedere”





...la storia della ketamina in una locandina

Zelig
Zelig
Zelig
Zelig
ZELIG
Zelig

Una Produzione JACK ROLLINS • CHARLES H. JOFFE

WOODY ALLEN MIA FARROW

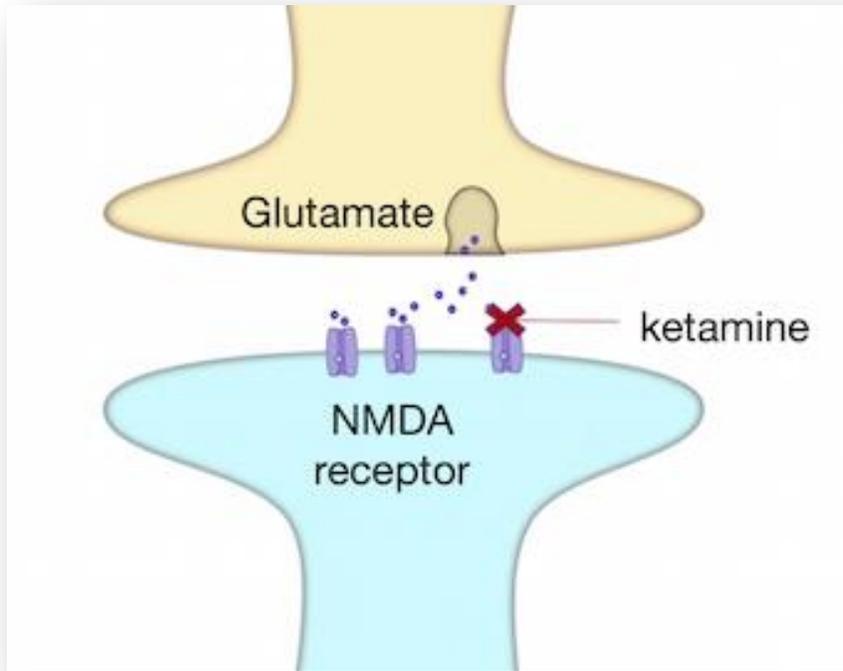
Montaggio SUSAN E. MORSE Costumi SANTO LOQUASTO Scenografia MEL BOURNE
Direttore della Fotografia GORDON WILLIS Produttore Esecutivo CHARLES H. JOFFE Prodotto da ROBERT GREENHUT
Scritto e Diretto da WOODY ALLEN
in QUADRY - The Winner Bros. Present
The Winner Bros. Company
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**un unico
farmaco
per molti
usi**



**meccanismi d'azione
della ketamina**



**BLOCCO NEURONI
GLUTAMMINERGICI
ECCITATORI
TRAMITE
ANTAGONISMO SU
NMDA_r**

**PROPOFOL,
MIDAZOLAM**

GABA_r

A close-up photograph of a car's accelerator pedal. The pedal is black with a prominent diamond-shaped grid pattern on its top surface. A metal rod is attached to the top of the pedal. To the right, another pedal, likely the brake or clutch, is partially visible but out of focus. The background is dark and indistinct.

PROPOFOL, MIDAZOLAM

Deprimono attività
corticale

Deprimono i riflessi
protettivi

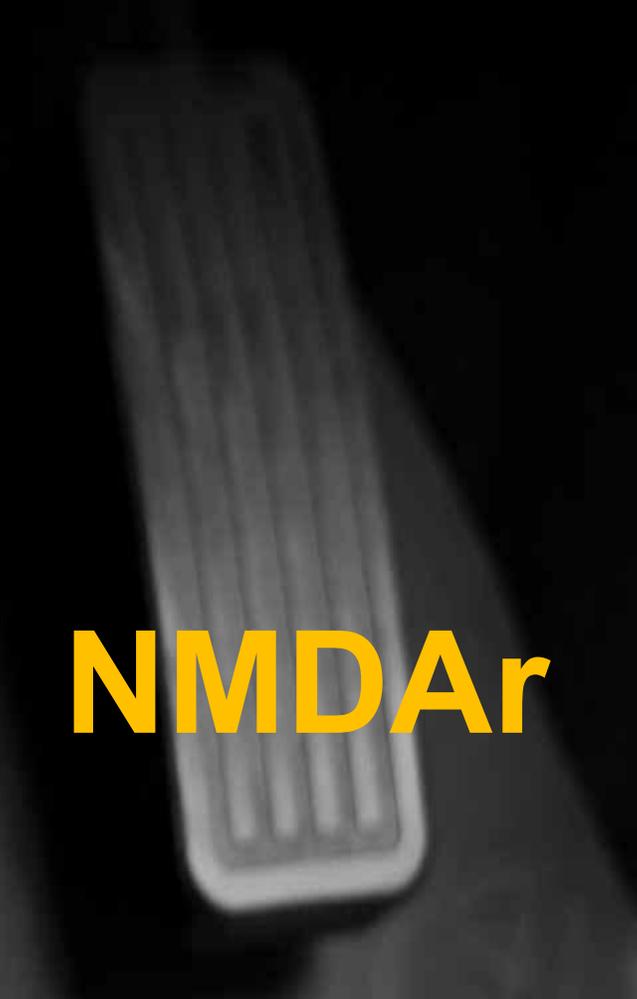
Deprimono attività
respiratoria

GABA_r



KETAMINA

Blocco comunicazione tra
periferia e corteccia
Corteccia attiva
Riflessi mantenuti
Attività respiratoria
conservata



NMDA_r



KETAMINA

Blocco comunicazione tra
periferia e corteccia

Corteccia attiva

Riflessi mantenuti

Attività respiratoria

conservata



NMDA_r

KETAMINA

1. inibizione dei recettori dell' N-Metil-D-Aspartico (NMDA)
2. potenziamento delle vie inibitorie discendenti (ossido nitrico)
3. antiinfiammatorio centrale e riduzione della sensibilizzazione centrale
4. potenziamento della via oppioide
5. Azione su recettori muscarinici, AMPAr, TORb...
6. Aumento livelli noradrenalina, serotonina, dopamina...



Dissociativo (Sedazione Procedurale)

**PERCHE' LA
KETAMINA
SPAVENTA?**



David S. Warner, M.D., Editor

Taming the Ketamine Tiger

Edward F. Domino, M.D.*

Pharmacologic Effects of CI-581, a New Dissociative Anesthetic, in Man. By E. F. Domino, P. Chodoff, G. Corssen. *Clin Pharmacol Ther* 1965; 6:279-91. Reprinted by permission from Macmillan Publishers Ltd., copyright 1965.

Abstract: Pharmacologic actions of CI-581, a chemical derivative of phencyclidine, were determined in 20 volunteers from a prison population. The results indicate that this drug is an effective analgesic and anesthetic agent in doses of 1.0 to 2.0 mg per kilogram. With intravenous administration the onset of action is within 1 min and the effects last for about 5 to 10 min, depending on dosage level and individual variation. No tachyphylaxis was evident on repeat doses. Respiratory depression was slight and

transient. Hypertension, tachycardia, and psychic changes are undesirable characteristics of the drug. Whether these can be modified by preanesthetic medication was not determined in this study. Recovery from analgesia and coma usually took place within 10 min, although from electroencephalographic evidence it may be assumed that subjects were not completely normal until after 1 to 2 h. No evidence of liver or kidney toxicity was obtained. CI-581 produces pharmacologic effects similar to those reported for phencyclidine, but of shorter duration. The drug deserves further pharmacologic and clinical trials. It is proposed that the words "dissociative anesthetic" be used to describe the mental state produced by this drug.

THOSE who anesthetize¹ patients with ketamine (originally given the clinical investigation number CI-581) realize it is a unique pharmacological agent. Ever since its introduction into human clinical anesthesia, ketamine has had a turbulent history. One only has to witness ketamine anesthesia emergence delirium to realize this agent produces unique psychic effects. Nevertheless, the value and safety of ketamine in the anesthetic management of a specific subset of surgical and critical care patients is recognized. After 45 yr of ketamine use in veterinary and human clinical anesthesia, its value and side effects are well known. Why has this drug survived? What can we learn from the past? Can knowledge about ketamine guide us in the future to help in the mission of anesthesiology to relieve pain and suffering? What are its

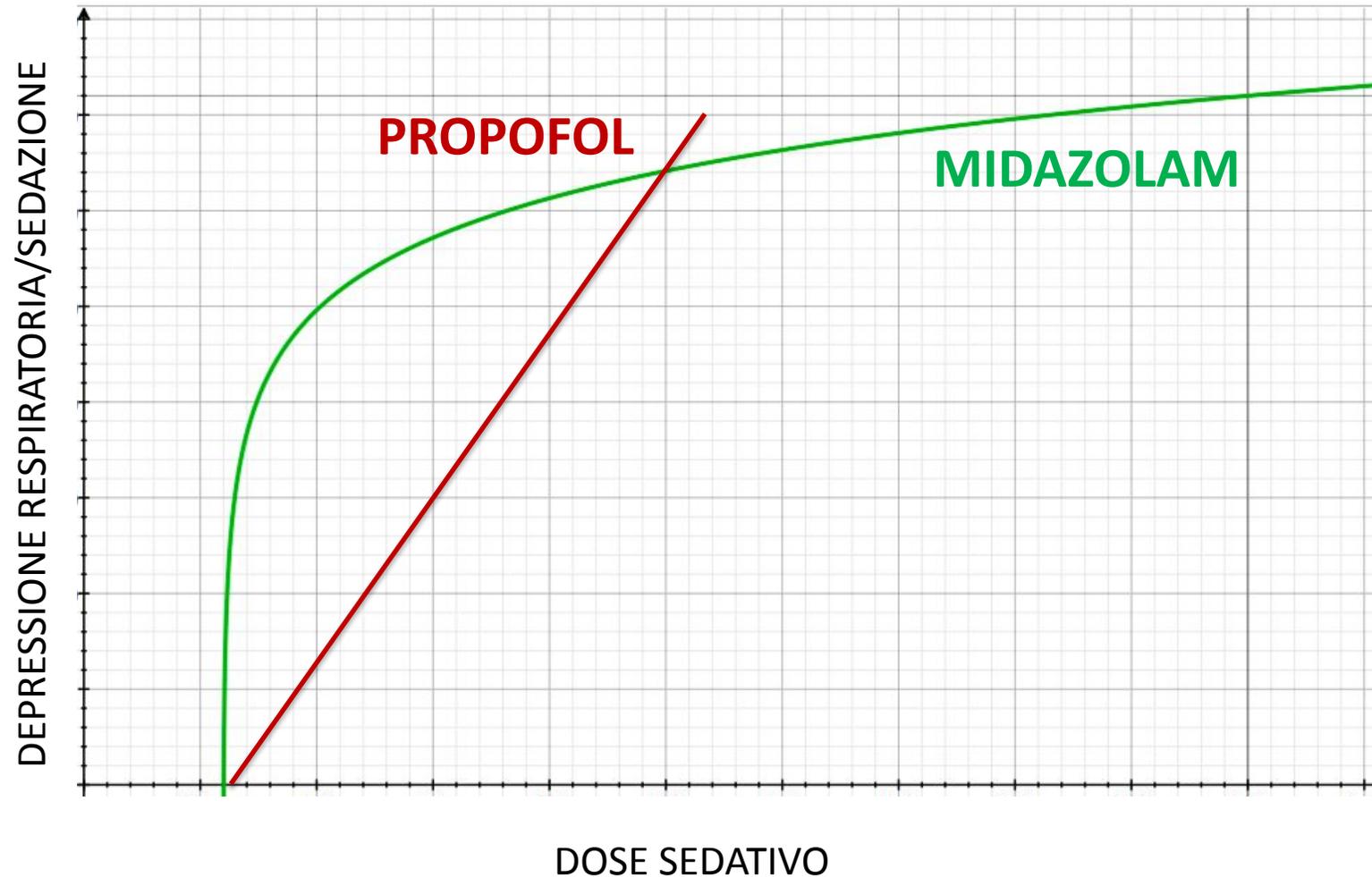
* Professor, Department of Pharmacology, University of Michigan, Ann Arbor, Michigan.

Received from Department of Pharmacology, University of Michigan. Submitted for publication March 16, 2010. Accepted for publication May 28, 2010. Support was provided solely from institutional and/or departmental sources.

Address correspondence to Dr. Domino: Department of Pharmacology, 1301 MSRB III, 1150 W. Medical Center Dr., University of Michigan, Ann Arbor, Michigan 48109-5632. efdabdc@umich.edu. This article may be accessed for personal use at no charge through the Journal Web site, www.anesthesiology.org.



CON I GABAERGICI E' CORRETTO E SICURO UN APPROCCIO DI CAUTELE, BASATO SU TITOLAZIONE



KETAMINA: DOSE PIENA



MAI SOTTODOSARE

KETAMINA

1-2

mg/kg

e.v.

KETAMINA

5-10

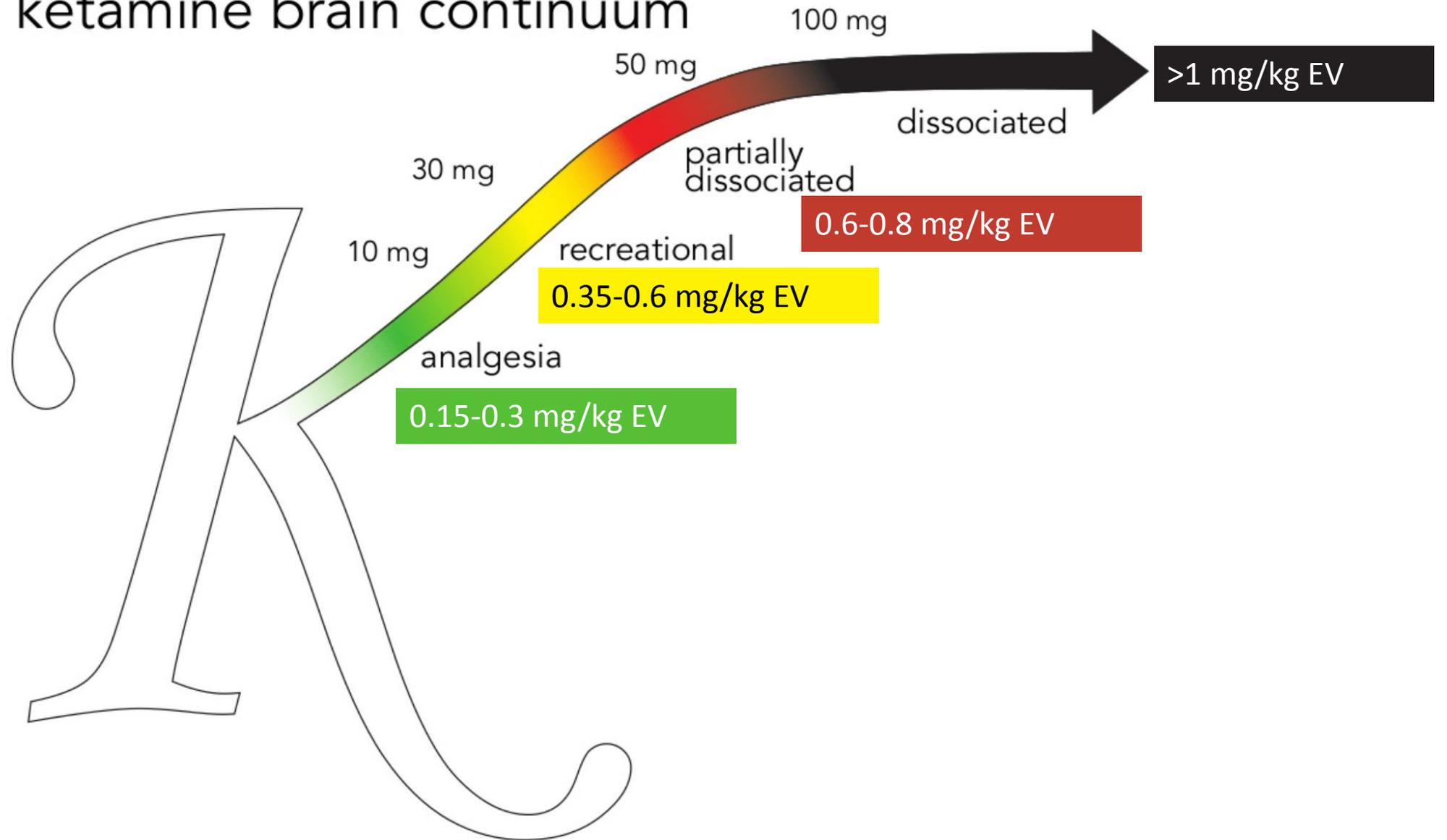
mg/kg

i.m.

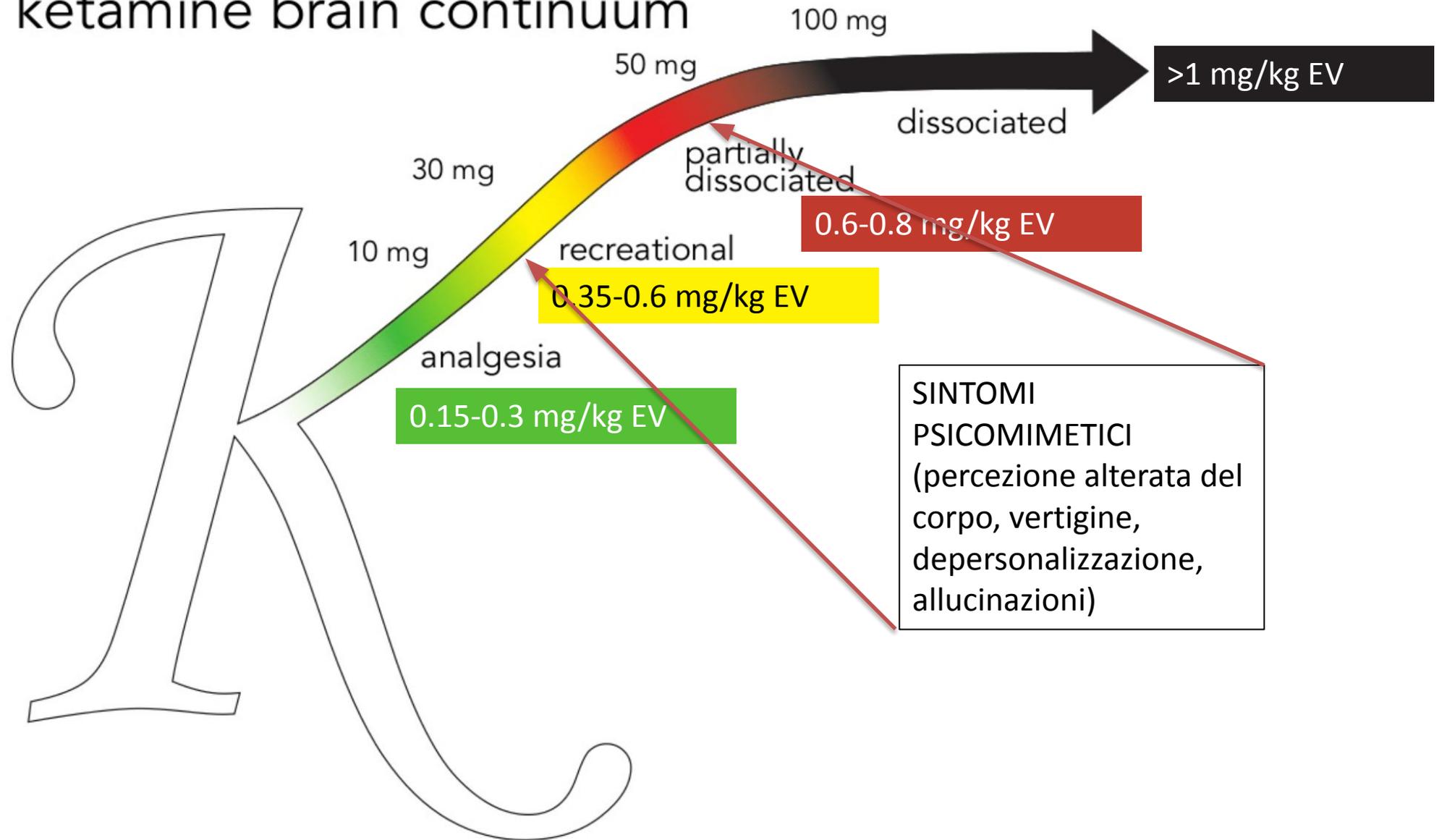
A young girl with long, wavy brown hair and bangs is shown in a laboratory setting. She is wearing a grey V-neck sweater over a white collared shirt and a red and yellow striped tie. She is holding a glass beaker in her right hand, pouring a green liquid into a test tube held in her left hand. The background features several white laboratory sinks and a tiled wall. The text "una questione di dosaggio" is overlaid in large white font across the center of the image.

**una questione di
dosaggio**

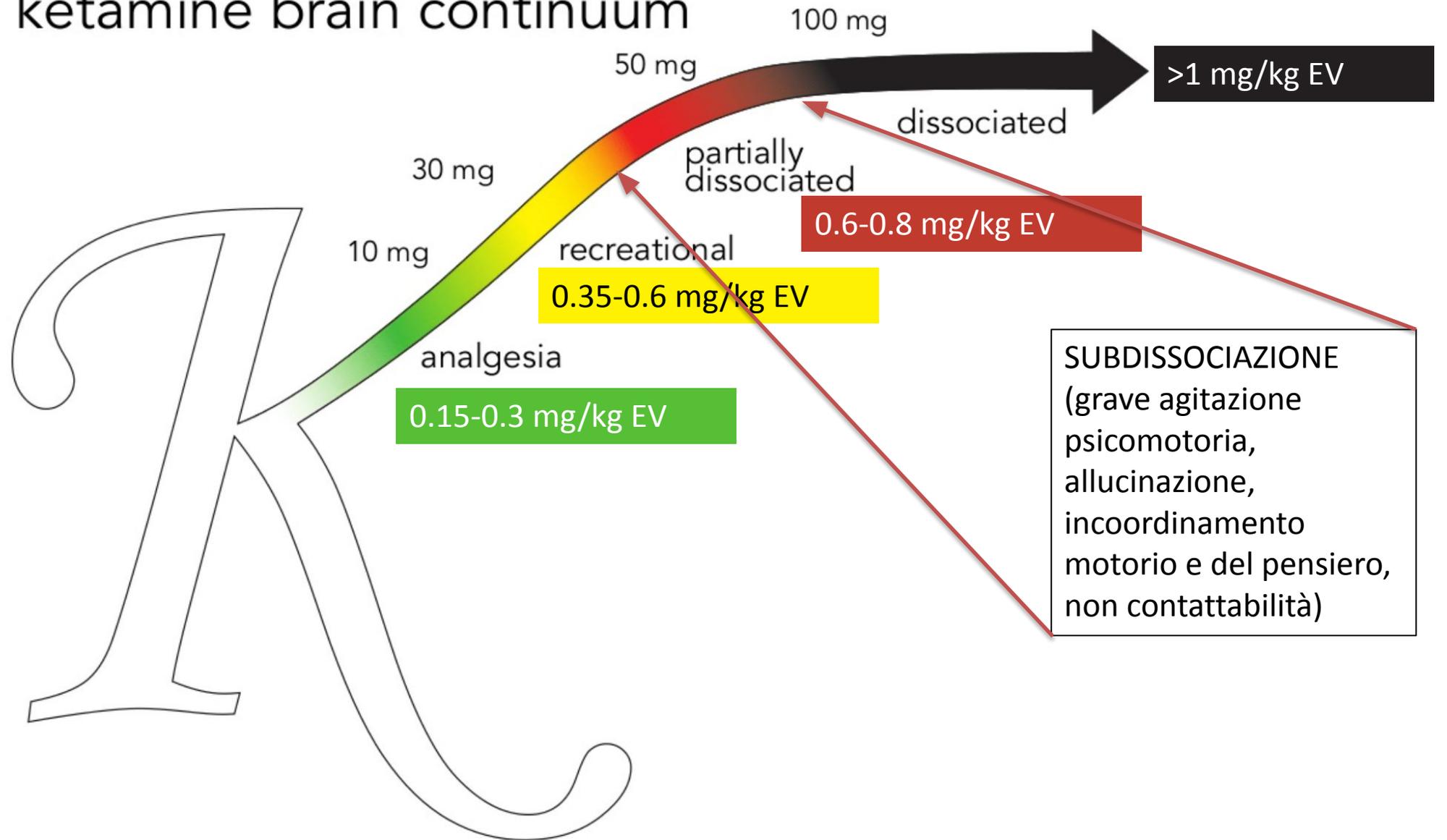
ketamine brain continuum



ketamine brain continuum



ketamine brain continuum



Basta che
funzioni



Sedativo

DELIRIO

IPERATTIVO



court tv
RECORDING 11 11 2011

MORTALITA'

14%

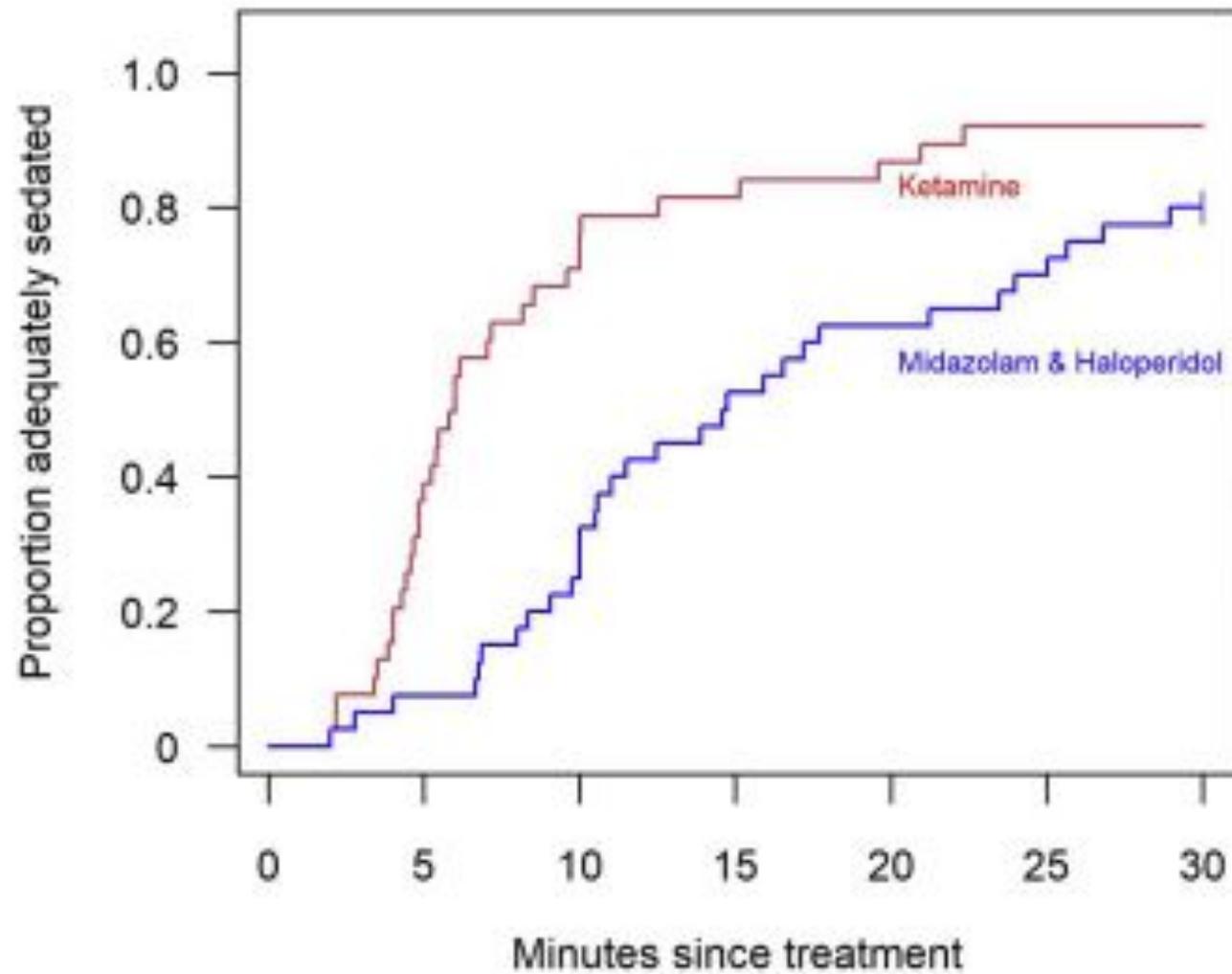
come l'embolia polmonare massiva

Rapid Agitation Control With Ketamine in the Emergency Department: A Blinded, Randomized Controlled Trial



David Barbic, MD, MSc*; Gary Andolfatto, MD; Brian Grunau, MD, MSCH; Frank X. Scheuermeyer, MD, MHSc; Bill Macewan, MD;
Hong Qian, MSc; Hubert Wong, PhD; Skye P. Barbic, PhD; William G. Honer, MD

*Corresponding Author. E-mail: david.barbic@ubc.ca.



POPOLAZIONE DELLO STUDIO: 308 pazienti

NEL DELIRIO ECCITATO IL PAZIENTE HA

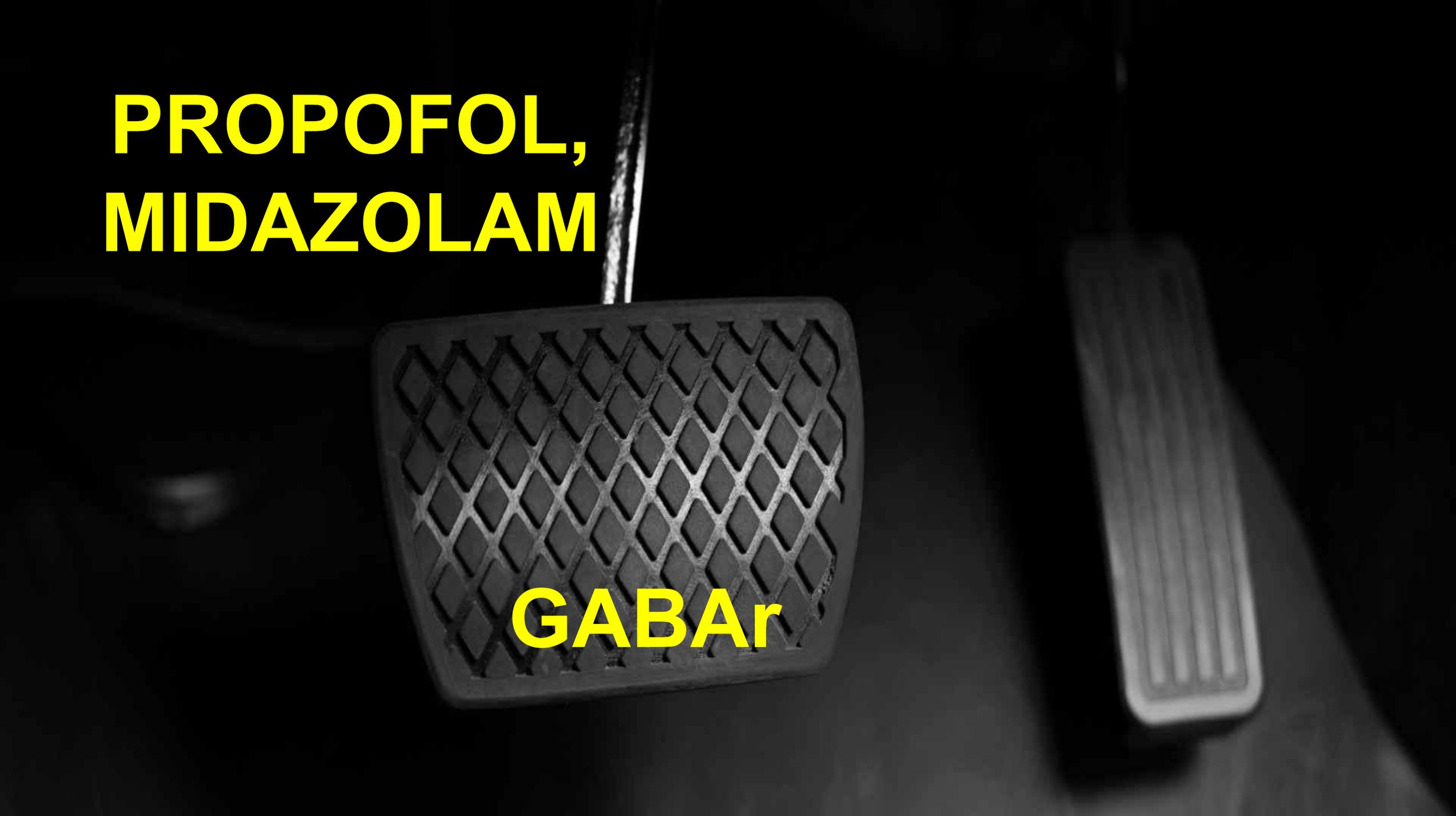
- IPOVOLEMIA
- ACIDOSI METABOLICA
- DISONIA
- RABDOMIOLISI
- INSUFFICIENZA RENALE ACUTA
- DEPLEZIONE CATECOLAMINERGICA

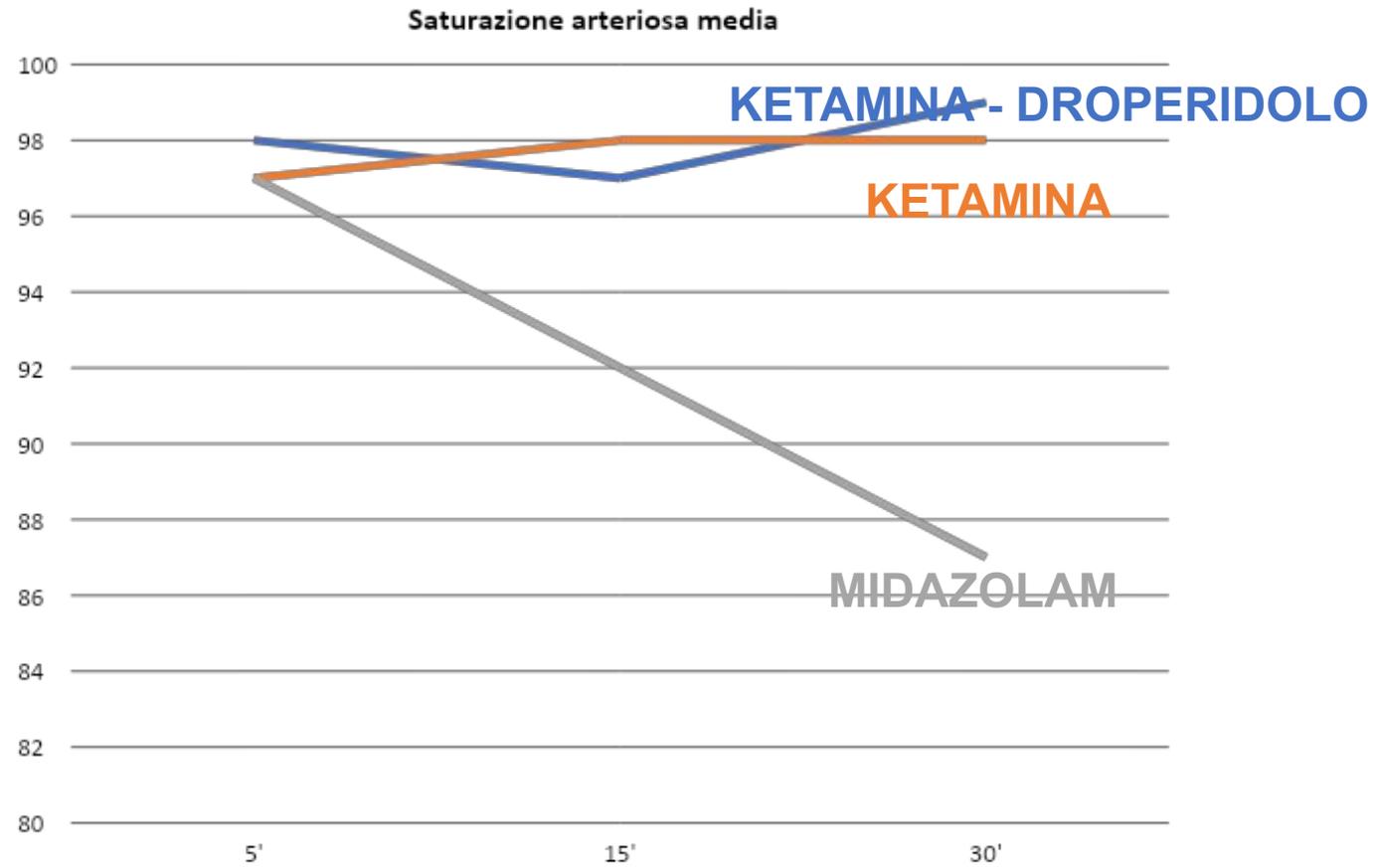


SYSTEM FAILURE

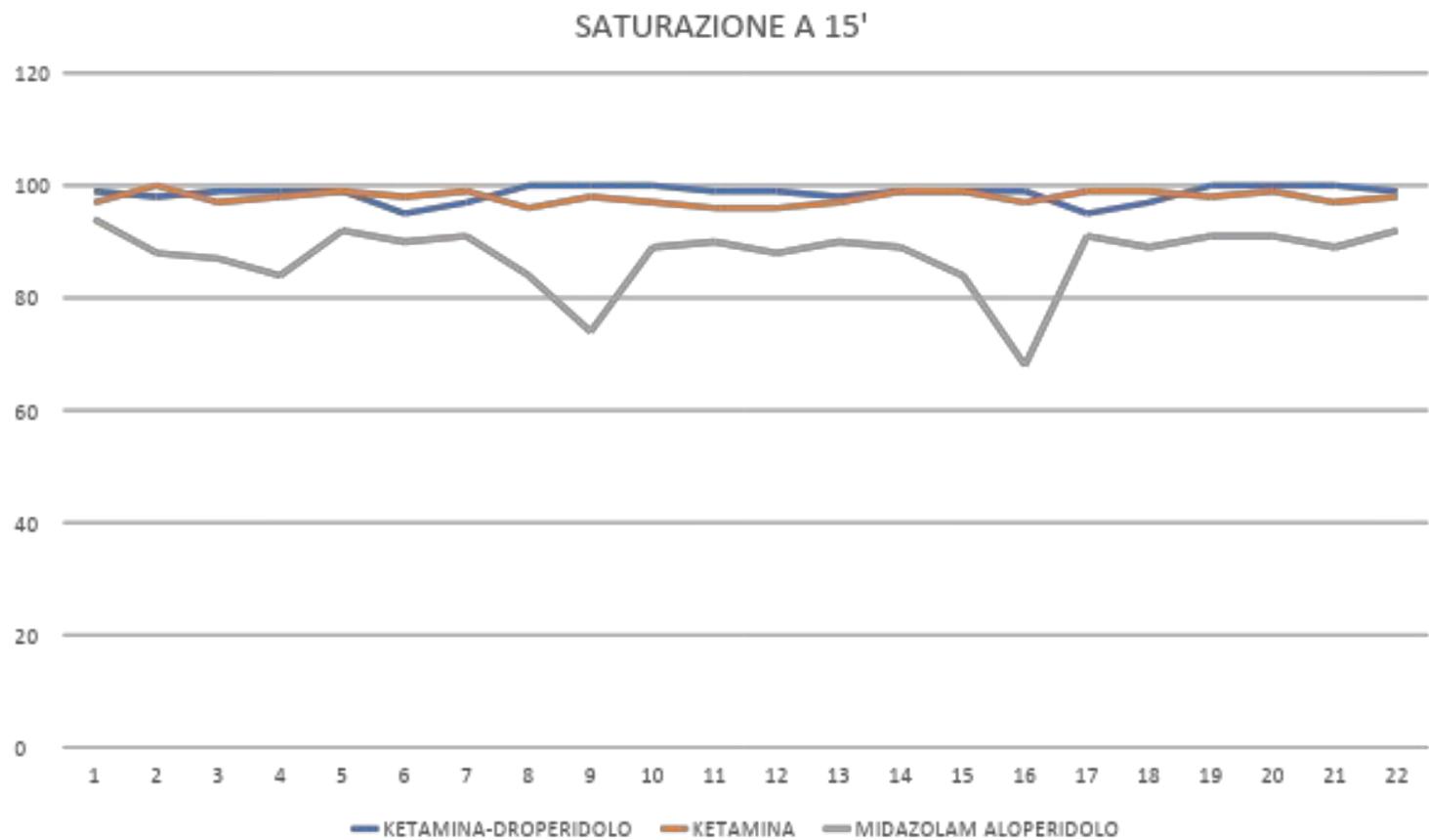
**PROPOFOL,
MIDAZOLAM**

GABA_r





DATI DELL'AUTORE (multicentrico ligure su grave agitazione psicomotoria RASS 4)



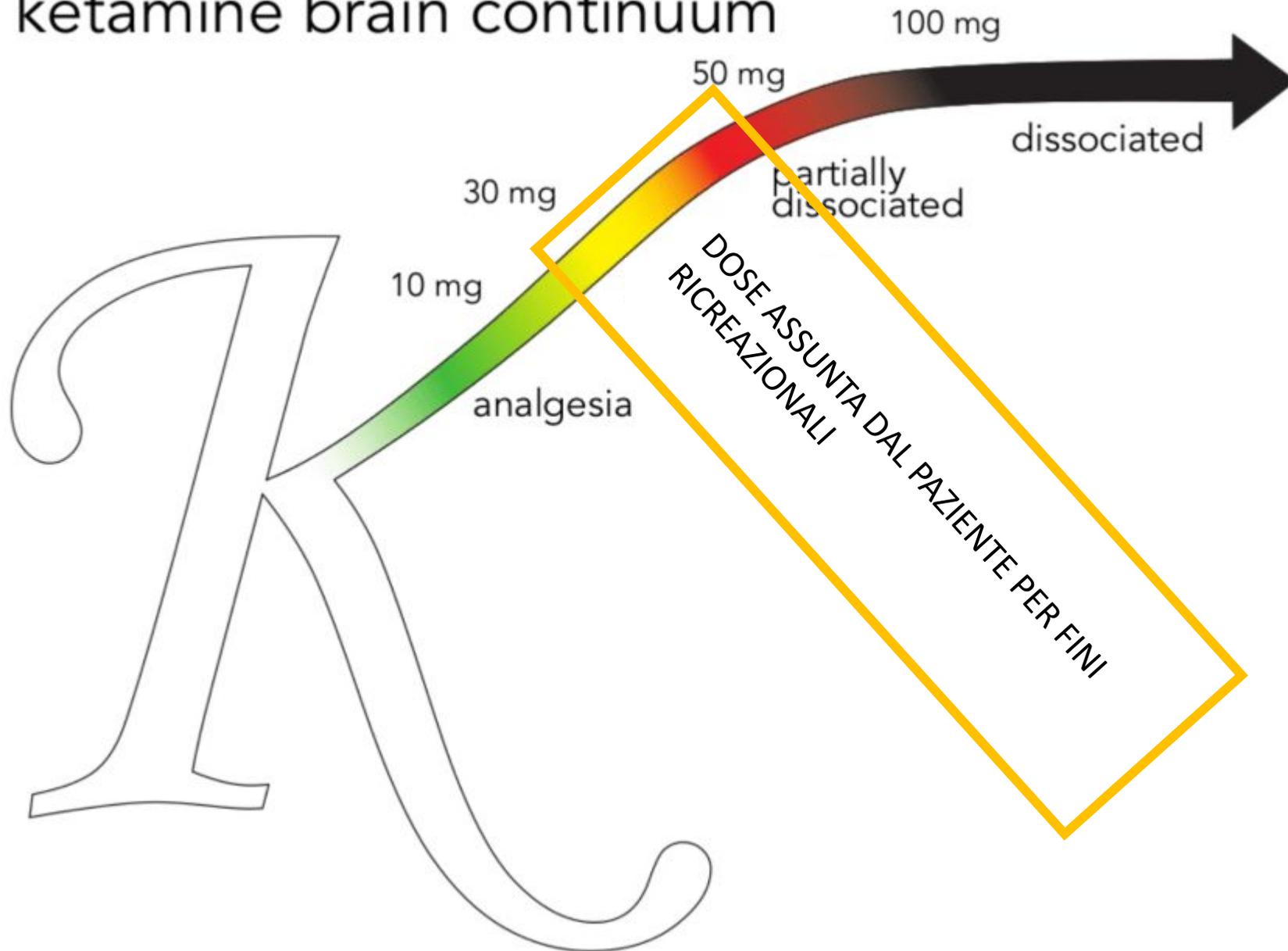
DATI DELL'AUTORE (multicentrico ligure su grave agitazione psicomotoria RASS 4)
Gruppo MIDAZOLAM: 3 apnee con necessità di ventilazione

5-10 mg/kg
intramuscolari

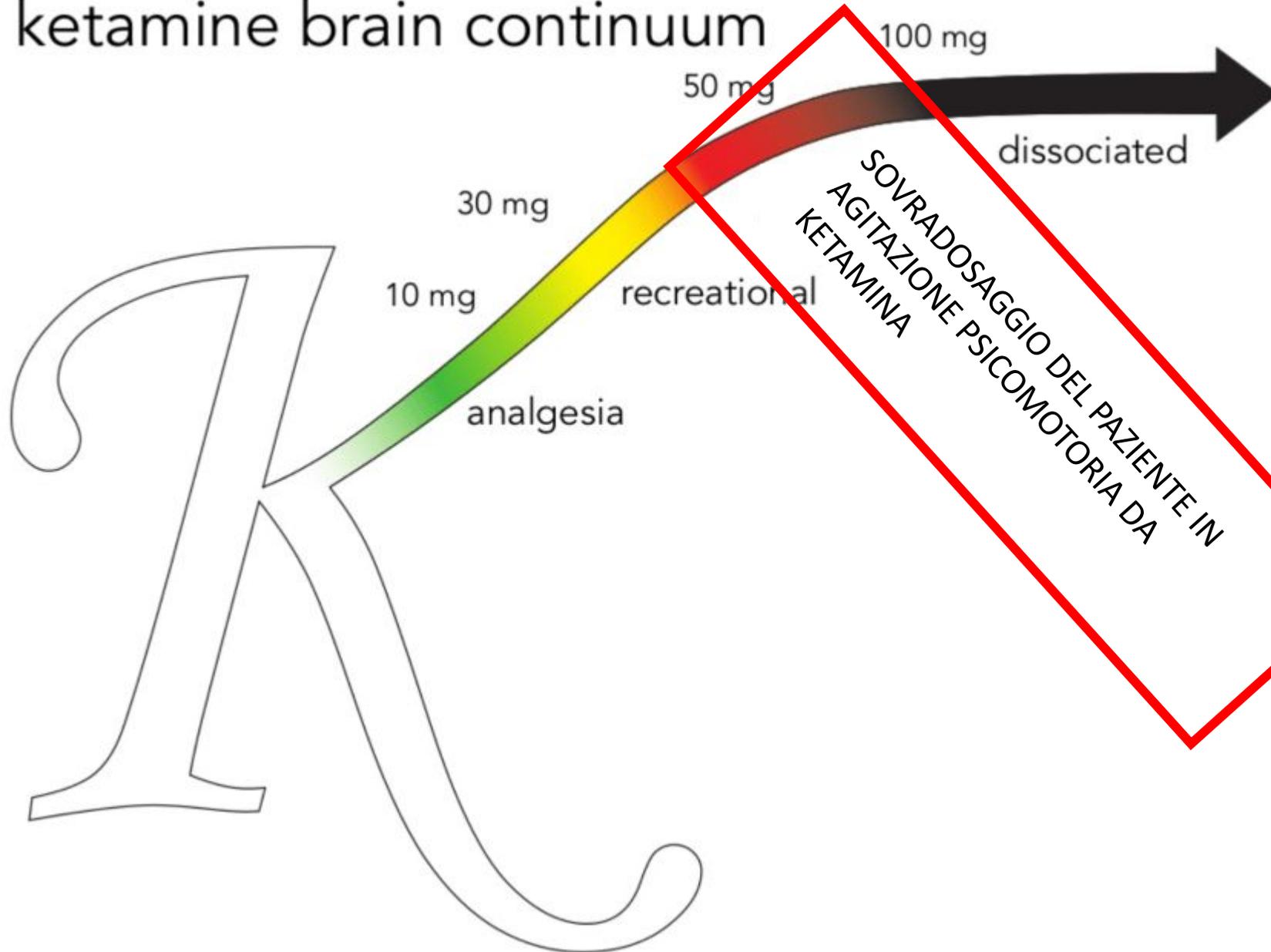
**1-2 mg/kg
endovenosi**

e se il paziente
agitato ha assunto
KETAMINA?

ketamine brain continuum



ketamine brain continuum

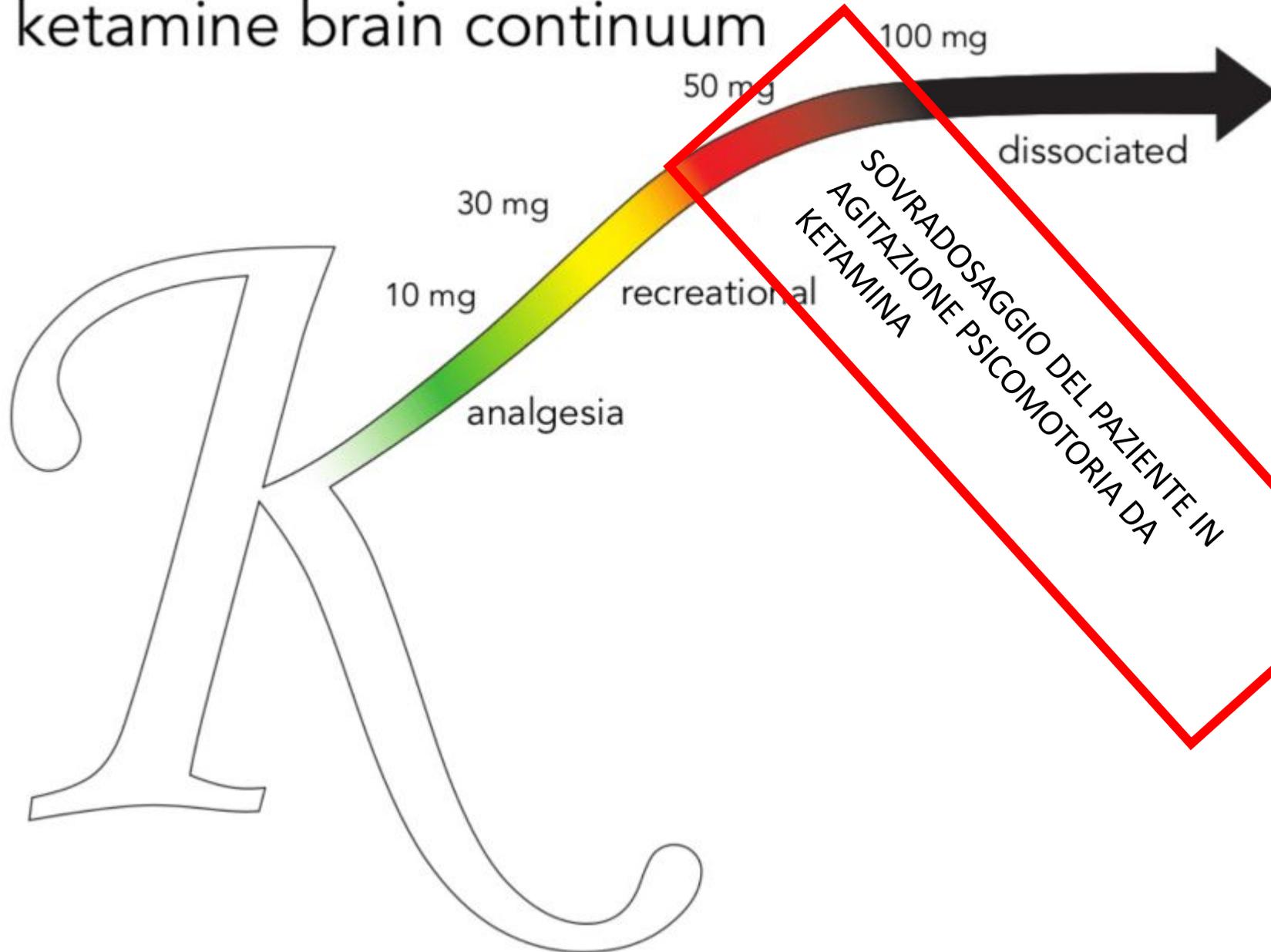


**se avesse assunto
una dose ancora
maggiore, sarebbe
dissociato**

ovvero nel

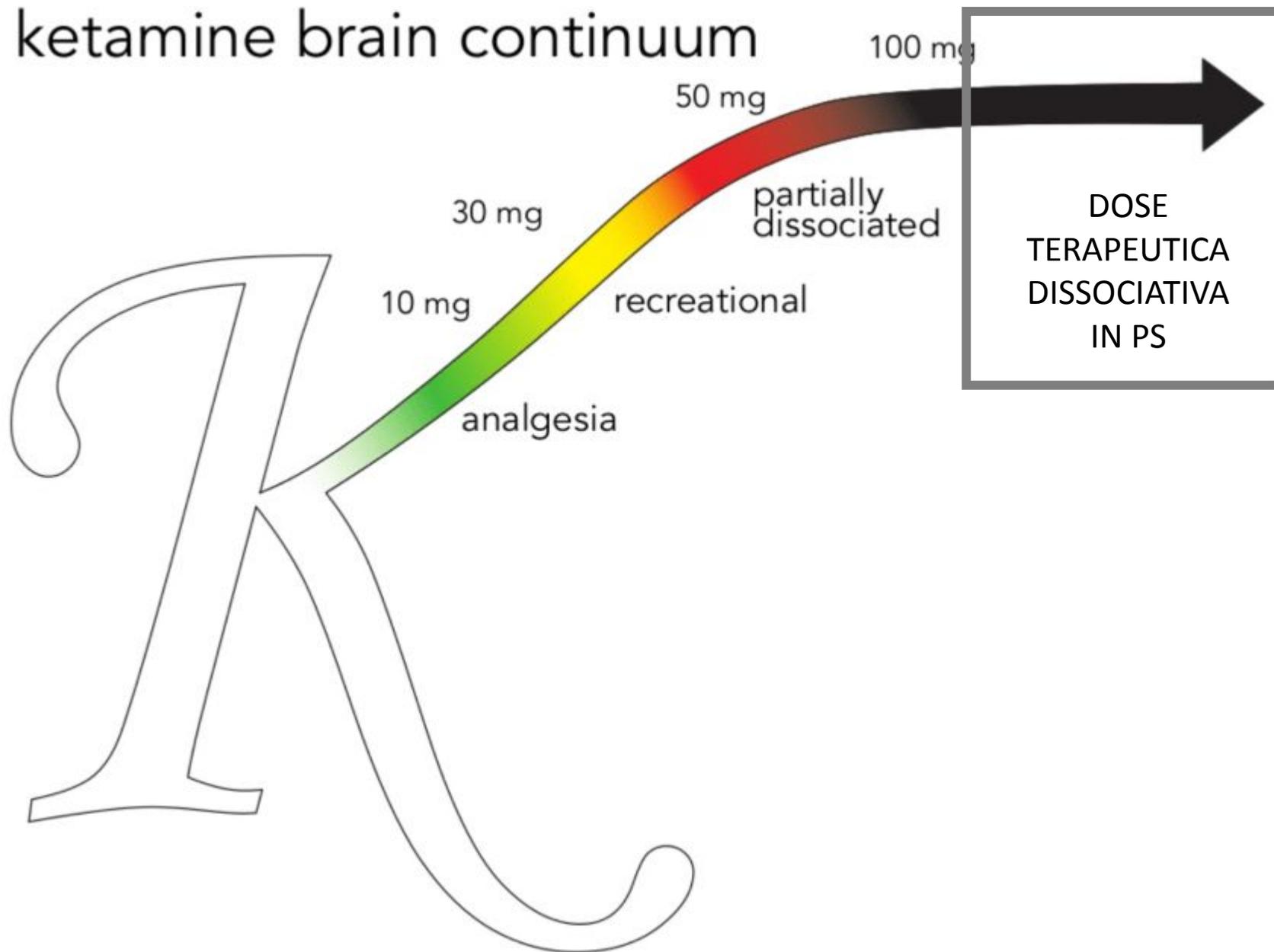
K-HOLE

ketamine brain continuum



SOVRADOSAGGIO DEL PAZIENTE IN
AGITAZIONE PSICOMOTORIA DA
KETAMINA

ketamine brain continuum



Ketamine Safety and Use in the Emergency Department for Pain and Agitation/Delirium: A Health System Experience

Hanjie Mo, PharmD*
Matthew J. Campbell, PharmD*
Baruch S. Fertel, MD, MPA†
Simon W. Lam, PharmD*
Elizabeth J. Wells, PharmD*
Elizabeth Casserly, PharmD*
Stephen W. Meldon, MD†

*Cleveland Clinic, Department of Pharmacy, Cleveland, Ohio
†Cleveland Clinic, Emergency Services Institute, Cleveland, Ohio

Western Journal of Emergency Medicine

Volume 21, No. 2: March 2020

Several patients also received ketamine doses above the recommended range. This may not portend harm as once dissociation is achieved, there is no further depth to sedation with increased ketamine administration. Additionally, protocol

**SEDATIVO-ANESTETICO PRIVO DI AZIONE LINEARE DOSE
DIPENDENTE SULLA DEPRESSIONE RESPIRATORIA**

Steven M Green, MD^{*}
Richard Clark, MD[†]
Mark A Hostetler, MD[§]
Michael Cohen, MS^{||}
Douglas Carlson, MD[¶]
Steven G Rothrock, MD[¶]

Inadvertent Ketamine Overdose in Children: Clinical Manifestations and Outcome

Conclusion: No adverse outcomes were noted in 9 healthy children treated in the ED who inadvertently received 5 to 100 times the intended dose of ketamine. Toxicity manifested as prolonged sedation in all 9 and brief respiratory depression in 4. The margin of safety in ketamine overdose may be wide, although less common and more serious outcomes cannot be excluded by this small, self-reported sample.

**Nessuna segnalazione di decesso per
uso medico di ketamina**

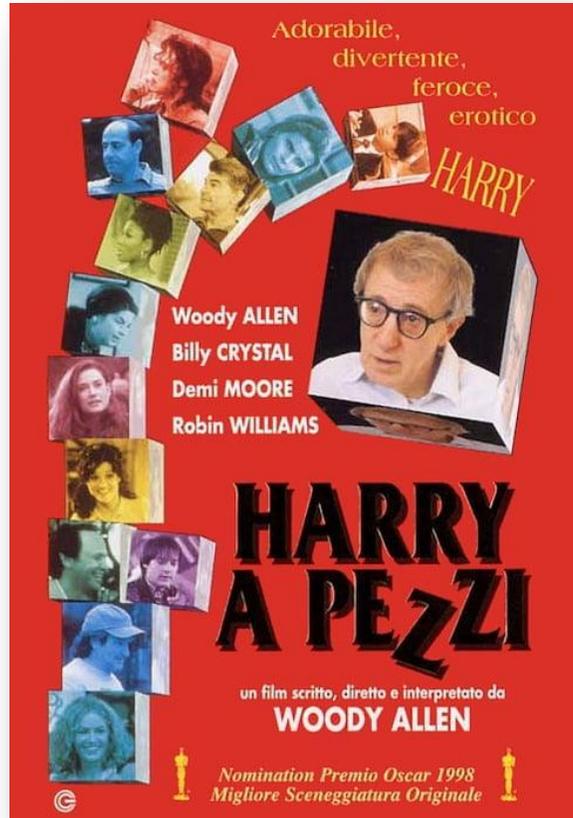
>40 mg/kg EV

**Dose pericolosa
dedotta da modelli animali
(primati)**

I decessi legati
all'abuso sono
connessi ad eventi
traumatici per lo
stato
subdissociativo o
psicomimetico *



*è vero che non deprime l'attività respiratoria anche a dosaggi dissociativi, ma non avendo branchie, la vasca da bagno non è da considerarsi sicura



Analgesic

0,2-0,3
mg/kg e.v.
bolo

1

mg/kg

intranasale

RESEARCH ARTICLE

The Effects of Low-Dose Ketamine on Acute Pain in an Emergency Setting: A Systematic Review and Meta-Analysis

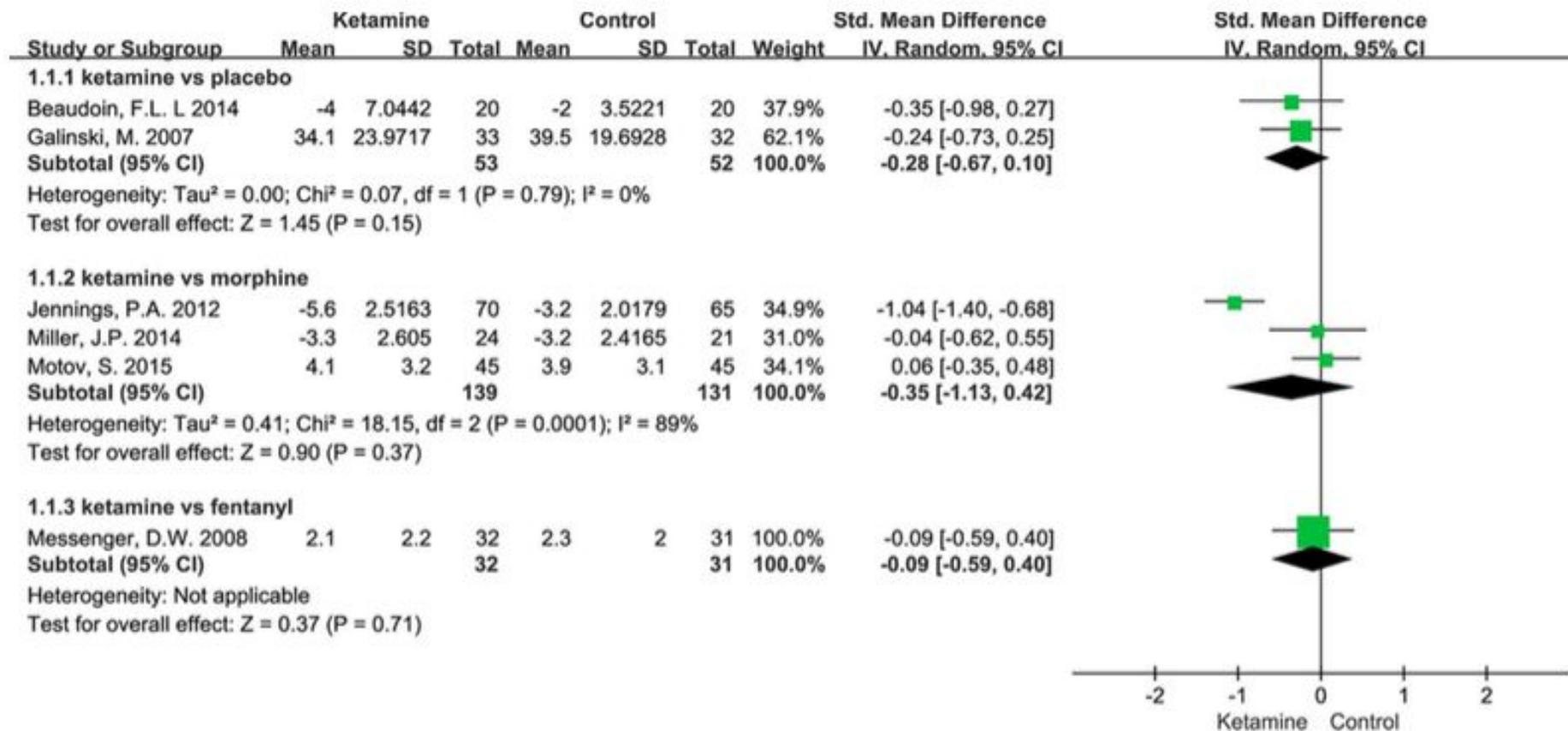
Eun Nam Lee¹*, Jae Hoon Lee²*,

1 Department of Nursing, Dong-A University, Daesin Gonwon-Ro, Seo-Gu, Busan, South Korea,

2 Department of Emergency Medicine, Dong-A university College of Medicine, Daesin Gonwon-Ro, Seo-Gu, Busan, South Korea

PLOS ONE, 2016

efficace
come la
morfina
in bolo



Lee, PLOS ONE, 2016

REGIONAL ANESTHESIA AND ACUTE PAIN

SPECIAL ARTICLE

OPEN

Consensus Guidelines on the Use of Intravenous Ketamine Infusions for Acute Pain Management From the American Society of Regional Anesthesia and Pain Medicine, the American Academy of Pain Medicine, and the American Society of Anesthesiologists

Eric S. Schwenk, MD, Eugene R. Viscusi, MD,* Asokumar Buvanendran, MD,† Robert W. Hurley, MD, PhD,‡
Ajay D. Wasan, MD, MSc,§ Samer Narouze, MD, PhD,|| Anuj Bhatia, MD, MBBS,** Fred N. Davis, MD,††
William M. Hooten, MD,‡‡ and Steven P. Cohen, MD§§*

SYSTEMATIC REVIEWS (WITH OR WITHOUT META-ANALYSES)

A Systematic Review and Meta-analysis of Ketamine as an Alternative to Opioids for Acute Pain in the Emergency Department

Nicholas Karlow, MPHS, Charles H. Schlaepfer, Carolyn R. T. Stoll, MPH, MSW,
Michelle Doering, MA, Christopher R. Carpenter, MD, Graham A. Colditz, DrPH, MD,
Sergey Motov, MD, Joshua Miller, MD, and Evan S. Schwarz, MD

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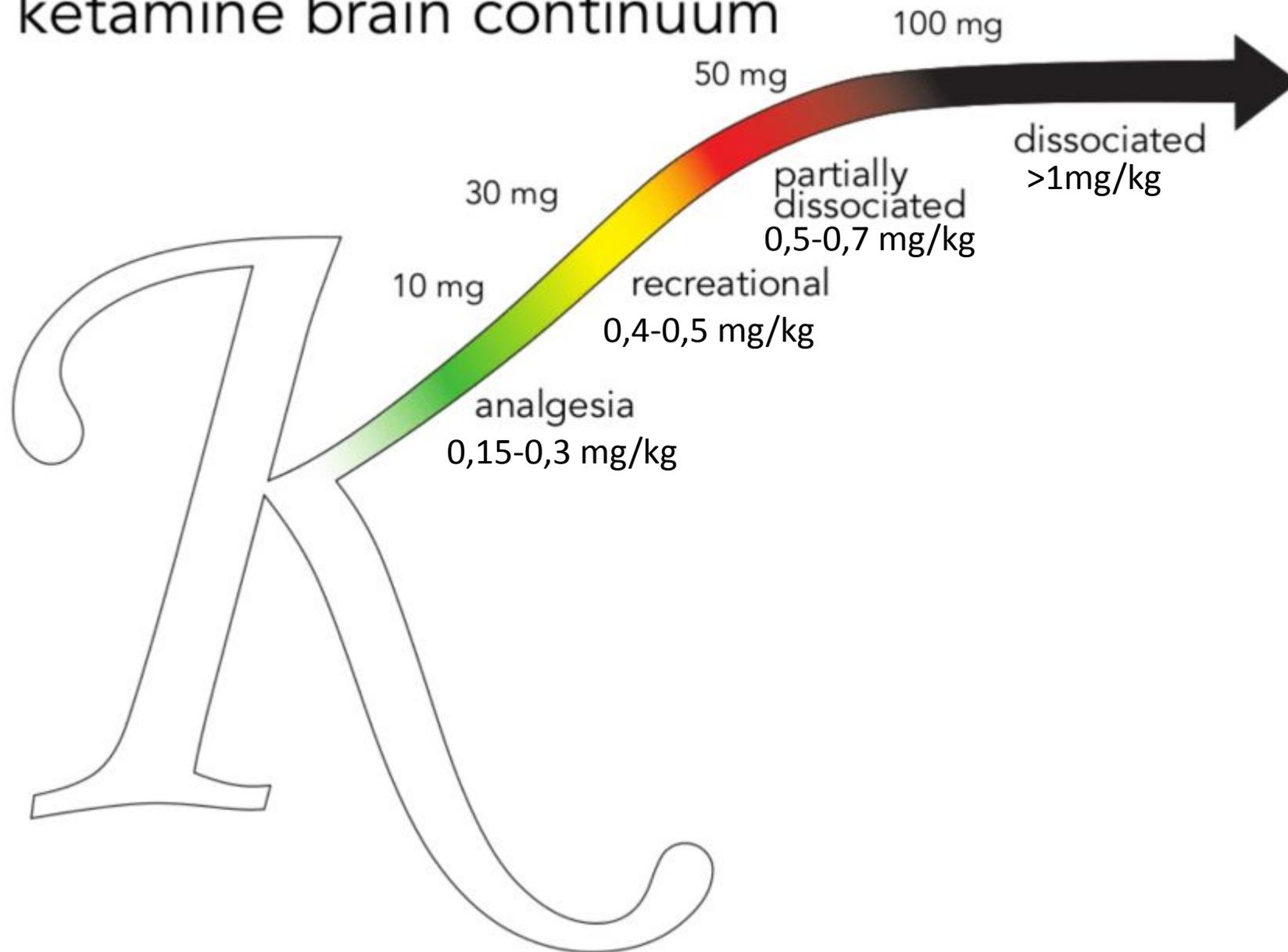
KETAMINA

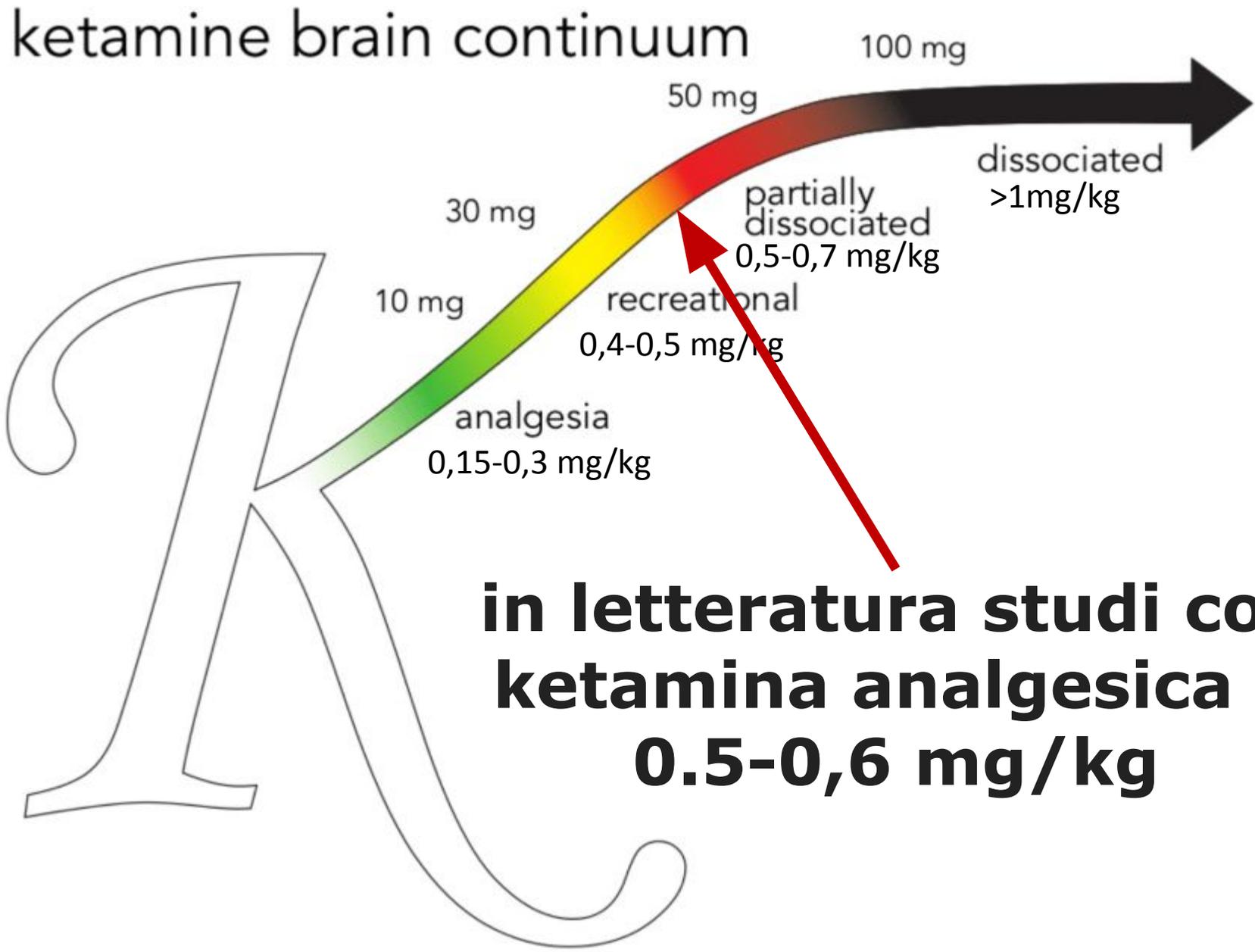
EVENTI AVVERSI

- vertigine
- nausea/vomito
- sensazione di de-personalizzazione

soprattutto a dosaggi maggiori

ketamine brain continuum





**in letteratura studi con
ketamina analgesica a
0.5-0,6 mg/kg**

A stylized illustration of a man in a suit, shown from the chest up. He is wearing a dark suit jacket, a white shirt, and a dark tie. From the top of his head, a large plume of colorful smoke or steam rises, composed of several thick, wavy bands of color: magenta, blue, green, red, yellow, cyan, and red. The background is a solid light blue color.

**la vera
rivoluzione**

Ketamine Infusions for Chronic Pain: A Systematic Review and Meta-analysis of Randomized Controlled Trials

Vwaire Orhurhu, MD, MPH,* Mariam Salisu Orhurhu, MD, MPH,† Anuj Bhatia, MD, FRCPC,‡
and Steven P. Cohen, MD§||

0,15-0,3
mg/kg/h e.v.
infusione

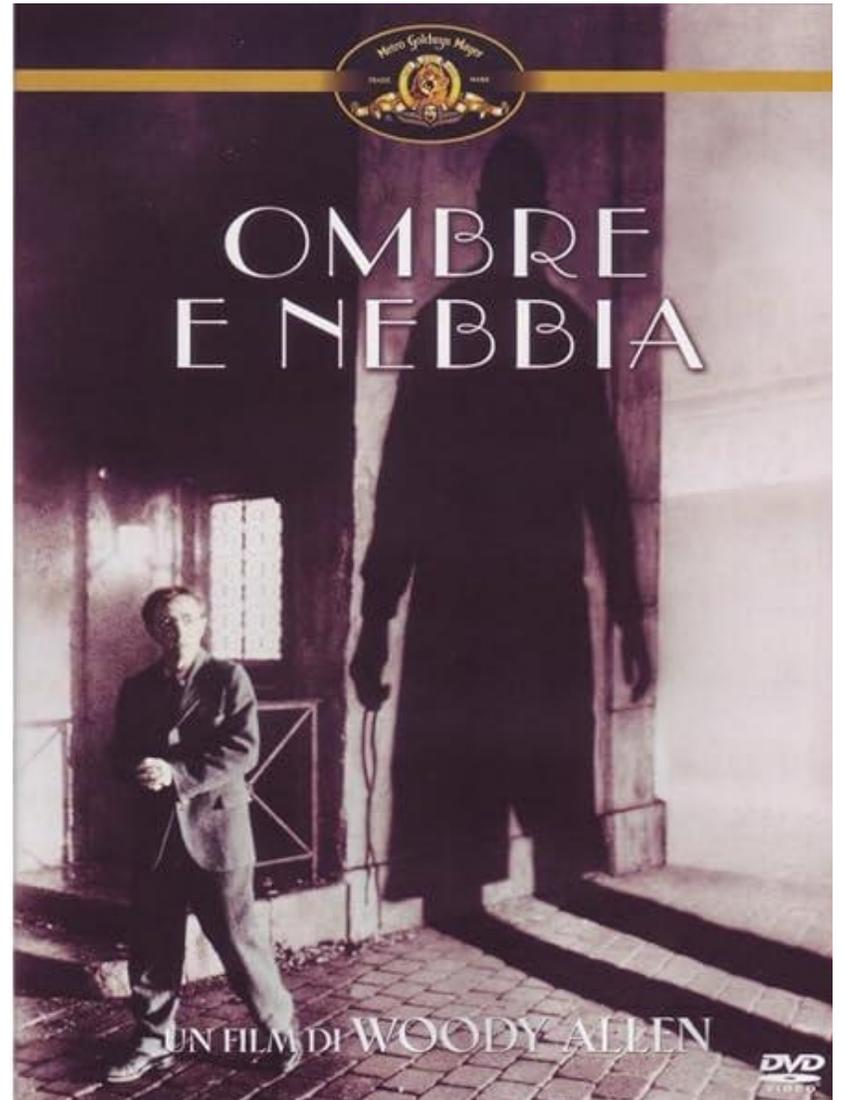
The median (range) duration of ketamine infusion for all 7 studies was 5 hours (range, 0.5–100 hours), and the median number of days over which ketamine was administered, continuously or intermittently, was 1 day (range, 1–10 days). The median (range) dose of ketamine during the infusion using a 70-kg patient as the reference was 0.35 mg·kg⁻¹ (0.23–0.6 mg·kg⁻¹).

Ketamine is a cytochrome P450 dependent drug. It is metabolized in the liver by CYP3A4, CYP2B6 and CYP2C9 to norketamine (via *N*-demethylation) with subsequent metabolism of norketamine into 4-, 5- and 6-hydroxynorketamine (by CYP2A6 and CYP2B6). Norketamine is produced within minutes after intravenous administration of ketamine and may exceed the ketamine concentration particularly after long term infusion [4, 8, 12]. Elimination of norketamine and the hydroxynorketamines occurs after glucuronidation in the liver, through the kidney and bile [16–18]. Inhibitors of the CYP enzymes involved in the metabolism of ketamine increase ketamine plasma concentrations [19]. In contrast, induction of the CYP system has limited effect on the plasma concentration of ketamine as the hepatic clearance of ketamine before

**La ketamina in infusione per
100 ore controlla il dolore
cronico **fino a 3 mesi dalla
sospensione del farmaco.****

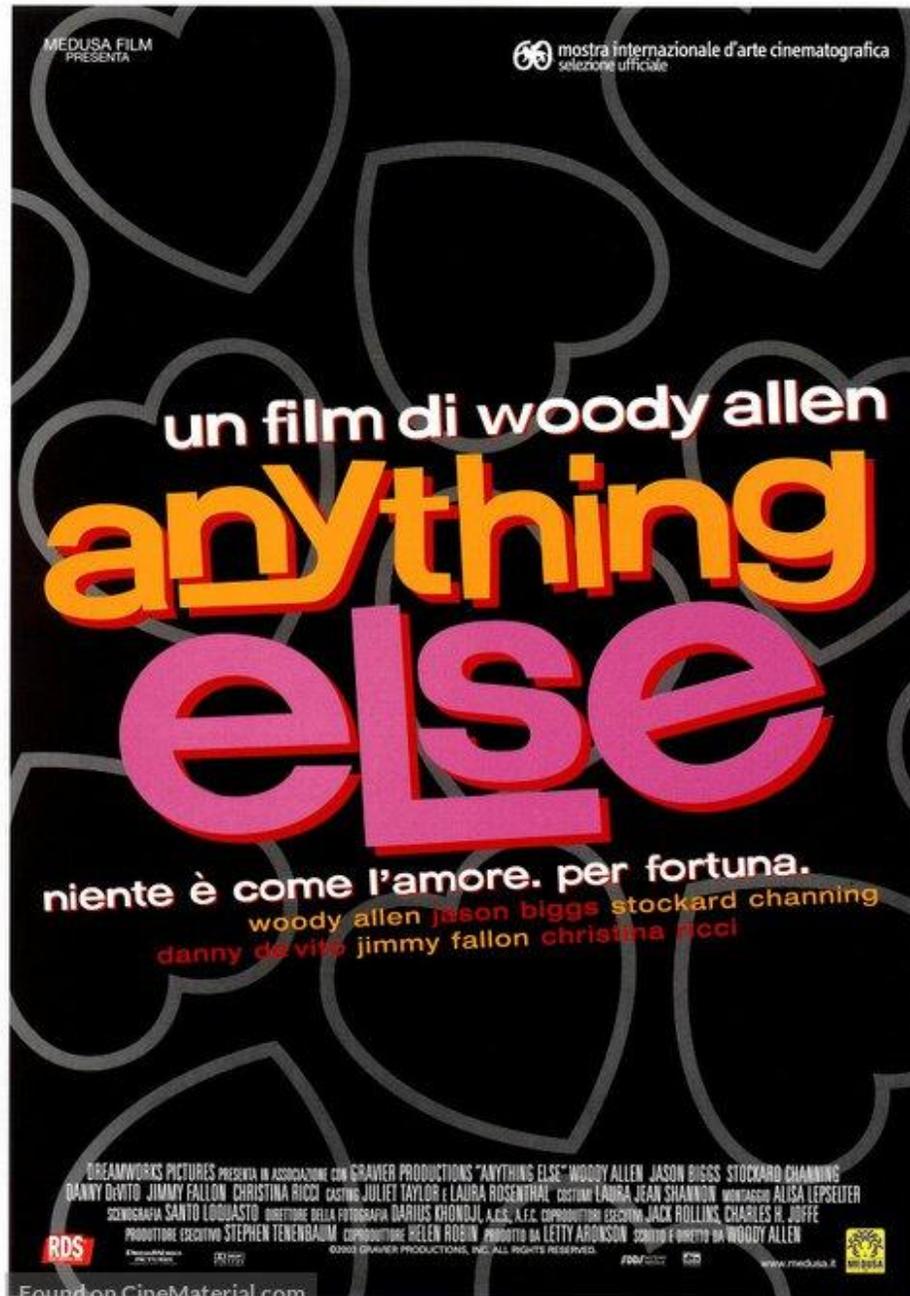
**Infusioni di durata minore (8-12
ore) controllano il dolore
cronico **fino a 2 settimane dalla
sospensione del farmaco.****

**COSA NON
SAPPIAMO**



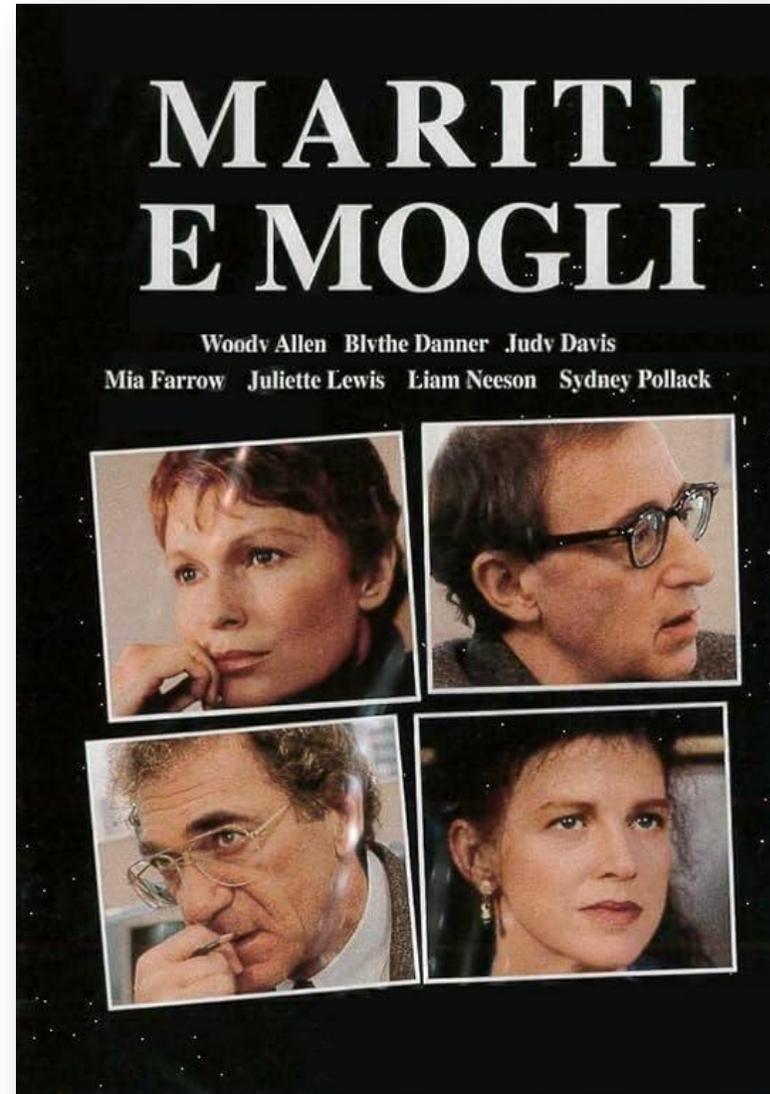
**>100 ore di
infusione
aumento
delle
transaminasi**

Evidence indicates that ketamine should be avoided in individuals with poorly controlled cardiovascular disease (grade C evidence, moderate level of certainty) and pregnancy or active psychosis (grade B evidence, moderate level of certainty). For hepatic dysfunction, evidence supports that ketamine infusions should be avoided in individuals with severe disease (eg, cirrhosis) and used with caution (ie, with monitoring of liver function tests before infusion and during infusions in surveillance of elevations) in individuals with moderate disease (grade C evidence, low level of certainty). Evidence indicates that ketamine should be avoided in individuals with elevated intracranial pressure and elevated intraocular pressure (grade C evidence, low level of certainty). Relative contraindications are shown in Table 5.



**ABBIAMO
ALTRO DA
DIRE?**

LE ASSOCIAZIONI



KETOFOL

1:1

0.5 mg/kg

0.5 mg/kg



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American Journal of Emergency Medicine

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



Original Contribution

Ketamine-propofol combination (ketofol) vs propofol for procedural sedation and analgesia: systematic review and meta-analysis ☆☆☆☆☆

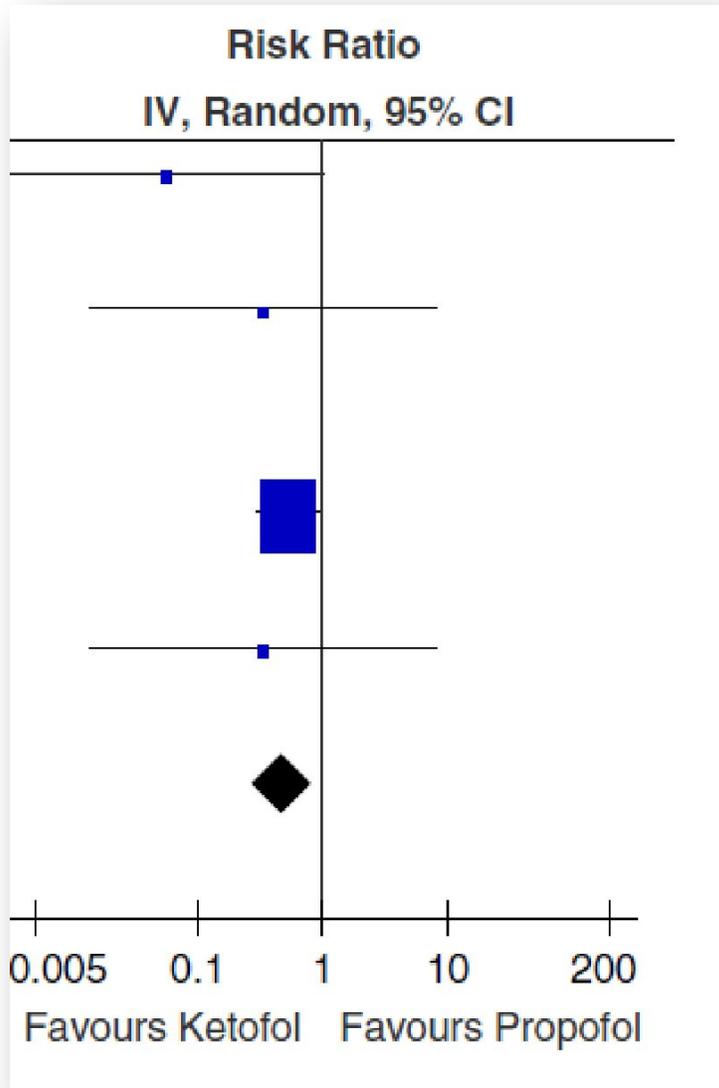


Mohammad Jalili, MD ^a, Maryam Bahreini, MD ^a, Amin Doosti-Irani, Msc, PhD candidate ^b,
Rasoul Masoomi, PhD ^c, Mona Arbab, MD ^a, Hadi Mirfazaelian, MD ^{a,*}

^a Department of Emergency Medicine, Tehran University of Medical Sciences, Tehran, Iran

^b Department of Epidemiology and Biostatistics, School of Public Health, Tehran University of Medical Sciences, Tehran, Iran

^c Department of Medical Educations, Tehran University of Medical Sciences, Tehran, Iran



AZIONE SINERGICA DEI DUE FARMACI CON SEDAZIONE COMPLETA E RAPIDA

RIDUZIONE EVENTI IPOTENSIVI DA PROPOFOL O IPERTENSIVI DA KETAMINA

RIDUZIONE EVENTI DEPRESSORI RESPIRATORI DA PROPOFOL

RIDUZIONE EVENTI DI AGITAZIONE DA KETAMINA

RECUPERO PIU' LENTO RISPETTO AL SOLO PROPOFOL

KETADEX

(per la sedazione del paziente in NIV)



Brief Report

Uncovering the Benefits of the Ketamine–Dexmedetomidine Combination for Procedural Sedation during the Italian COVID-19 Pandemic

Alessandro Riccardi ¹ , Sossio Serra ² , Fabio De Iaco ³, Andrea Fabbri ⁴, Dana Shiffer ^{5,6} and Antonio Voza ^{5,6,*†}  on behalf of the Study and Research Center of the Italian Society of Emergency Medicine (SIMEU)

	KETA-DEX Group	KET Group	DEX Group
Patients (<i>n</i>)	22	22	22
Male % (<i>n</i>)	40.9 (9)	40.9 (9)	45.5 (10)
Mean age (years)	78.33 ± 8.72	79.41 ± 10.76	77.21 ± 12.33
Hypertension % (<i>n</i>)	86.4 (19)	68.2 (15)	72.7 (16)
Diabetes % (<i>n</i>)	36.3 (8)	27.3 (6)	22.7 (5)
Neoplasm history % (<i>n</i>)	22.7 (5)	27.3 (6)	31.8 (7)
Heart failure % (<i>n</i>)	40.9 (9)	27.7 (6)	36.3 (8)
Mean P/F before sedation	145.45 ± 23.46	138.59 ± 20.67	147.45 ± 26.25
Mean RASS	-5 ± 0	-5 ± 0	-1.96 ± 0.21
10' RASS	-5 ± 0	-5 ± 0	0
30' RASS	-5 ± 0	-5 ± 0	-0.82 ± 0.39
60' RASS	-5 ± 0	-5 ± 0	-1.81 ± 0.39
Desaturation (<i>n</i>)	0	0	0
Change in blood pressure (<i>n</i>)	0	10 (hypertension)	10 (hypotension)

Data are expressed as absolute numbers (*n*), percentages (%), or mean ± standard deviation.

EQUILIBRIO TRA L'AZIONE IPOTENSIVA DELLA DEXMEDETOMIDINA E QUELLA IPERTENSIVA DELLA KETAMINA

RIDUZIONE EVENTI DI DELIRIUM DA KETAMINA

un film scritto, diretto e interpretato da

Woody Allen

TUTTI DICONO I LOVE YOU

Alan Alda

Woody Allen

Drew Barrymore

Lukas Haas

Goldie Hawn

Gaby Hoffmann

Natasha Lyonne

Edward Norton

Natalie Portman

Julia Roberts

Tim Roth

David Ogden Stiers





GRAZIE PER
L'ATTENZIONE