



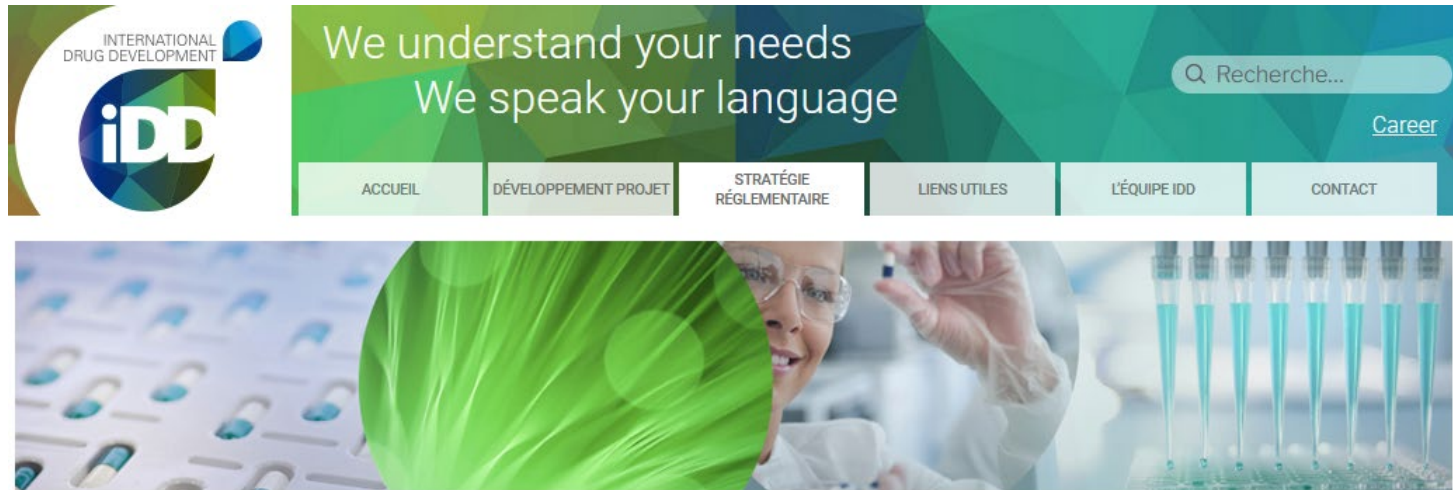
# Eskétamine en médecine d'urgence

Georges Mion

Hôpital Cochin  
Paris



# Georges Mion est consultant pour International Drug Development (IDD)



## EXPLOITATION ET STRATÉGIE RÉGLEMENTAIRE

Notre cœur de métier : le dossier d'AMM



HAUTE AUTORITÉ DE SANTÉ

## COMMISSION DE LA TRANSPARENCE

**21 JUILLET 2021**

*eskétamine*

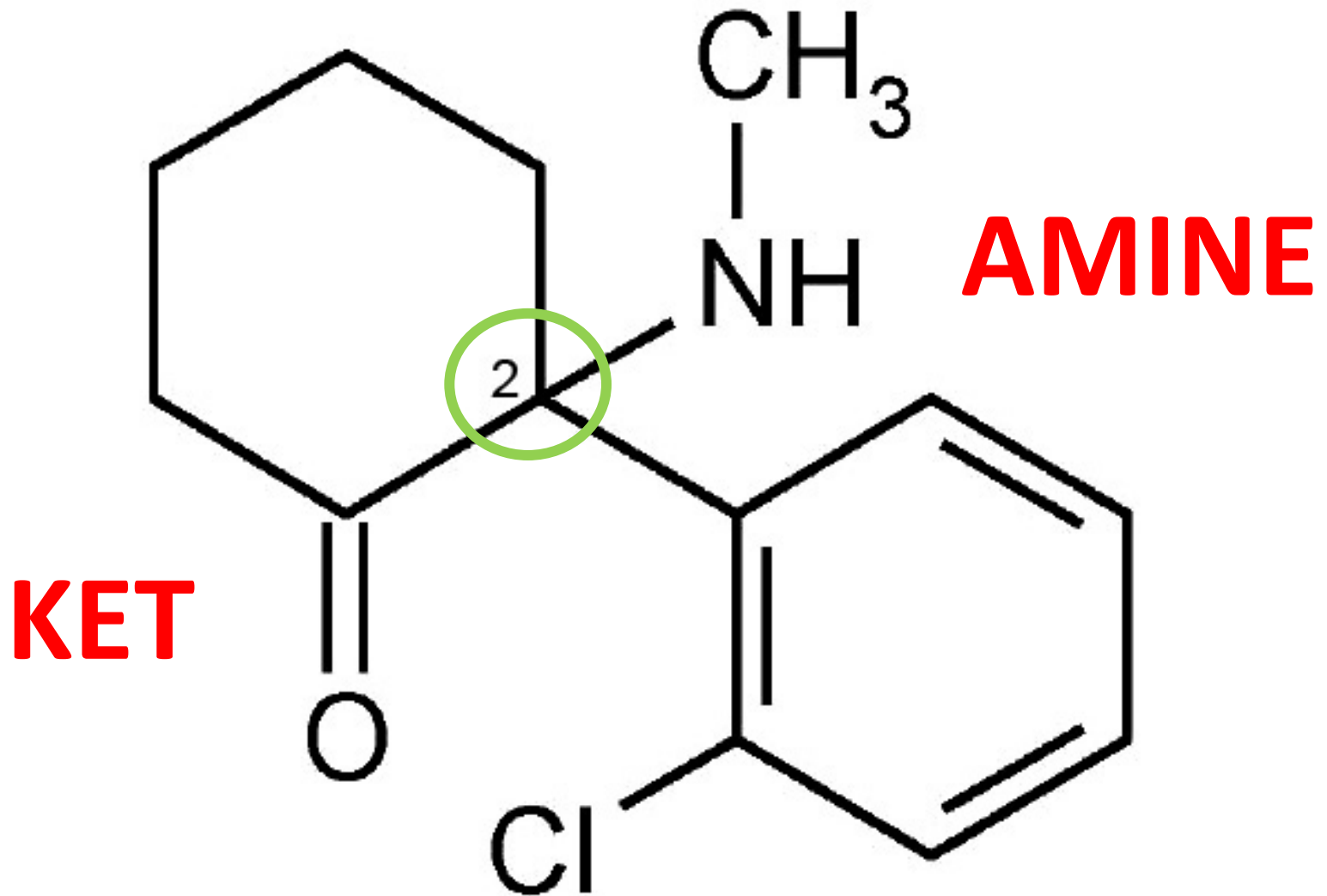
**ESKETAMINE** IDD 5 mg/ ml et 25 mg/ ml, solution injectable pour perfusion

Avis favorable au remboursement dans :

- induction et maintien de l'anesthésie générale, comme seul anesthésique ou en association avec des hypnotiques ;
- anesthésie et soulagement de la douleur (analgésie) en médecine d'urgence ;
- contrôle de la douleur liée à la respiration artificielle (intubation).

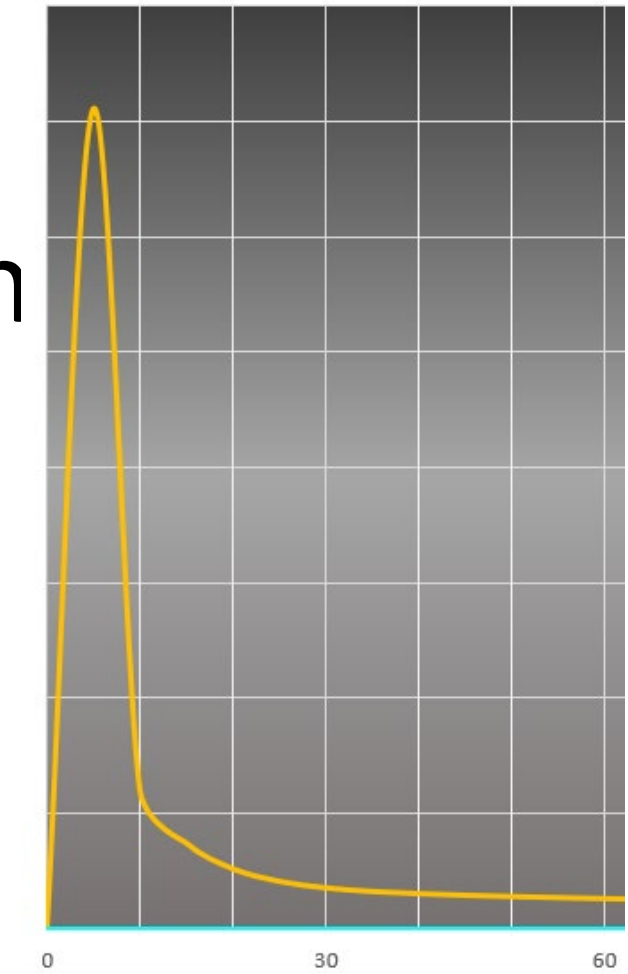


# 2 - ortho-chlorophényl - 2 - méthylamino - cyclohexanone



# Pharmacocinétique

- $t_{1/2} \alpha$  : 10 min
- délai d'action : 1 min
- $t_{1/2} \beta$  : 1-2 h
- Métabolisme hépatique
  - Cytochrome P450
  - NOR-kétamine



# Action analgésique

- **Inhibition** non compétitive **NMDA-R**
- **Activation syst. monoaminergiques desc.**
- **Effet anesthésique local** (canaux sodiques)
- **Effets anti-proinflammatoires (NfκB)**
- **Effet antidépresseur**

2 énantiomères

**S(+)** vs **R(-)**

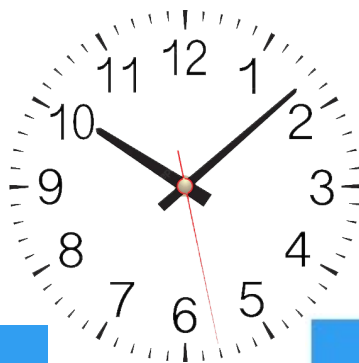
# Que veut dire



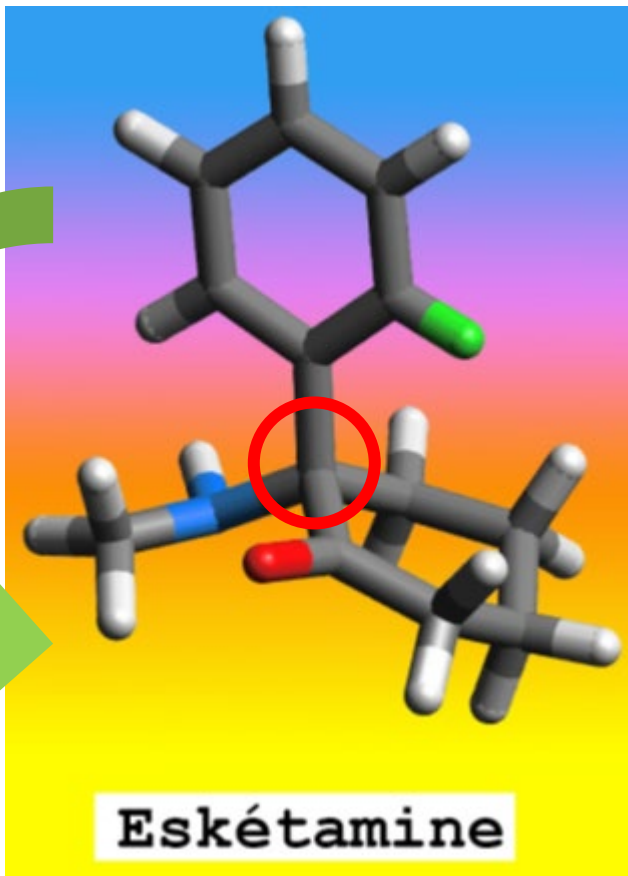
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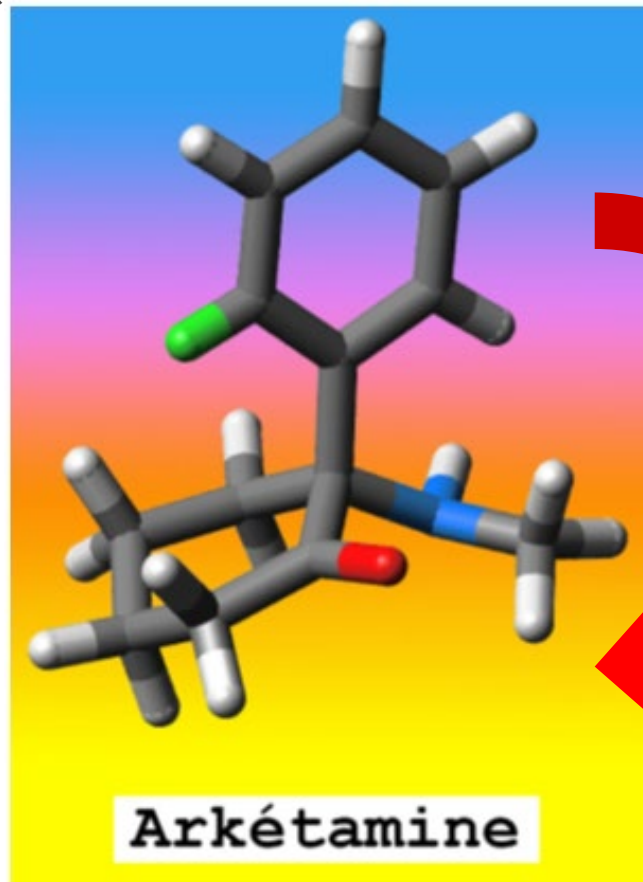
S



R



Dextrogyre (+)



Lévogyre (-)

# L'Eskétamine bloque plus efficacement le récepteur NMDA



4 fois plus que l'arkétamine  
2 fois plus que le racémique

# Anesthesia with S(+)-ketamine

E. Pfenninger and S. Himmelseher<sup>1</sup>

Many clinical trials have proven that the use of isolated S(+)-ketamine offers the opportunity of administering half the dose of racemic ketamine with the same pharmacologic effects as racemic ketamine. As a consequence, the introduction of S(+)-ketamine into the German commercial market followed in 1997.

Moitié de la dose

# COMPARATIVE PHARMACOLOGY OF THE KETAMINE ISOMERS

*Studies in Volunteers*

P. F. WHITE, J. SCHÜTTLER, A. SHAFER, D. R. STANSKI, Y. HORAI AND  
A. J. TREVOR

*Br. J. Anaesth.* (1985), 57, 197-203

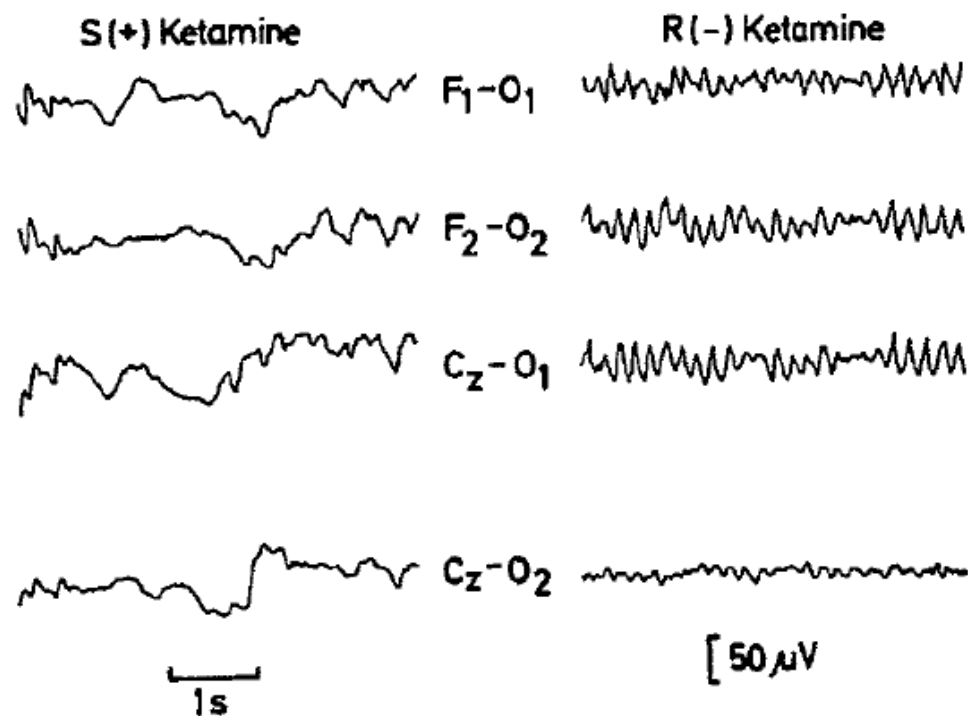


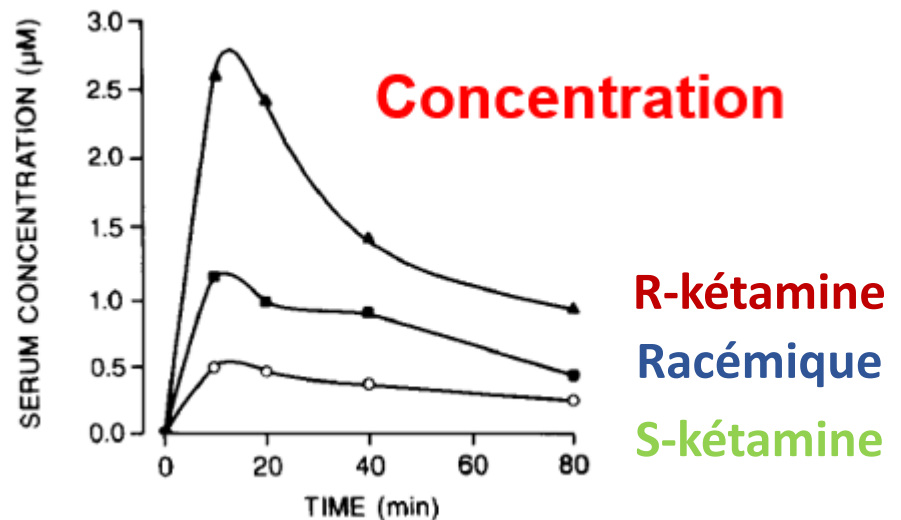
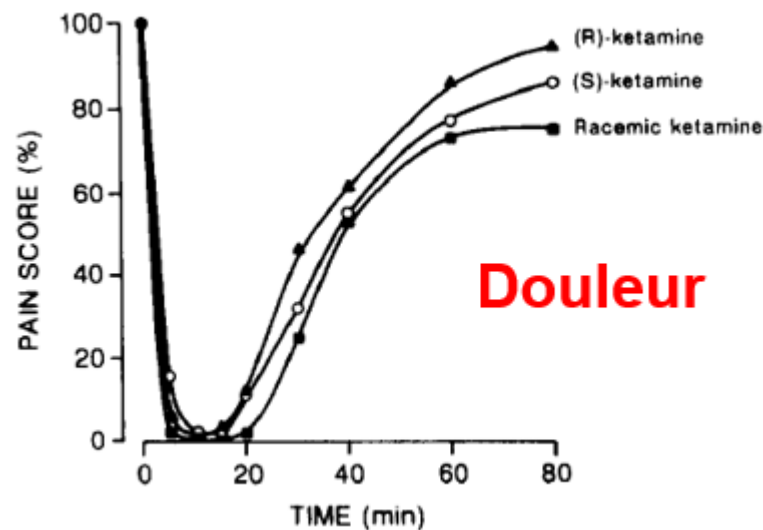
FIG. 2. A typical four-lead EEG pattern demonstrating the maximal slowing during or immediately after the infusion of S(+) ketamine or the R(-) isomer i.v.

# Effect of ketamine, an NMDA receptor inhibitor, in acute and chronic orofacial pain

Lene Cecilie Mathisen <sup>a,1</sup>, Per Skjelbred <sup>b</sup>, Lasse A. Skoglund <sup>c</sup> and Ivar Øye <sup>a,\*</sup>

*Pain*, 61 (1995) 215–220

The various forms of ketamine were given on an individual basis, either **i.m. or intravenously** (i.v.) as a single dose sometimes followed by **continuous infusion**. The patients recorded their pain on the VAS described above and the treatment goal was to obtain analgesia for a time period of at least 15 min. This study was regarded as a pilot investigation. It was not blinded, placebo was not included, and the





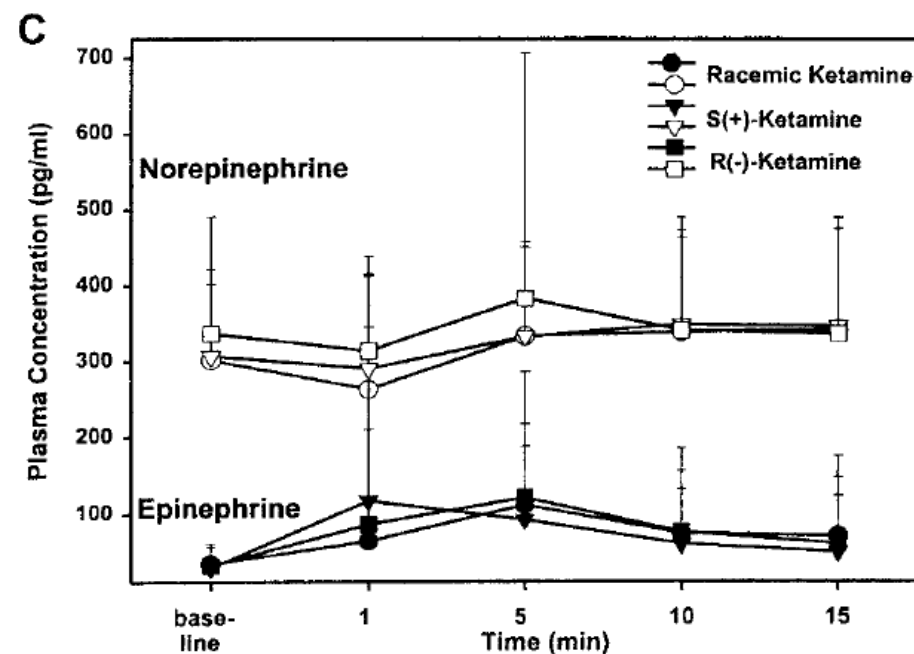
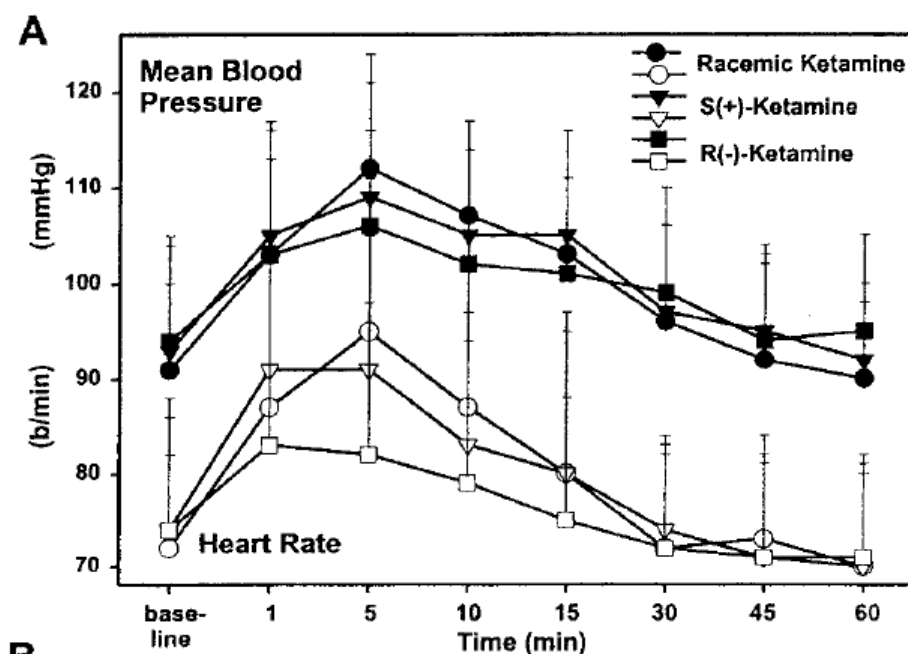
# Effets cardiovasculaires

# Cognitive Impairment after Small-dose Ketamine Isomers in Comparison to Equianalgesic Racemic Ketamine in Human Volunteers

Ernst G. Pfenninger, M.D.,\* Marcel E. Durieux, M.D., Ph.D.,† Sabine Himmelseher, M.D.‡

Anesthesiology 2002; 96:357-66

**Methods:** Twenty-four subjects received intravenous 0.5 mg/kg racemic, 0.25 mg/kg S(+)-, and 1.0 mg/kg R(-)-ketamine in a prospective, randomized, double-blind, crossover study. Hemo-



# *Actions of Ketamine and Its Isomers on Contractility and Calcium Transients in Human Myocardium*

Gudrun **Kunst**, M.D.,\* Eike Martin, M.D.,† Bernhard M. Graf, M.D.,‡ Siegfried Hagl, M.D.,§  
Christian F. Vahl, M.D.||

Anesthesiology 1999; 90:1363–71

Aux concentrations  
cliniques,  
l'eskétamine  
est inotrope +

**Results:** Compared with the initial control maximal isometric developed force, maximal isotonic shortening amplitude, contractility, and relaxation **increased by 12.5–22.4%** after perfusion with S(+)-ketamine at the concentration of 73  $\mu\text{M}$  ( $P < 0.05$ ). In contrast **no changes** were seen after addition of 73  $\mu\text{M}$  R(–)-ketamine. The effect of racemic ketamine (73  $\mu\text{M}$ ) was between that of the two isomers. **At the highest concentration (730  $\mu\text{M}$ ) ketamine and its isomers decreased maximal isometric developed force, maximal shortening amplitude, contractility, and relaxation by 26.8–57.4% ( $P < 0.05$ ), accompanied by a significant decrease of the intracellular calcium transient (by 21.0–32.2%,  $P < 0.05$ ).**

**Conclusions:** In contrast to R(–)-ketamine, S(+)-ketamine increased isometric force, isotonic shortening, contractility, and relaxation at low concentrations (73  $\mu\text{M}$ ) compared with the initial control. At higher concentrations (730  $\mu\text{M}$ ) a direct negative inotropic action was observed after perfusion with ketamine and its isomers, which was accompanied by a decreased intracellular  $\text{Ca}^{2+}$  transient. (Key words: Force; intravenous anesthetics; stereoisomers.)

# ***Ketamine Stereoselectively Affects Vasorelaxation Mediated by ATP-sensitive $K^+$ Channels in the Rat Aorta***

Mayuko Dojo, M.D.,\* Hiroyuki Kinoshita, M.D.,† Hiroshi Iranami, M.D.,‡ Katsutoshi Nakahata, M.D.,§  
Yoshiki Kimoto, M.D.,§ Yoshio Hatano, M.D.||

Anesthesiology 2002; 97:882-6

**Methods:** Rings of the rat aorta with or without endothelium were suspended for isometric force recording. During contraction to phenylephrine ( $3 \times 10^{-7}$  M), vasorelaxation in response to an ATP-sensitive  $K^+$  channel opener levcromakalim ( $10^{-8}$  to  $10^{-5}$  M) or a nitric oxide donor sodium nitroprusside ( $10^{-10}$  to  $10^{-5}$  M) was obtained. Glibenclamide ( $10^{-5}$  M), S(+) ketamine ( $10^{-4}$  M), or ketamine racemate ( $10^{-5}$  to  $10^{-4}$  M) was applied 15 min before addition of phenylephrine.

Aux concentrations cliniques, le racémique inhibe la VD induite par l'ischémie

**Conclusion:** In the isolated rat aorta, clinically relevant concentrations of ketamine racemate can inhibit relaxation induced by an ATP-sensitive  $K^+$  channel opener, whereas S(+) ketamine did not produce any inhibitory effect on this vasorelaxation. These results suggest that ketamine stereoselectively alters vasodilation *via* ATP-sensitive  $K^+$  channels in the conduit artery.

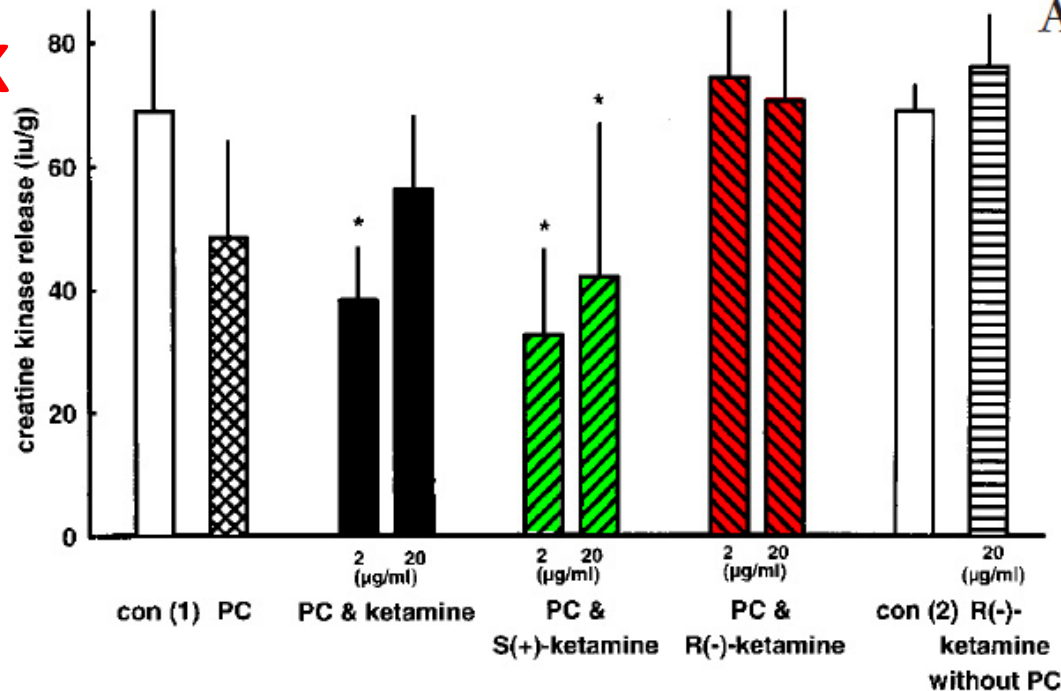


# Effects of Ketamine and Its Isomers on Ischemic Preconditioning in the Isolated Rat Heart

Andrei Molojavyi, M.D.,\* Benedikt Preckel, M.D., D.E.A.A.,† Thomas Comfère,‡ Jost Müllenheim, M.D.,† Volker Thämer, M.D., Ph.D.,§ Wolfgang Schlack, M.D., Ph.D., D.E.A.A.¶

Anesthesiology 2001; 94:623

CPK



Aux concentrations cliniques, l'arkétamine et le racémique Inhibent le preconditioning

Fig. 3. Cumulative creatine kinase release during reperfusion as a variable of cellular damage. Data are mean values and standard deviation,  $n = 8$ ; \* $P < 0.05$  versus control group; PC = ischemic preconditioning.

$\pm 8$ ,  $30 \pm 14$ ,  $41 \pm 25$  IU/g). After administration of 20 µg/ml ketamine and 2 or 20 µg/ml R(-)-ketamine, the protective effects of preconditioning were abolished (LV developed pres-



# Effets Cérébraux

## Current trends in emergency and intensive care medicine

Helmut Trimmel · Raimund Helbok · Thomas Staudinger · Wolfgang Jaksch · Brigitte Messerer · Herbert Schöchl · Rudolf Likar

<i>Analgesia</i>	In trauma patients fractures, burns, soft tissue trauma, etc.
<i>Analgo-sedation</i>	During extrication from vehicles, invasive measures in uncooperative patients
<i>Anesthesia</i>	In hypovolemic status and cardiogenic shock
<i>Asthma</i>	Induction of anesthesia in asthmatic status, additive to analgo-sedation in patients with bronchospasm
<i>Disasters</i>	Proven worldwide as analgesic and anesthetic in mass casualties, disaster relief and war surgery

**Table 5** Typical indications for S(+)-ketamine in emergency medicine

### *Severe brain trauma*

S(+)-ketamine is a suitable and safe substance in patients with brain injuries if ventilation and oxygenation are sufficient, even in the hands of less experienced emergency physicians. Contrary to earlier assumptions, therapy with S(+)-ketamine with controlled ventilation does not raise intracranial pressure [36]. As described, due to the blockade of the NDMA receptor, not only an anti-nociceptive effect but also a neuroprotective effect is achieved.

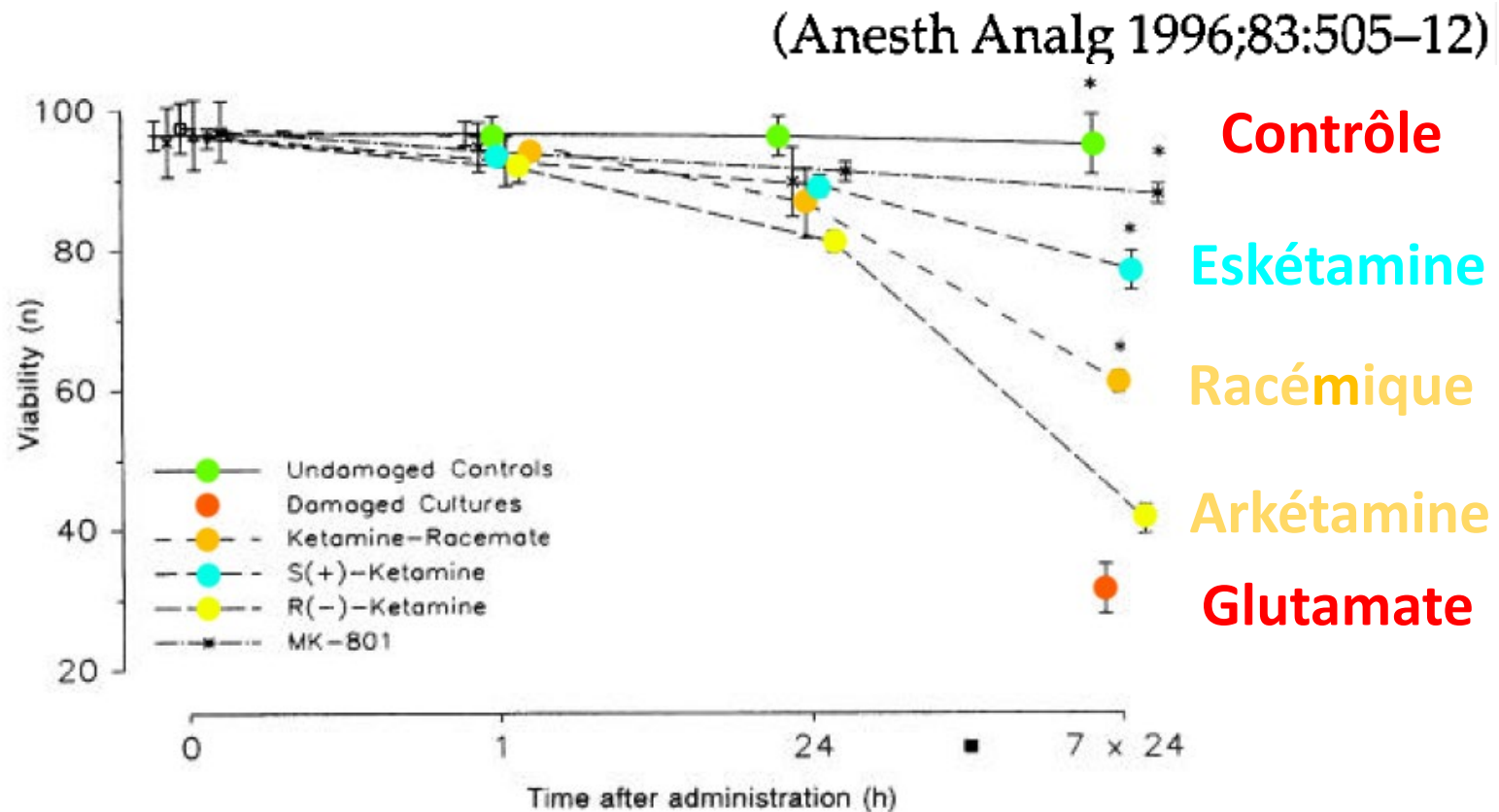
### Revising a Dogma: Ketamine for Patients with Neurological Injury?

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

(Anesth Analg 2005;101:524–34)

# The Effects of Ketamine-Isomers on Neuronal Injury and Regeneration in Rat Hippocampal Neurons

Sabine Himmelseher, MD, Ernst Pfenninger, MD, and Michael Georgieff, MD



**Figure 2.** Survival of undamaged controls, glutamate-induced reduction in live cells of glutamate-exposed, untreated cultures, and glutamate-exposed cells treated with  $10^{-4}$  M ketamine-racemate,  $10^{-4}$  M S(+)-ketamine,  $10^{-4}$  M R(-)-ketamine, and  $10^{-6}$  M MK-801. Drugs were added after glutamate-exposure, and on postinjury

# S(+)-ketamine/propofol maintain dynamic cerebrovascular autoregulation in humans

Kristin Engelhard MD, Christian Werner MD, Oliver Möllenberg MD, Eberhard Kochs MD

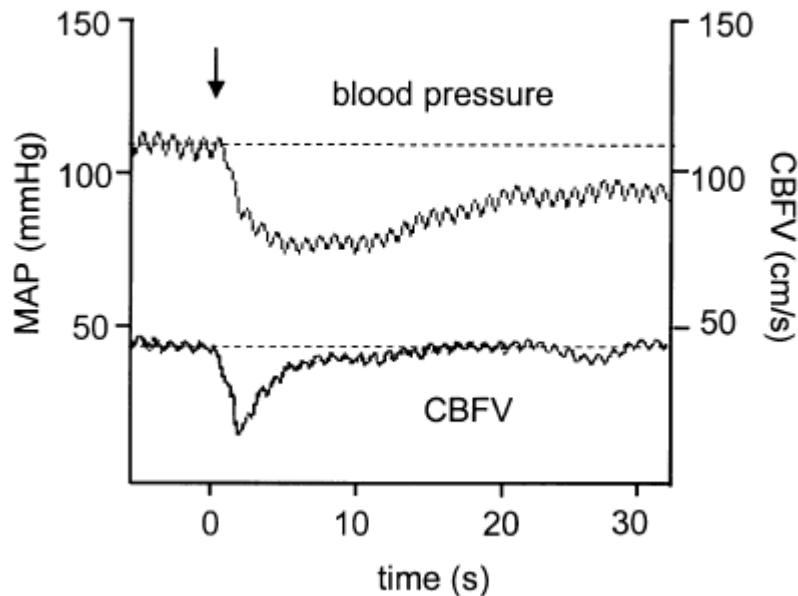
CAN J ANESTH 2001 / 48: 10 / pp 1034–1039

was obtained in 24 patients (ASA physical status I–II) scheduled for elective abdominal surgery. Patients

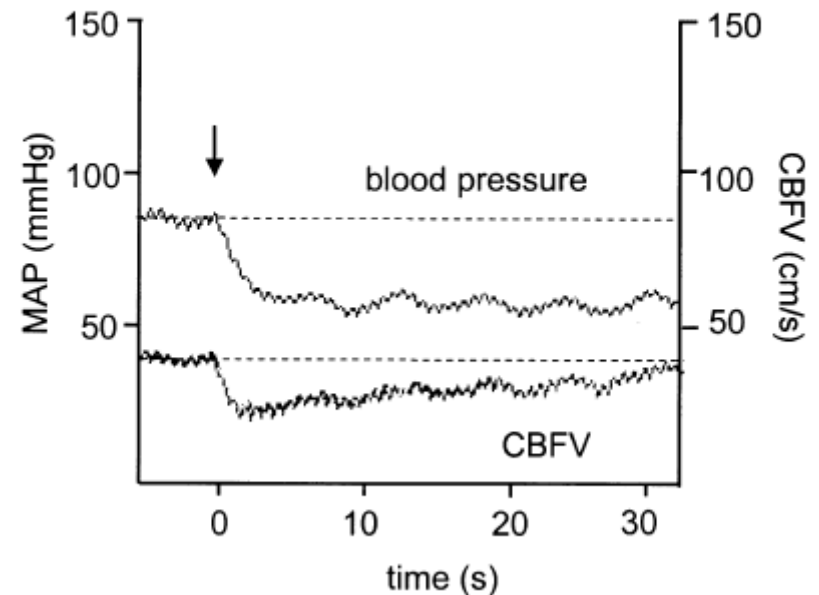
To assess dynamic cerebrovascular autoregulation the middle cerebral artery (MCA) blood flow velocity (CBFV) was measured by the transtemporal approach using a 2-MHz transcranial Doppler system (TCD,

To activate autoregulatory vasodilation a non-pharmacological sudden decrease in MAP of 15–20 mmHg was induced by rapid (<0.5 sec) deflation of large cuffs placed around both thighs, previously inflated to supra-systolic blood pressure levels for three minutes.<sup>9,10</sup> With

**S(+)-ketamine/propofol**



**sevoflurane**



# Effets neurocognitifs



# Pharmacology of Ketamine Isomers in Surgical Patients

Paul F. White, M.D., Ph.D.,\* Jay Ham, M.D.,† Walter L. Way, M.D.,‡ Anthony J. Trevor, Ph.D.§

equianesthetic doses of

racemic ketamine (RK), 2 mg/kg,

(+)ketamine (PK), 1 mg/kg,

(-)ketamine (MK), 3 mg/kg,

randomized,

were administered intravenously to 60 healthy patients

double-blind

Patients received no premedicant

Anesthesiology

52:231-239, 1980

1980

The durations of anesthesia ( $35 \pm 4$  min) were the same in all three groups; drug needed ranged from 2.4 mg/kg in the PK group to 8.5 mg/kg in the MK group.

At the termination of anesthesia, mean plasma levels of the parent compounds were 0.9 (RK), 0.5 (PK), and  $1.7 \mu\text{g/ml}$  (MK),

consistent with a PK:MK potency ratio of 3.4:1.

PK was judged to produce more effective anesthesia than RK or MK (95 vs. 75 vs. 68 per cent).

Verbal responses in the postanesthetic period suggested significantly

more psychic emergence reactions after MK than after RK or PK (37 vs. 15 vs. 5 per cent).

MK produced more agitated behavior than did RK or PK (26 vs. 10 vs. 0 per cent).

Postoperative pain occurred more commonly in the RK (10 per cent) and MK (16 per cent) groups than in the PK group (0 per cent).

The incidences of dreaming (84 per cent) were the same in all three groups.

The slopes of the plasma decay curves were not significantly different among the three groups.

similarities in the patterns of appearance and excretion of the ketamine metabolites suggest that the differences were due to pharmacodynamic factors.

Moins de douleur  
Avec l'eskétamine

Moins de  
problèmes  
d'émergence  
et d'agitation  
avec l'eskétamine

# Nonstereoselective Inhibition of Neuronal Nicotinic

## Acetylcholine Receptors by Ketamine Isomers (Anesth Analg 2000;91:741–8)

Toshio Sasaki, MD, Tomio Andoh, MD, PhD, Itaru Watanabe, MD, Yoshinori Kamiya, MD, Hideki Itoh, MD, Tomoko Higashi, MD, and Takayuki Matsuura, MD

These results indicate that the inhibitory action of ketamine isomers on neuronal nAChRs is not stereoselective. Although our findings do not deny possible involvement of these receptors in ketamine anesthesia, they suggest that inhibition of neuronal nAChRs is not primarily responsible for the anesthetic action of this anesthetic.

## Synergistic Inhibition of Muscarinic Signaling by Ketamine Stereoisomers and the Preservative Benzethonium Chloride

Marcel E. Durieux, M.D.,\* Gregor W. Nietgen, M.D.†

Anesthesiology  
1997; 86:1326–33

**Methods:** Rat m1 muscarinic acetylcholine receptors were expressed recombinantly in *Xenopus laevis* oocytes.

**Results:** The  $IC_{50}$  was  $125 \pm 33 \mu M$  for S(+) ketamine, and  $91 \pm 19 \mu M$  for R(–) ketamine. This difference was not statistically significant, indicating that muscarinic inhibition by ketamine is not stereoselective. The R(–)/S(+) mixture had an  $IC_{50}$  of  $48 \pm 1 \mu M$ , and thus the stereoisomers interact synergistically.

# Différences pharmacocinétiques

# Pharmacokinetics of ketamine and its major metabolites norketamine, hydroxynorketamine, and dehydronorketamine: a model-based analysis

Jasper Kamp\*, Kelly Jonkman, Monique van Velzen, Leon Aarts, Marieke Niesters, Albert Dahan and Erik Olofsen

Received: 7 March 2020 Accepted: 19 June 2020

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## Abstract

**Background:** Recent studies show activity of ketamine metabolites, such as hydroxynorketamine, in producing rapid relief of depression-related symptoms and analgesia. To improve our understanding of the pharmacokinetics of ketamine and metabolites norketamine, dehydronorketamine, and hydroxynorketamine, we developed a population pharmacokinetic model of ketamine and metabolites after i.v. administration of racemic ketamine and the S-isomer (esketamine). Pharmacokinetic data were derived from an RCT on the efficacy of sodium nitroprusside (SNP) in reducing the psychotomimetic side-effects of ketamine in human volunteers.

**Methods:** Three increasing i.v. doses of esketamine and racemic ketamine were administered to 20 healthy volunteers, and arterial plasma samples were obtained for measurement of ketamine and metabolites. Subjects were randomised to receive esketamine/SNP, esketamine/placebo, racemic ketamine/SNP, and racemic ketamine/placebo on four separate occasions. The time–plasma concentration data of ketamine and metabolites were analysed using a population compartmental model approach.

**Results:** The pharmacokinetics of ketamine and metabolites were adequately described by a seven-compartment model with two ketamine, norketamine, and hydroxynorketamine compartments and one dehydronorketamine compartment with metabolic compartments in-between ketamine and norketamine, and norketamine and dehydronorketamine main compartments. Significant differences were found between S- and R-ketamine enantiomer pharmacokinetics, with up to 50% lower clearances for the R-enantiomers, irrespective of formulation. Whilst SNP had a significant effect on ketamine clearances, simulations showed only minor effects of SNP on total ketamine pharmacokinetics.

**Conclusions:** The model is of adequate quality for use in future pharmacokinetic and pharmacodynamic studies into the efficacy and side-effects of ketamine and metabolites.

**Clinical trial registration:** Dutch Cochrane Center 5359.

**Expérience clinique  
en médecine d'urgence**



# Analgesia in adult trauma patients in physician-staffed Austrian helicopter rescue: a 12-year registry analysis

Scandinavian Journal of Trauma,  
Resuscitation and Emergency Medicine

(2021) 29:28

Christopher Rugg<sup>1</sup>, Simon Woyke<sup>1</sup>, Wolfgang Voelckel<sup>2</sup>, Peter Paal<sup>3,4</sup> and Mathias Ströhle<sup>1,4\*</sup>

**Background:** Sufficient analgesia is an obligation, but **oligoanalgesia** (NRS > 3) is frequently observed prehospitally. Potent analgesics may cause severe adverse events. Thus, analgesia in the helicopter emergency medical service (HEMS) setting is challenging. Adequacy, efficacy and administration safety of potent analgesics pertaining to injured patients in HEMS were analysed.

**Methods:** Observational study evaluating data from 14 year-round **physician-staffed helicopter bases in Austria** in a 12-year timeframe.

**Results:** Overall, 47,985 (34.3%) patients received analgesics, 26,059 of whom were adult patients, injured and not mechanically ventilated on site. Main drugs administered were opioids ( $n=20,051$ ; 76.9%), **esketamine** ( $n=9082$ ; **34.9%**), metamizole ( $n=798$ ; 3.1%) and NSAIDs ( $n=483$ ; 1.9%). **Monotherapy with opioids or esketamine was the most common regimen** ( $n=21,743$ ; **83.4%**), while **opioids together with esketamine** ( $n=3591$ ; **13.8%**) or metamizole ( $n=369$ ; 1.4%) were the most common combinations. Females received opioids less frequently than did males ( $n=6038$ ; 74.5% vs.  $n=14,013$ ; 78.1%;  $p < 0.001$ ). Pain relief was often sufficient (> 95%), but females more often had moderate to severe pain on arrival in hospital ( $n=34$ ; 5.0% vs.  $n=59$ ; 3.2%;  $p=0.043$ ). Administration of potent analgesics was safe, as indicated by MEES, SpO<sub>2</sub> and respiratory rates. On 10% of all missions, clinical patient assessment was deemed sufficient by HEMS physicians and monitoring was spared.

**Conclusions:** **Opioids and esketamine alone or in combination were the analgesics of choice** in physician-staffed HEMS in Austria. Analgesia was often sufficient, but females more than males suffered from oligoanalgesia on hospital arrival. Administration safety was high, justifying liberal use of potent analgesics in physician-staffed HEMS.

# Analgesia in pediatric trauma patients in physician-staffed Austrian helicopter rescue: a 12-year registry analysis

Christopher Rugg<sup>1</sup>, Simon Woyke<sup>1</sup>, Julia Ausserer<sup>1</sup>, Wolfgang Voelckel<sup>2,3,4</sup>, Peter Paal<sup>5,6</sup> and Mathias Ströhle<sup>1,3,6\*</sup> 

*Scandinavian Journal of Trauma, Resuscitation and Emergency Medicine* (2021) 29:161

**Background:** As pediatric patients are typically rare among helicopter emergency medical systems (HEMS), children might be at risk for oligo-analgesia due to the rescuer's lack of experience and the fear of side effects.

**Methods:** In this retrospective analysis, data was obtained from the ÖAMTC HEMS digital database including 14 physician staffed helicopter bases in Austria over a 12-year timeframe. Primary missions involving pediatric trauma patients (< 15 years) not mechanically ventilated on-site were included. Analgesia was assessed and compared between the age groups 0–5, 6–10 and 11–14 years.

**Results:** Of all flight missions, 8.2% were dedicated to children < 15 years. Analgetic drugs were administered in 31.4% of all primary missions (3874 of 12,324), wherefrom 2885 were injured and non-ventilated (0–5 yrs.: n = 443; 6–10 yrs.: n = 902; 11–14 yrs.: n = 1540). The majority of these patients (> 75%) suffered moderate to severe pain, justifying immediate analgesia. HEMS physicians typically chose a monotherapy with an opioid (n = 1277; 44.3%) or Esketamine (n = 118; 41.1%) followed by the combination of both (n = 324; 11.2%). Opioid use increased (37.2% to 63.4%) and Esketamine use decreased (66.1% to 48.3%) in children < 6 vs. > 10 years. Esketamine was more often administered in extremity (57.3%) than in head (41.5%) or spine injuries (32.3%). An intravenous access was less often established in children < 6 years (74.3% vs. 90.8%; p < 0.001). Despite the use of potent analgesics, 396 missions (13.7%) were performed without technical monitoring. Particularly regarding patient data at handover in hospital, merely < 10% of all missions featured complete documentation. Therefore, sufficient evaluation of the efficacy of pain relief was not possible. Yet, by means of respiratory measures required during transport, severe side effects such as respiratory insufficiency, were barely noted.

**Conclusions:** In the physician-staffed HEMS setting, pediatric trauma patients liberally receive opioids and Esketamine for analgesia. With regard to severe respiratory insufficiency during transport, the application of these potent analgesics seems safe.

# Paediatric procedural sedation and analgesia by emergency physicians in a country with a recent establishment of emergency medicine

Maybritt I. Kuypers<sup>a,b</sup>, Gaël J.P. Smits<sup>c</sup>, Eva P. Baerends<sup>f</sup>, Erick Oskam<sup>g</sup>, Eef P.J. Reijners<sup>h</sup>, Lisette A.A. Mignot-Evers<sup>i</sup>, Wendy A.M.H. Thijssen<sup>c</sup>, Frans B. Plötz<sup>j</sup> and Erik H.M. Korsten<sup>d,e</sup>

**Objectives** Paediatric patients receive less procedural sedation and analgesia (PSA) in the emergency department compared with adults, especially in countries where emergency medicine is at an early stage of development. The objectives of this study were to evaluate the adverse events and efficacy of paediatric PSA in a country with a recent establishment of emergency medicine and to describe which factors aided implementation.

**Methods** This is a prospective, multicentre, observational study of paediatric patients undergoing PSA by the first trained emergency physicians (EPs) in The Netherlands. A standardized data collection form was used at all participating hospitals to collect data on adverse events, amnesia, pain scores, and procedure completion. A survey was used to interpret which factors had aided PSA implementation.

**Results** We recorded 351 paediatric PSA. The mean age was 9.5 years (95% confidence interval: 9.1–10.0). Esketamine was most frequently used (42.4%), followed by propofol (34.7%). The adverse event rate was low (3.0%). Amnesia was present in 86.8%. The median pain score was 2 (out of 10) for patients without amnesia. Procedures were successfully completed in 93.9% of the cases.

Eur J Emerg Med 2019;26:168-173.



# The use of esketamine sedation in the emergency department for manipulation of paediatric forearm fractures: A 5 year study

Dhawal Patel<sup>a,\*</sup>, Christopher Talbot<sup>b</sup>, Weisang Luo<sup>a</sup>, Shirley Mulvaney<sup>c</sup>, Eileen Byrne<sup>c</sup>

*Liverpool L9 7AL, United Kingdom*

*Injury 52 (2021) 1321–1330*

The purpose of this study is to assess the use of esketamine as procedural sedation for the reduction of paediatric forearm fractures in the emergency department (ED). A retrospective analysis was undertaken of forearm fractures between 1<sup>st</sup> January 2012 to 31<sup>st</sup> December 2016 which were treated with manipulation in ED using esketamine sedation. Patient demographics and fracture configuration were collected. Patient radiographs were evaluated and cast index calculated. 151 patients (103 male, 48 female) were included (average age of 8.5 [1 to 15]). Four (2.6%) patients were lost to final follow up. 11 (7%) fractures were not accepted after initial manipulation and required formal surgical management under general anaesthetic. At one week follow up, a further 5 (3%) fractures displaced requiring operative management. 100% of patients who slipped at one week had a cast index greater than 0.8 [average 0.86, 95% CI 0.80–0.92]. At final follow up successful reduction was achieved in 89.1% (131/144) of patients. No adverse events occurred following administration of esketamine. This study provides evidence that manipulation of paediatric forearm fractures using esketamine as procedural sedation in the ED is comparable to other methods in achieving acceptable outcomes. This is in addition to the potential for cost savings. However, future studies formally assessing cost effectiveness and patient outcomes are needed.

The patient has intravenous access established by trained members of the accident and emergency team. The procedure is undertaken in the department's minor operations room. Esketamine is administered at an initial dose of 1.0–1.5mg/kg intravenously by an ED consultant. During administration, the patient has continuous blood pressure and oxygen saturations monitored. The emergency

# Prehospital analgesia using nasal administration of S-ketamine – a case series

Joakim Johansson<sup>1,2\*</sup>, Jonas Sjöberg<sup>2</sup>, Marie Nordgren<sup>2</sup>, Erik Sandström<sup>2</sup>, Folke Sjöberg<sup>3,4</sup> and Henrik Zetterström<sup>2,5</sup>

*Scandinavian Journal of Trauma, Resuscitation and Emergency Medicine 2013, 21:38*

## Abstract

Pain is a problem that often has to be addressed in the prehospital setting. The delivery of analgesia may sometimes prove challenging due to problems establishing intravenous access or a harsh winter environment. To solve the problem of intravenous access, intranasal administration of drugs is used in some settings. In cases where vascular access was foreseen or proved hard to establish (one or two missed attempts) on the scene of the accident we use nasally administered S-Ketamine for prehospital analgesia. Here we describe the use of nasally administered S-Ketamine in 9 cases. The doses used were in the range of 0,45-1,25 mg/kg. 8 patients were treated in outdoor winter-conditions in Sweden. 1 patient was treated indoors. VAS-score decreased from a median of 10 (interquartile range 8-10) to 3 (interquartile range 2-4). Nasally administered S-Ketamine offers a possible last resource to be used in cases where establishing vascular access is difficult or impossible. Side-effects in these 9 cases were few and non serious. Nasally administered drugs offer a needleless approach that is advantageous for the patient as well as for health personnel in especially challenging selected cases. Nasal as opposed to intravenous analgesia may reduce the time spent on the scene of the accident and most likely reduces the need to expose the patient to the environment in especially challenging cases of prehospital analgesia. Nasal administration of S-ketamine is off label and as such we only use it as a last resource and propose that the effect and safety of the treatment should be further studied.

**Eskétamine intranasale : 0,45 – 1,25 mg/Kg**



# Posologie (AMM)

## *Sédation en médecine d'urgence*

*La RCP propose 0,125 à 0,25 mg/kg en IV lente*

*ou 0,25 à 0,5 mg/kg en IM*

*Je propose, éventuellement associé au midazolam ou au propofol :*

Bolus titré : titration de 1 à 3 mg d'eskétamine  
toutes les minutes jusqu'à atteinte de l'objectif d'analgésie

Dans une seringue de 5 mL d'eskétamine à 5 mg/mL,  
chaque graduation (0,2 mL) représente 1 mg

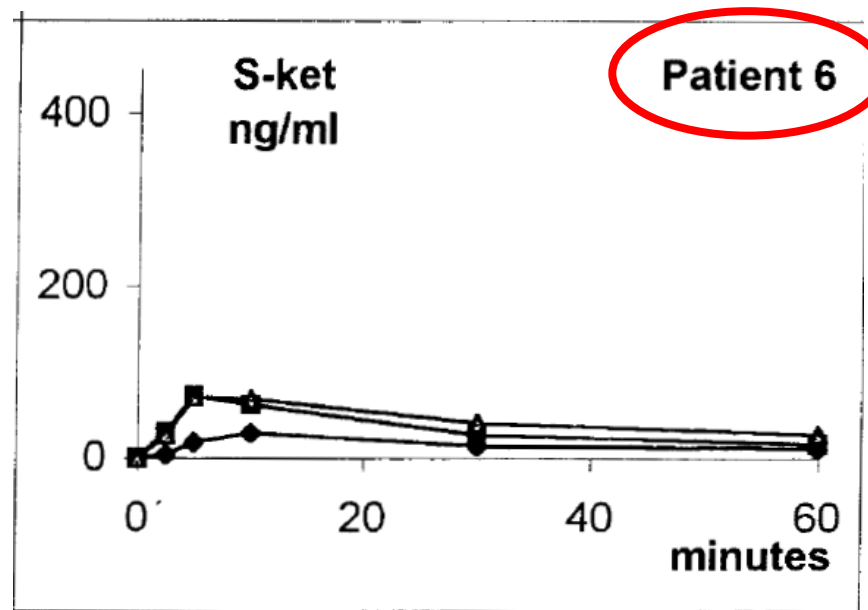
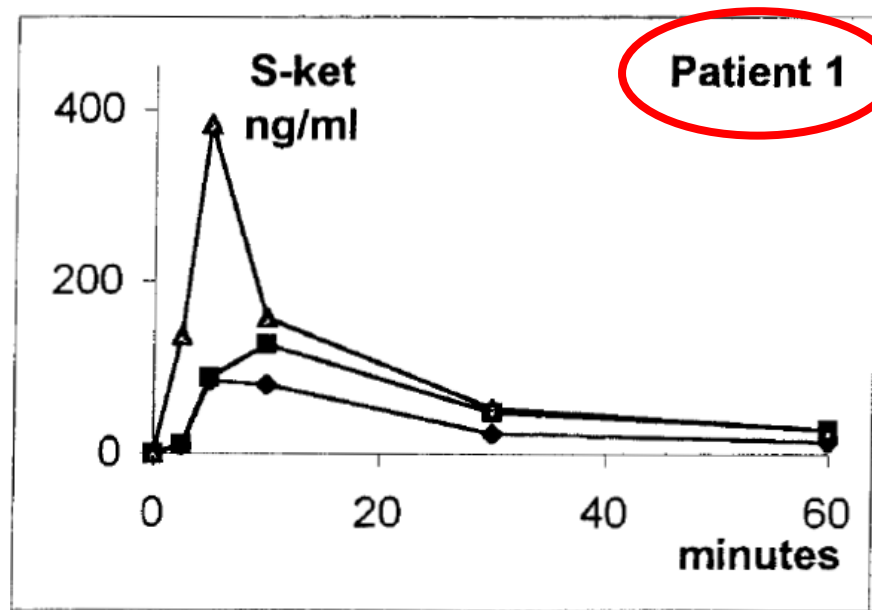
Entretien : 0,125 à 0,25 mg/kg/h

# TITRATION +++

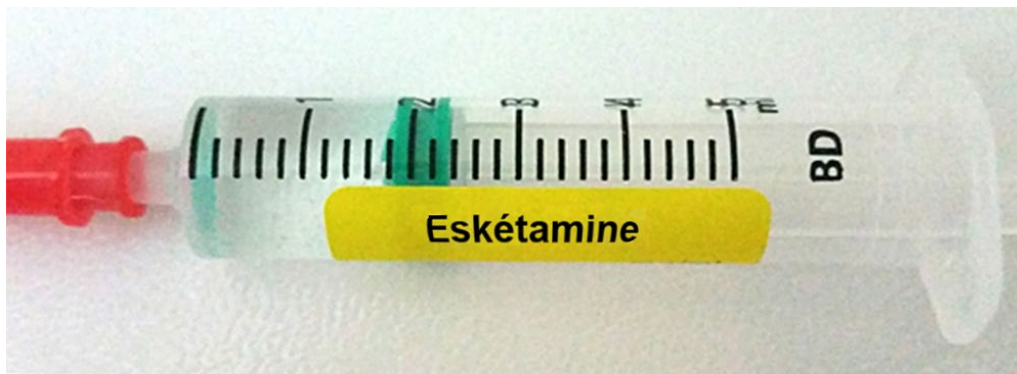
# The analgesic effect of racemic ketamine in patients with chronic ischemic pain due to lower extremity arteriosclerosis obliterans

J. PERSSON, J. HASSELSTRÖM, B. WIKLUND, A. HELLER, J.-O. SVENSSON and L. L. GUSTAFSSON

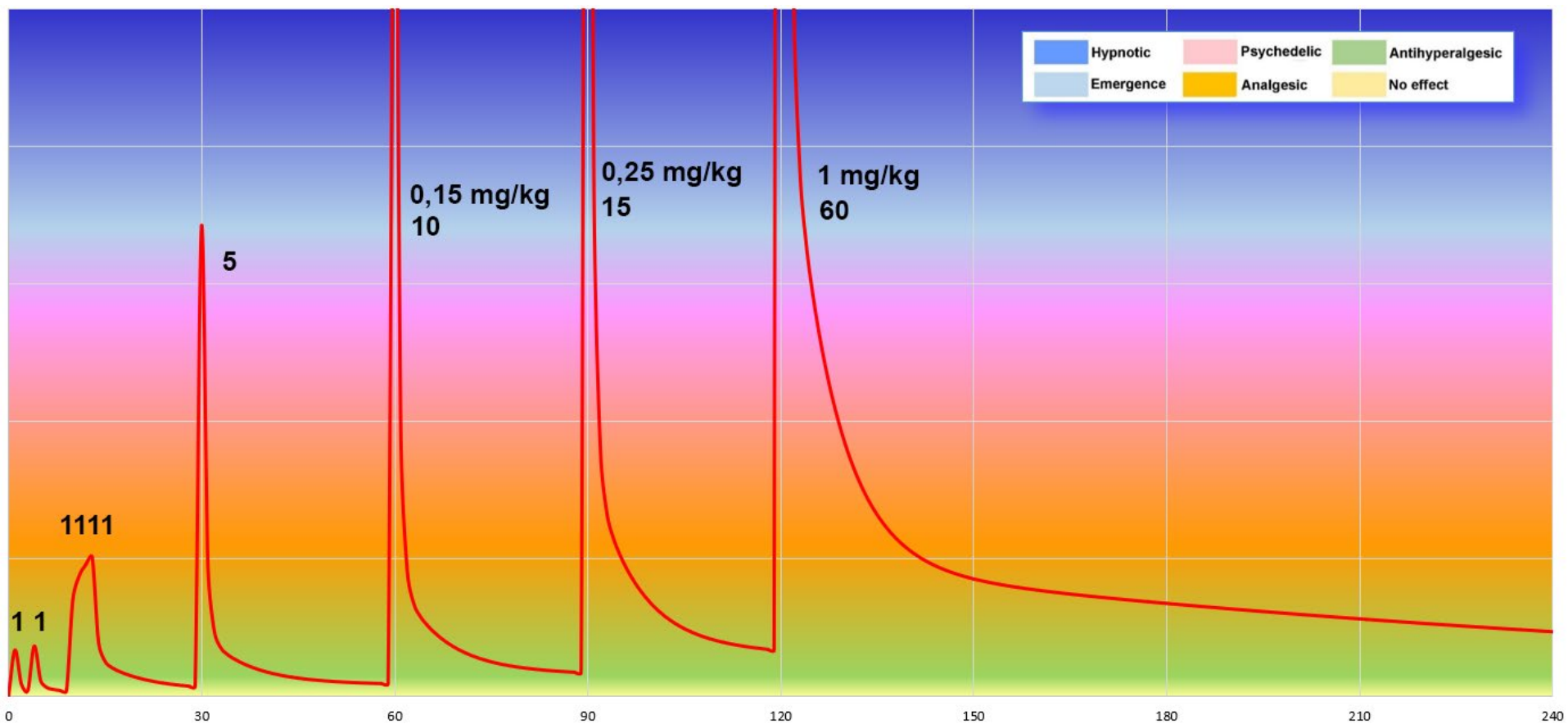
*Acta Anaesthesiol Scand* 1998; 42: 750–758



**Methods:** Eight patients with rest pain in the lower extremity due to arteriosclerosis obliterans were given sub-dissociative doses of 0.15, 0.30, or 0.45 mg/kg racemic ketamine and morphine 10 mg as a 5-min infusion on four separate days in a cross-over, double-blind, randomised protocol. Plasma levels of (S)- and (R)-ketamine and their nor-metabolites were analysed with



5 mg/mL



# Conclusion

- différence essentielle : **l'eskétamine est deux fois plus active** que le racémique en termes d'analgésie et de narcose
- L'eskétamine a un **meilleur profil** sur les **systèmes circulatoire et nerveux** et sur les **troubles cognitifs**
- l'eskétamine a une **clairance plus élevée** que le racémique.  
Dans plusieurs études cliniques, cet avantage s'est accompagné d'une émergence plus rapide et plus calme
- En médecine d'urgence, si le malade reste éveillé, **la titration est importante**

A propos de la [note eskétamine de la SFAR](#)

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Mion G

[Eskétamine](#)

Conférence 2023

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Merci

Mion G

[Histoire des antagonistes NMDA et perspectives.](#)

Conférence au symposium CDM LAVOISIER / IDD, congrès annuel de la SFAR, Paris, 22 septembre 2022.

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Proposition de [protocoles d'utilisation](#) (respectant l'AMM)

Proposition de protocoles [pour la douleur chronique](#) (hors AMM)