



# KETAMINE SEDATION FOR AGITATED PATIENTS REQUIRING AEROMEDICAL RETRIEVAL



# Ketamine sedation for patients with acute agitation and psychiatric illness requiring aeromedical retrieval

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## ABSTRACT

**Objective** Aeromedical retrieval services face the difficult problem of appropriate levels of sedation for transport of acutely agitated patients to definitive care. This paper describes a technique using ketamine, which is titratable and avoids problems associated with airway management.

**Method** A 3-year review of a new technique of ketamine sedation by aeromedical retrieval teams from the Cairns base of the Queensland section of the Royal Flying Doctor Service of Australia. Clinical records were systematically reviewed for ketamine administration and signs of adverse events during transport and in the subsequent 72 h.

**Results** 18 patients were sedated during retrieval with intravenous ketamine. Effective sedation was achieved in all cases, with no significant adverse events noted during retrieval or 72 h afterwards.

**Conclusion** Ketamine sedation is effective and safe in agitated patients with a psychiatric illness in the aeromedical setting and does not lead to worsening agitation in the subsequent 72-h period.

benzodiazepine therapy. There is, however, a small subset of agitated patients who do not respond adequately to these first-line agents but require urgent air transport to progress their mental health care. In this situation the resort to general anaesthesia and intubation has often been made despite its attendant risks.

This study seeks to describe an alternative approach using ketamine sedation and outline its safety profile.

## MATERIALS AND METHODS

The Cairns RFDS base transferred 135 patients with a mental health International Classification of Diseases, version 10 diagnosis between January 2007 and April 2010. During this period Cairns RFDS base began utilising ketamine sedation as an alternative strategy when first-line sedation (benzodiazepine and/or antipsychotic agents) had failed to control agitation. Due to weather conditions it is not uncommon for aeromedical retrievals to be delayed for up to 12 h and so first-line sedation of the patient would often be prescribed for

## RFDS OVERVIEW

### *RFDS Bases*

#### 8 Operational Bases

- Clinic / Retrieval Base
  - Cairns (est 1972 relocated from Charters Towers)
  - Charleville (est 1942)
  - Mt Isa (est 1965 relocated from Cloncurry)
  - Townsville (est 1996)
- Retrieval Only Bases
  - Brisbane (est 1995)
  - Rockhampton (est 1995)
  - Bundaberg (est 2002)
- Clinic Only Bases
  - Longreach (est 2004)



## Beechcraft Super King Air B200 SE

- \* Average Cruise Speed - 480 km/hr
- \* Max Range ~3,400 km
- \* Max Altitude - 35,000 ft
- \* Fuel Consumption - 340 Lt JetA1 /hr

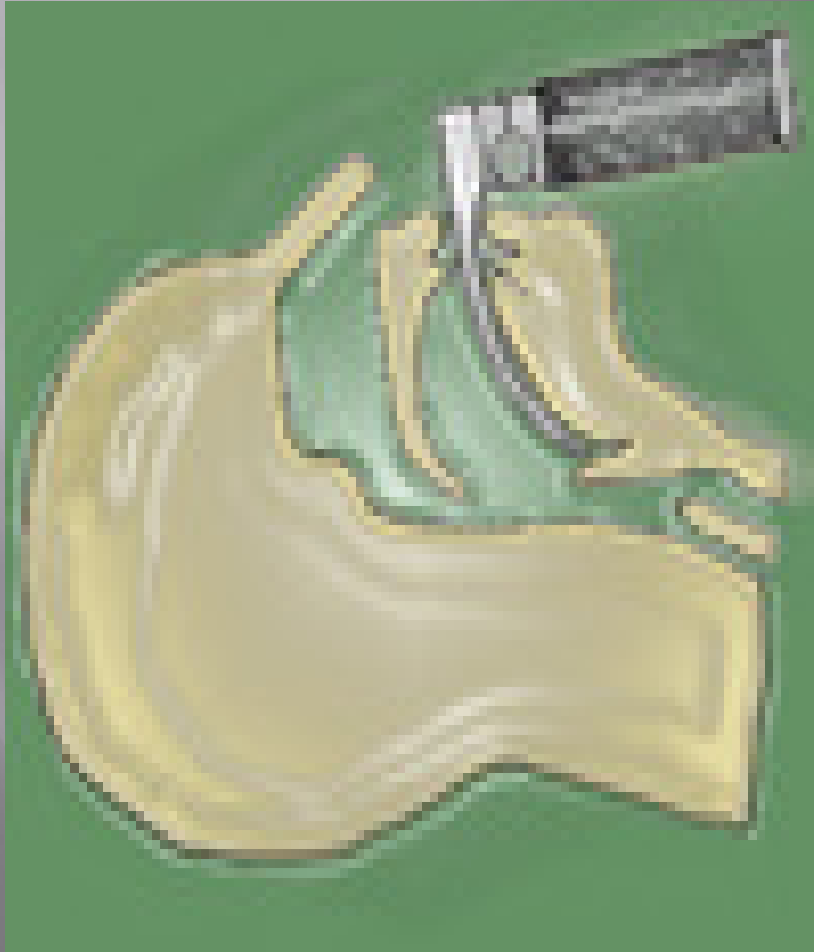


- \* 2 Stretcher Capacity with comprehensive Medical Equipment Cabin Fit

**Royal Flying Doctor Service of Australia (Queensland Section)**  
**Number of Mental Health Transports by RFDS Base and Year**  
**All Bases**  
**1 January 2007 to 31 December 2009**

	<b>2007</b>	<b>2008</b>	<b>2009</b>	<b>Total</b>
<b>BN</b>	24	17	25	<b>66</b>
<b>BU</b>	9	4	5	<b>18</b>
<b>CS</b>	40	40	55	<b>135</b>
<b>CV</b>	10	5	6	<b>21</b>
<b>MA</b>	34	45	29	<b>108</b>
<b>RK</b>	16	25	33	<b>74</b>
<b>TL</b>	23	17	16	<b>56</b>
<b>Total</b>	<b>156</b>	<b>153</b>	<b>169</b>	<b>478</b>

# Why do this study?



# QLD Coroner's report, Mr AF, 1<sup>st</sup> December 2001

- ▣ Suicidal mental health patient, cut both wrists
- ▣ Required pepper spray by police
- ▣ Brought into RBH ED, ETOH intoxicated++
- ▣ Combative +++
- ▣ Sedated with ?IMI midazolam?haloperidol
- ▣ Began vomiting+++
- ▣ Aspirated and died despite oral ETI attempts with suxamethonium and a surgical airway attempt by ED staff
- ▣ Autopsy: gastric content aspiration, BAL 0.27

# A more recent case of sedation related death

December 2009



Government of Western Austral  
Department of Health

From Death We Learn  
2009

# What happened?

An obese adult man with a history of recurrent psychosis presented to a rural centre Emergency Department by ambulance with the assistance of the police. He was noncompliant, and required physical restraint in order to prevent him leaving medical care.

The history available was that he had been prevented from attempting to hang himself. Examination revealed a man of approximately 130 kg with no physical injury; however, he was thought-disordered, disorganised, and anxious and

A duty of care decision was made to sedate the man in order to prevent him leaving and harming himself, and he was referred to a psychiatric institution in Perth under the *Mental Health Act 1996*. He was initially sedated with intramuscular major tranquillisers [Haloperidol] and short acting sedatives [Midazolam]. Due to the location, transport could not be arranged for 6 to 8 hours.

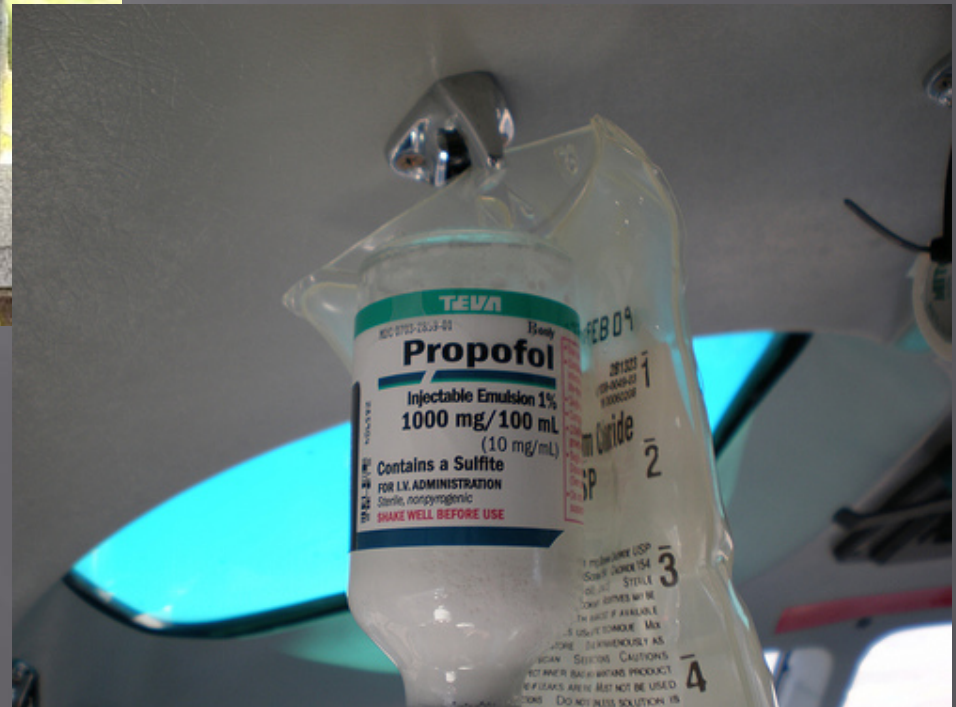
## That seems reasonable?...

The patient was difficult to restrain and sedate. After repeat doses of Midazolam and Haloperidol intramuscularly he received intermittent doses of intravenous Midazolam, then a Midazolam infusion. For the next four hours he was managed in the Emergency Department on oxygen 10 l/min by mask with ECG and oxygen saturation monitoring. Observation charts record a progressive fall in GCS from 15 on arrival, to 8.

When the transport service arrived, positional upper airway obstruction and poor airway reflexes were noted. The respiratory rate is recorded as 15 and GCS 6. He was intubated and ventilated for transport direct to a metropolitan ICU where chest x-ray identified right upper lobe pulmonary collapse and possible aspiration.

The patient remained on ICU for 5 days being treated for aspiration syndrome and sepsis. He was discharged extubated to the medical ward on day 6 awaiting psychiatric review. While mobilising on the ward he had a cardio respiratory arrest and died. Post mortem examination identified the cause of death as pulmonary embolus.

# And this sedation misadventure



# The limits of benzodiazepine and antipsychotic sedation

- ▣ Substance abusers often tolerant to first line sedatives
- ▣ ETOH abusers often tolerant to everything!
- ▣ Need to consider the realm of procedural sedation at this point...or general anaesthesia



# What we did

- ▣ Since 2007 alternative emergency sedation using ketamine
- ▣ Bolus and/or infusions
- ▣ Fasting status was not exclusion criteria
- ▣ Doctor administered only

# Study design

- ▣ 3 year retrospective chart audit 2007-2010
- ▣ Retrieval records systematically reviewed for ketamine use
- ▣ Preflight and inflight sedation
- ▣ Adverse events during retrieval
- ▣ 72hr post retrieval hospital chart review by two psychiatrists

# What did we find

- ▣ 18 cases collated over 3 years
- ▣ Medium to very high risk scores
- ▣ One reported case of inflight vomit (positioning required)
- ▣ One reported case of generalised muscle rigidity
- ▣ Initial bolus range : 10mg – 100mg
- ▣ Infusions : 20- 200mg /hr
- ▣ No reported cases of oxygen desaturation or hypotension
- ▣ No reported case of airway intervention required

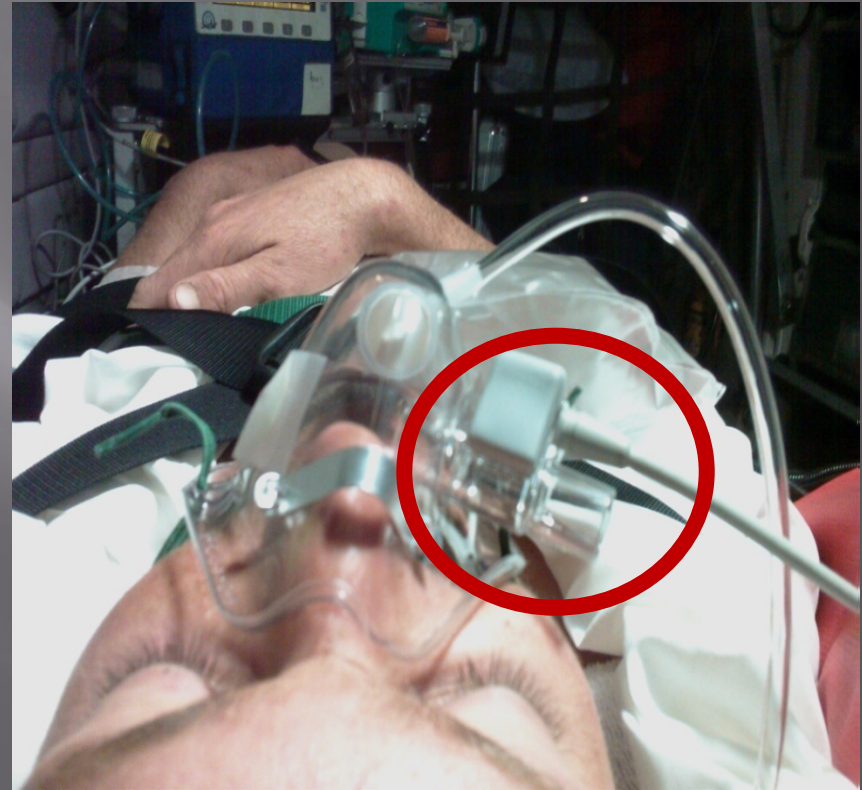
Aeromedical retrieval sedation details	Pre-flight sedatives administered(12hrs pre-flight) + dosages	Total In-flight sedatives administered + cumulative dosages	Duration of flight	Diagnosis
<b>Patient J</b> Retrieval: 25/8/09	PO olanzapine 10mg PO diazepam 20mg	IV diazepam 20mg + IV ketamine 400mg +IV midazolam 59mg +IV haloperidol 5mg	2 hrs	Schizophrenia
<b>Patient K</b> Retrieval: 26/08/09	PO olanzapine 10mg PO diazepam 10mg IV diazepam 10mg IV haloperidol 10mg IV ketamine 30mg	IV midazolam 6mg + IV ketamine 630mg	1 hr 35mins	Suicide attempt
<b>Patient L</b> Retrieval: 03/09/09	2/9 PO olanzapine 20mg + PO diazepam 20mg 3/9 IMI olanzapine 10mg + IVI midazolam 1mg	IV midazolam 2.5mg IV ketamine 20mg	1 hr	Schizophrenia
<b>Patient M</b> Retrieval: 16/10/09	PO olanzapine 10mg	IV midazolam 7 mg IV ketamine 240mg	2 hrs	Schizophrenia
<b>Patient N</b> Retrieval: 21/01/10	PO olanzapine 10mg x 4 = 40mg PO diazepam 10mg x 4 = 40mg	IV ketamine 230mg + IV midazolam 4mg	3 hrs	Schizophrenia
<b>Patient O</b> Retrieval: 04/02/10	PO olanzapine 5mg PO diazepam 10mg IV diazepam 5mg	IV ketamine 70mg	1 hr 50mins	Schizophrenia

# What about the 72hrs post ketamine sedation?

- ▣ Mild hypertension noted in about 10% for 1-6hrs
- ▣ No cases of worsening agitation attributable to ketamine ( pre-ketamine agitation =post ketamine agitation)

# Ketamine sedation tips

- ▣ 0.5-1.5mg/kg initial IV dose ( best preflight test dose)
- ▣ Adjuncts : midazolam, atropine(optional)
- ▣ Monitoring : cardiac rhythm, SaO<sub>2</sub>, BP, ETCO<sub>2</sub> ( see image)
- ▣ Preketamine sedation vital in minimising delirium  
(IMPORTANCE OF ADEQUATE PRE-TRANSPORT SEDATION)



# What is our ongoing experience?

- ▣ Highest recorded ketamine infusion rate  
=400mg/hr
- ▣ Has not replaced intubation but dramatically reduced need
- ▣ No post sedation delirium
- ▣ Rapid recovery in ED
- ▣ Atropine needed once for secretions

# Our conclusions

- ▣ Ketamine is a safe and effective emergency sedation agent for acute agitation
- ▣ It has reduced need for resort to intubation as a method of restraint
- ▣ When used as second line sedation there is a very low/negligible incidence of delirium

# SPECIAL K



# History

- ▣ 1959, search for safe sedative led to phencyclidine class.
- ▣ 1965, ketamine derived from this class by Parke, Davis & Company.
- ▣ Fallen out of favour in developed world anaesthesia but used extensively elsewhere
- ▣ Notorious recreational drug nowadays

# Ketamine sedation

- ▣ Powerful sedative
- ▣ Maintains respiratory drive to a degree
- ▣ Seems to work when first line sedatives fail
- ▣ Problems: hangover, nausea, delirium

## The combative multitrauma patient: a protocol for prehospital management

Eitan Melamed, Yahav Oron, Ron Ben-Avraham, Amir Blumenfeld and Guy Lin

**Objective** To describe the management of the combative trauma patient in the prehospital setting, and to suggest a protocol for management.

**Methods** A retrospective, prehospital case series conducted in Israel among military medical teams over the course of nearly 2 years, between January 2000 and October 2002. We collected a case series of patients who became combative following traumatic injury. Following data collection, we summoned an expert panel and developed a protocol for physicians and paramedics upon encountering a combative trauma patient.

**Results** Available data were found for 11 patients and these were included in the analysis. Most victims included in this study were injured under military or geographical circumstances mandating a long time interval from injury to definitive care, namely 114 min (range 38–225 min). Five patients received intravenous ketamine, in three of which it

more agitated after administration. No adverse effects were recorded by the prehospital caregivers.

**Conclusions** In this article, an algorithmic approach to the treatment of the patient's agitation is outlined, using ketamine as the principal sedating agent, either alone or combined with midazolam. The combination of both drugs is suggested for the effective sedation of adult prehospital combative patient population. *European Journal of Emergency Medicine* 14:265–268 © 2007 Wolters Kluwer Health | Lippincott Williams & Wilkins.

*European Journal of Emergency Medicine* 2007; 14:265–268

Keywords: agitation, combative patient, ketamine, prehospital care, trauma

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## KETAMINE CHEMICAL RESTRAINT TO FACILITATE RESCUE OF A COMBATIVE "JUMPER"

John L Hick, Jeffrey D Ho

*Prehospital Emergency Care*; Jan-Mar 2005; 9, 1; Career and Technical Education

pg. 85

# Ketamine in delirium???



## White Paper Report on Excited Delirium Syndrome

ACEP Excited Delirium Task Force

September 10, 2009

The ante-mortem diagnosis in the prehospital or emergency department setting depends upon clinical characteristics and the exclusion of alternative disease processes. It is our consensus that rapid and appropriate but limited control measures, and immediate administration of IV benzodiazepines or ketamine, IM ketamine, or intranasal midazolam, can be lifesaving.

<b>Clark County (Las Vegas), NV</b>	Midazolam (Versed) 2mg IV or 5mg IM/IN [may repeat]	Normal saline	Evaporative Cooling Cold packs	
<b>Columbus, OH</b>	Midazolam (Versed) 2-5mg IN, IV, pr [max 10mg]	Normal saline 500cc over 20min	Evaporative Cooling Cold packs	sodium bicarb. ½ amp (25meq) per liter of Normal saline
<b>Minneapolis, MN</b>	ketamine 5mg/kg IM or 2mg/kg IV	Normal saline up to 2 liter bolus IV	Evaporative Cooling Cold packs	sodium bicarb. 2 amps (100meq) IV push
<b>Rochester, MN</b>	Lorazepam (Ativan) 1-4mg IV/IM or midazolam (Versed) 1-5mg IV/IM	Normal saline	Evaporative Cooling Cold packs	sodium bicarbonate 1meq/kg IV push in cardiac arrest

# Does ketamine worsen mental illness?

The Schizophrenia Ketamine Challenge Study Debate

William T. Carpenter, Jr.

*subjects were drawn.* Biol Psychiatry 1999;46:1081-1091 © 1999 Society of Biological Psychiatry

Long-Term Outcome of Patients Who Receive Ketamine during Research

Adrienne C. Lahti, Dale Warfel, Tamara Michaelidis, Martin A. Weiler, Kristin Frey, and Carol A. Tamminga

*Conclusions: In a controlled environment and paying close attention to subject safety features, administering subanesthetic doses of ketamine causes no adverse events and little distress to schizophrenic volunteers. This study strongly indicates that administering ketamine does not change any aspect of the course of schizophrenic illness.*  
Biol Psychiatry 2001;49:869-875 © 2001 Society of Biological Psychiatry

- ❑ No in the short term
- ❑ No in the long term
- ❑ Audit of ketamine use on psychiatric retrievals

# Ketamine With and Without Midazolam for Emergency Department Sedation in Adults: A Randomized Controlled Trial

Serkan Sener, MD, Genker Eken, MD, Carl H. Schultz, MD, Mustafa Serinken, MD, Murat Ozsarac, MD

*From the Department of Emergency Medicine, Acibadem University School of Medicine, Acibadem Bursa Hospital, Bursa, Turkey (Sener); the Department of Emergency Medicine, Akdeniz University Hospital, Antalya, Turkey (Eken); the Center for Disaster Medical Sciences, Department of Emergency Medicine, UC Irvine School of Medicine, Orange, CA (Schultz); the Department of Emergency Medicine, Pamukkale University Hospital, Denizli, Turkey (Serinken); and the Department of Emergency Medicine, Ege University Hospital, Izmir, Turkey (Ozsarac).*

**Conclusion:** Coadministered midazolam significantly reduces the incidence of recovery agitation after ketamine procedural sedation and analgesia in ED adults (number needed to treat 6). Adverse events occur at similar frequency by the IV or IM routes. [Ann Emerg Med. 2011;57:109-114.]

# A Randomized Add-on Trial of an *N*-methyl-D-aspartate Antagonist in Treatment-Resistant Bipolar Depression

*Nancy Diazgranados, MD, MS; Lobna Ibrahim, MD; Nancy E. Brutsche, MSN; Andrew Newberg, MD; Phillip Kronstein, MD; Sami Khalife, MD; William A. Kammerer, MD; Zenaide Quezado, MD; David A. Luckenbaugh, MA; Giacomo Salvadore, MD; Rodrigo Machado-Vieira, MD, PhD; Hussein K. Manji, MD, FRCPC; Carlos A. Zarate Jr, MD*

**Conclusion:** In patients with treatment-resistant bipolar depression, robust and rapid antidepressant effects resulted from a single intravenous dose of an *N*-methyl-D-aspartate antagonist.

**Trial Registration:** [clinicaltrials.gov](http://clinicaltrials.gov) Identifier: NCT00088699

*Arch Gen Psychiatry. 2010;67(8):793-802*

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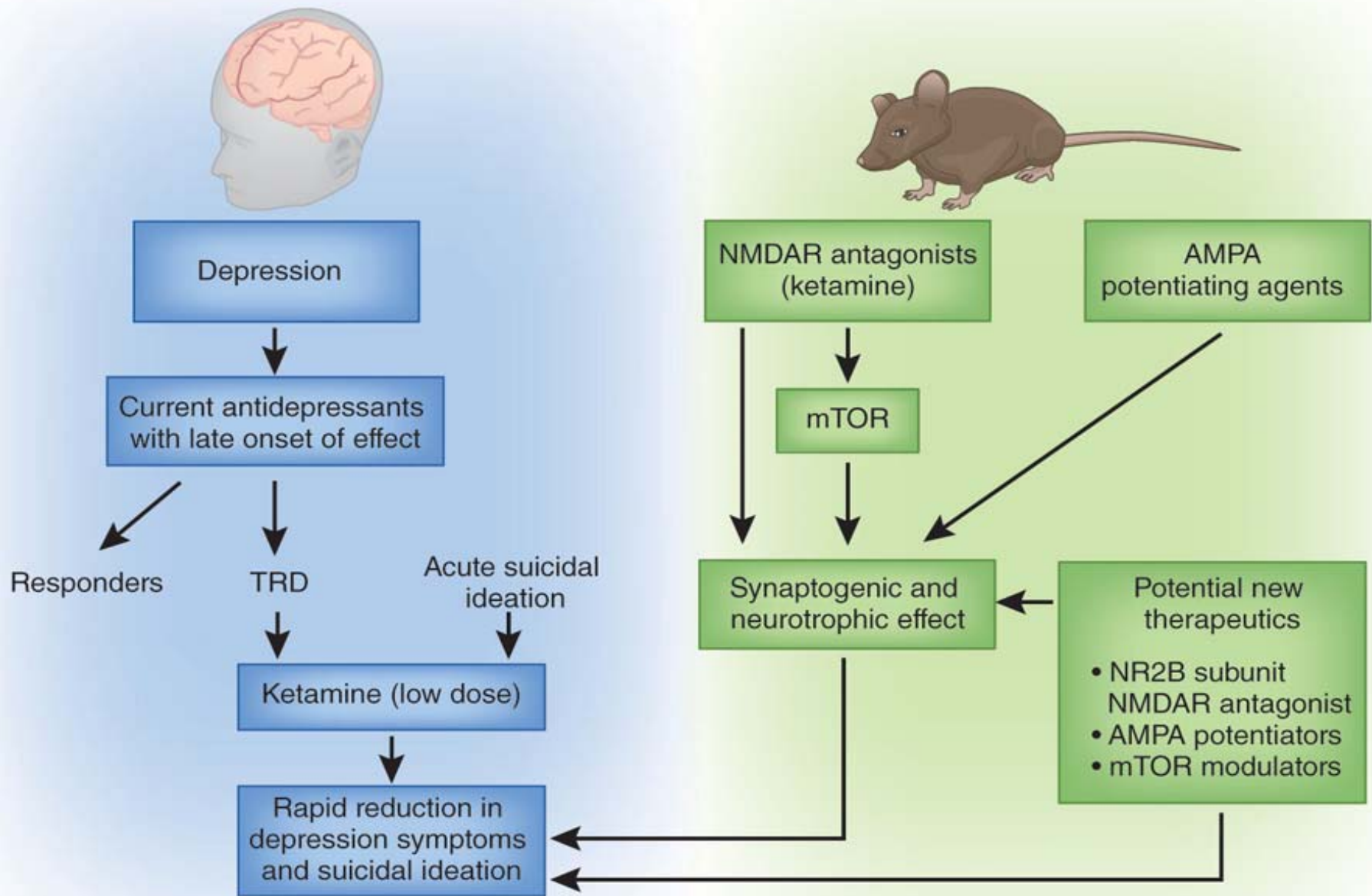
## A Prospective Open Label Trial of Low Dose Ketamine for Acute Suicidal States In the Emergency Department

Larkin GL, Beautrais AL, Powsner SM, Sanacora G, Krystal JH, Turelli RR, Lippmann MJ/Yale University School of Medicine, New Haven, CT

Ann Emerg Med 2010, 56(3):S53

Methods: Design: Prospective open-label case series. Subjects were 15 consecutive ED patients who presented with a primary complaint of depression and/or suicidal ideation. All patients were administered a single sub-anesthetic IV bolus of ketamine (0.20 mg/kg over 1-2 minutes) with continuous monitoring of

patients at 40, 80, 120 and 240 minutes post-infusion. Suicidal ideation was completely resolved in 14/15 subjects by 40 minutes and this reduction was sustained at 10 days in 13 of the 14 subjects followed to 10 days. Of 14 subjects



# Interesting trends emerging

- ▣ 2 cases of patients previously transported intubated
- ▣ Last 12 months both retrieved on ketamine infusion successfully
- ▣ Close liason with psychiatrists

# Aurukun clinic case



# RFDS retrieval sedation guidelines 2010

- ▣ Addition to Clinical Practice guidelines
- ▣ Collaborative work between RFDS and Cairns remote psychiatric service consultants (Professor Ernest Hunter, FRANZCP, Dr Bruce Gynther, FRANZCP)
- ▣ Expert input from retrieval anaesthetist (Dr Peter Schuller, FANZCA) and ED physicians (Dr Geoff Ramin, FACEM, Dr Steve Rashford, FACEM, Dr Mark Elcock, FACEM)

# Sedation training- RFDS style



- ▣ Handover
- ▣ Airway assessment
- ▣ Resuscitation gear preparation
- ▣ Monitoring
- ▣ Medical assessment
- ▣ Fasting status
- ▣ Sedation/ Agitation scoring
- ▣ Target sedation level/ score

**TABLE 1. RICHMOND AGITATION-SEDATION SCALE**

Score	Term	Description
+4	Combative	Overtly combative or violent; immediate danger to staff
+3	Very agitation	Pulls on or removes tube(s) or catheter(s) or has aggressive behavior toward staff
+2	Agitated	Frequent nonpurposeful movement or patient-ventilator dyssynchrony
+1	Restless	Anxious or apprehensive but movements not aggressive or vigorous
0	Alert and calm	
-1	Drowsy	Not fully alert, but has sustained (more than 10 seconds) awakening, with eye contact, to voice
-2	Light sedation	Briefly (less than 10 seconds) awakens with eye contact to voice
-3	Moderate sedation	Any movement (but no eye contact) to voice
-4	Deep sedation	No response to voice, but any movement to physical stimulation
-5	Unarousable	No response to voice or physical stimulation

Procedure

1. Observe patient. Is patient alert and calm (score 0)?  
Does patient have behavior that is consistent with restlessness or agitation (score +1 to +4 using the criteria listed above, under DESCRIPTION)?
2. If patient is not alert, in a loud speaking voice state patient's name and direct patient to open eyes and look at speaker. Repeat once if necessary. Can prompt patient to continue looking at speaker.  
Patient has eye opening and eye contact, which is sustained for more than 10 seconds (score -1).  
Patient has eye opening and eye contact, but this is not sustained for 10 seconds (score -2).  
Patient has any movement in response to voice, excluding eye contact (score -3).
3. If patient does not respond to voice, physically stimulate patient by shaking shoulder and then rubbing sternum if there is no response to shaking shoulder.  
Patient has any movement to physical stimulation (score -4).  
Patient has no response to voice or physical stimulation (score -5).

# What are the risks of procedural sedation during aeromedical retrieval?

- ▣ Case reports only
- ▣ Flying Doctor Emergency Retrieval Sedation Registry by RFDS QLD
- ▣ Funded for 3 years
- ▣ Prospective study of all retrieval sedations, using new guidelines
- ▣ Safe and efficacious?

# I hope I have...

- ▣ Given you something to think about
- ▣ Motivated you to consider research into this area
- ▣ Provided a glimpse at one model of better practice