

Original Research Article

A novel use of ketamine sedation for patients with acute agitation 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. We describe a novel technique using ketamine which is titratable and avoids problems associated with airway management. We report our experience with this technique, emphasising safety profile during transport and impact on patients' mental state following the period after their arrival at definitive psychiatric care facility

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. Retrieval transport records were systematically reviewed for psychiatric diagnosis, ketamine administration and signs of adverse events during transport. The inpatient hospital records for the patients in this study were reviewed for evidence of worsening agitation or other adverse events over a 72 hr period following retrieval.

Results: A total of 18 patients were sedated during retrieval with intravenous ketamine, usually in combination with a benzodiazepine. 16 of the 18 patients had a diagnosis of schizophrenia. Effective sedation was achieved in all cases with no significant adverse events noted. Mild hypertension was noted in one third of the patients during and for up to 6 hrs after transport. There was no worsening of agitation or psychotic symptoms compared to the patients' pre-retrieval state.

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 hr period.

Keywords: ketamine; psychiatric; aeromedical; retrieval; sedation

Financial disclosures: None declared

Author contributions: ML collected and reviewed the aeromedical retrieval data and wrote the manuscript in conjunction with PS. EH and BG collected and reviewed the hospital admission data and provided input into the manuscript.

Acknowledgements: Leigh –Ann Onnis, research assistant to EH and BG, who collated all the hospital records and completed data sheets for review

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Introduction

Aeromedical transport of patients suffering acute mental illness is challenging due to the high degree of agitation that may exist, the large doses of sedative medications that are often used prior to transport and the risks involved if inadequate sedation is achieved during the flight. Although several published guidelines exist for sedation of the acutely agitated patient in the hospital setting (1), the optimal sedation strategy for the air transport of psychiatric patients remains unclear. This has led to sometimes starkly divergent approaches taken by aeromedical providers ranging from use of physical restraints, refusal to transport at all, through to general anaesthesia and tracheal intubation. Most patients with acute agitation can be transported safely using conventional 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 been often made despite its attendant risks. This study seeks to describe an alternative approach using ketamine sedation and outline its safety profile.

The Queensland (QLD) section of the Royal Flying Doctor Service (RFDS) of Australia has a total of 7 operational bases for aeromedical missions that cover a combined territory equivalent to three times the land area of France. The base in Cairns services a sparsely populated area in the far north of the state which is the size of Great Britain, yet has a population, outside of the major centre of the greater Cairns area, of only 20,000 people (2). This includes mining centres such as Weipa, indigenous settlements such as Aurukun & Lockhart River and scattered cattle stations. Where these sites have any health services at all, they are generally small community health centres staffed by remote-area nurses and visited by RFDS medical staff for several days a week only. These clinics are not staffed after hours, except for emergencies, and have no facilities to deal with acute presentations of major psychotic disorders. The exceptions are the small hospitals at Weipa, Bamaga and Thursday Island, which have several doctors and an after-hours ward, but no facilities for the acutely mentally disturbed patient and no secure areas. As a result, even a single presentation of a psychotic or suicidal patient places great strain on the local resources, especially if they require constant restraint and supervision after hours. Where a patient is so acutely unwell that they are deemed a risk to

themselves or others such that they require inpatients medical care or locked ward supervision, they are clearly a serious in-flight risk to aeromedical staff and the safety of the aircraft. Any patient who is deemed a risk to themselves or others such that they require transfer to a psychiatric facility is not, by definition, safe for travelling on an aircraft

RFDS QLD Policy on Transfer of the Disturbed Patient

Our preferred management of severely agitated patients is for them to be progressively sedated with antipsychotics and benzodiazepines, and only after that has been achieved, for the retrieval to be activated. Ideally, such patients are sedated to the point where they are cooperative and able to walk onto the aircraft, but drowsy enough such that when they see the transport stretcher they willingly lie down on it. A small extra dose of sedation is then given, and basic hand and wrist restraints are applied. They are closely monitored throughout the flight and small boluses of midazolam are usually sufficient for the patient to rest quietly for the several hours of the transfer. The RFDS Queensland's policy mandates both a doctor and nurse to be tasked to the flight, and where there is history or likelihood of violence, a police officer is requested to accompany the flight. In addition, night transfers are avoided. Ideally the pre-flight sedation takes place over a 12 -24 hour period prior to activation of the retrieval. More rapid attempts at sedation may fail due to either over-sedation, requiring airway support, or under-sedation, whereby they are still too agitated to be safe for travel by aircraft. However, due to the varied type and experience of staff at the various originating health centres, it is difficult to establish consistent and adequate sedation of patients before the arrival of the aeromedical team. In part, this is due to the concern of patients being over-sedated when there may be no medical staff present with adequate airway skills. As a result, there is little alternative for the evacuating aeromedical team but to perform rapid sedation of the patient, which is a difficult and unpredictable task, if the aim is to avoid intubation and ventilation. Intubation and ventilation as a means of safely transferring severely agitated patients is not without risk, both at the time of intubation and during the flight, and it also poses considerable logistical problems at the receiving hospital. Such patients cannot be sent directly to a psychiatric ward but must be woken and extubated in an acute environment, usually the Emergency department where they take up an acute resuscitation bed and several medical and security staff for what is often an erratic and noisy extubation process.

Materials and Methods

The Cairns RFDS base transferred 135 patients with a mental health ICD 10 diagnosis between January 2007 and April 2010. During this period the author (ML) and retrieval colleagues working out of Cairns RFDS base began utilising ketamine sedation as an alternative strategy when standard initial treatment had failed to control agitation. The 2009 Queensland Health Statewide guidelines for acute sedation in adult mental health inpatient settings stipulates first line sedation treatment consist of a benzodiazepine (lorazepam or diazepam) and/or antipsychotic (olanzapine). The initial ketamine dosing range given for retrieval sedation was 0.5-1mg/kg. If two doses were required within the first 60 minutes of initiation of sedation then an infusion was started with an initial rate of 1-1.5mg/kg/hour. The amount given was titrated to achieve a target sedation level which was a calm, cooperative patient who could still respond to verbal commands. Ethics approval to conduct formal audit of RFDS and Cairns Base Hospital records was sought and granted from Queensland Health Human Research Ethics Committee (Cairns). The RFDS records were reviewed by author (ML) for use of ketamine for transport sedation. The

following factors were systematically reviewed for each record: pre-flight sedation, in-flight sedation, duration of flight, primary diagnosis, blood pressure, heart rate, oxygen saturation and episodes of vomiting or complaints of nausea. The subsequent Cairns Base Hospital medical records for each case were then examined by authors (EH and BG, independently) for the following 72 hours after transport with systematic review of the following factors : In hospital sedation , clinical diagnosis, use of physical restraints, evidence of physical assault by patient, blood pressure , heart rate, oxygen saturations and overall clinical impression. When determining the overall clinical impression result, the reviewing clinician was asked to consider the following question: “Did the patient get worse in mental state between days 1 to day 3 of admission?” For each patient both psychiatrists determined whether there was any significant change in the patient’s mental state after treatment with ketamine, compared to their pre-retrieval mental state.

Results

19 retrieval cases were identified for the study period, involving 18 patients. The age range of the study group was from 12 to 43 years old. (See Table A). Sixteen (65%)patients had a primary retrieval diagnosis of exacerbation of schizophrenia. Two (10%) were suicidal, one had acute mania and one had a personality disorder. All patients received pre-flight sedation consisting of either olanzapine or haloperidol or both, in combination with a benzodiazepine. In each case the patients were transported for Involuntary Assessment or Treatment under the Queensland Mental Health Act. As per RFDS protocol, approved 4 points physical restraints were applied. Ketamine initial dosing ranged from 20 to 200mg IV followed by intermittent boluses averaging 60 mg per hour. Infusions were administered on 9 patients , at a rate varying from 40 to 120mg per hour. Continuous monitoring of blood pressure, pulse rate and oxygen saturations was undertaken. All patients were given supplemental oxygen of 2 -4 L/min. No patients had been formally fasted prior to sedation with ketamine.

Adverse events

Adverse events were defined as blood pressure readings of systolic < 90 mmHg or >140mmHg, pulse rate > 100/minute, oxygen saturation <90% and episodes of vomiting or complaints of nausea

Hypertension or tachycardia occurred in 4 patients. No corrective treatment was deemed necessary. There was one case of generalised body rigidity reported after the initial ketamine IV dose that resolved spontaneously within 1 minute. One patient vomited a small amount of gastric contents. This occurred mid-flight and without warning. This did not require active intervention as the patient turned his head and cleared the vomitus without assistance. This patient had both eaten and drunk within the hour before pre-flight sedation was administered. In the single paediatric patient , not only had the first line agents failed to sedate adequately, but his mental state had actually worsened before ketamine was given.

Table A

Aeromedical retrieval sedation details	Pre-flight sedatives administered(12hrs pre-flight) + dosages	Total In-flight sedatives administered + cumulative dosages	Duration of flight	Diagnosis	Any recorded BP <90 or >140 systolic	Heart rate recorded >100	Oxygen Saturation recorded <95	Vomiting or c/o nausea

Patient A Retrieval: 18/08/07	PO olanzapine 10mg PO diazepam 10mg	IV midazolam 9.5mg +IV ketamine 30mg	2 hrs	Acute Mania	No	No	No	No
Patient B Retrieval: 24/10/07	IV midazolam 7.5mg PO olanzapine 20mg	IV midazolam 7mg +IV ketamine 30mg	1.5hrs	Schizophrenia	No	No	No	No
Patient C Retrieval: 05/08/08	PO olanzapine 10mg PO diazepam 20mg	IV ketamine 420mg +IV midazolam 6mg	2 hrs	Psychosis	No	No	No	No
Patient D Retrieval: 10/10/08	PO olanzapine 10mg on 9/10 and 10mg on 10/10	V midazolam 12mg + IV ketamine 30mg	1hr 15mins	Cannabis induced psychosis	No	No	No	No
Patient E Retrieval: 6/12/2008	IMI olanzapine 10mg IMI diazepam 10mg	IV ketamine 40mg	30 mins	Psychosis	No	No	No	No
Patient F Retrieval: 02/03/09	Olanzapine PO 20mg Clonazepam PO 2mg	IV midazolam 10mg + IV ketamine 380mg	2.5 hrs	Personality disorder	No	No	No	Yes, small vomit x 1
Patient G Retrieval: 08/03/09	PO valproate 1g PO olanzapine 20mg PO diazepam 190mg	IV midazolam 7mg + IV ketamine 600mg	3 hrs	Schizoaffective	BP>140 once (last recording of flight)	Yes , whole retrieval duration	No	No
Patient H Retrieval: 28/4/09	IV haloperidol 5mg + IMI haloperidol 10mg + PO olanzapine 10mg + IV clonazepam 4mg	IV ketamine 200mg	30mins	Schizophrenia	BP 140-150	No	No	No
Patient H Retrieval: 18/07/09	PO Diazepam 20mg PO Olanzapine 20mg PO risperidone 2mg PO haloperidol 10mg + IV morphine 4mg + IV midazolam 2mg	IV ketamine 90mg	30 mins	Schizophrenia	No	No	No	No
Patient H Retrieval: 21/05/09	PO diazepam 20mg	IV midazolam 2.5mg	30 mins	Schizophrenia	No	No	No	No
Patient I Retrieval: 31/5/09	PO olanzapine 20mg PO diazepam 20mg	IV midazolam 19mg + IV ketamine 160mg	4 hrs	Schizophrenia	No	No	No	No

Aeromedical retrieval sedation details	Pre-flight sedatives administered(12hrs pre-flight) + dosages	Total In-flight sedatives administered + cumulative dosages	Duration of flight	Diagnosis	Any recorded BP <90 or >140 systolic	Heart rate recorded >100	Oxygen Saturation recorded <95	Vomiting or c/o nausea
Patient J 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	BP 140-150 initially then reduced to 130	HR >100 for 30 min initially after initial ketamine IV	No	No
Patient K 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	1hr 35mins	Suicide attempt	No	No	No	No
Patient L 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	No	No	No	No
Patient M Retrieval: 16/10/09	PO olanzapine 10mg	IV midazolam 7 mg IV ketamine 240mg	2 hrs	Schizophrenia	No	No	No	No
Patient N 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	YES = BP >140/ for most of retrieval but note that BP >140/ pre-retrieval	YES = HR >100 for 50 % of retrieval	No	No
Patient O Retrieval: 04/02/10	PO olanzapine 5mg PO diazepam 10mg IV diazepam 5mg	IV ketamine 70mg	1hr 50mins	Schizophrenia	No	No	No	No
Patient P Retrieval: 6/2/2010	IMI haloperidol 10mg IMI midazolam 10mg IVI Midazolam 5mg IVI diazepam 20mg IVI clonazepam 2mg	IV ketamine 240mg	30 mins	Schizophrenia	No	No	No	No
Patient Q Retrieval: 18/02/10	10mg PO diazepam on admission, then 2mg IV clonazepam + 10mg IV haloperidol, then over 12 hrs further 20mg IV diazepam	3mg IV midazolam + 20mg IV ketamine	35 mins	Suicidal ideation/Intentional self harm	No	No	No	No

Patient R Retrieval: 19/02/10	PO olanzapine 30mg PO diazepam 90mg IV diazepam 15mg	IV midazolam 9mg + IV ketamine 270mg	3 hrs	Schizophrenia	No	No	No	No
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During the 72 hrs after retrieval, 10 patients had at least one abnormal blood pressure or heart rate recording, most of which was in the first 24hrs. All resolved without treatment. One case developed a bradycardia of 42/min on arrival in the Emergency Department but had a blood pressure of 102/56. This spontaneously resolved over the next hour. It is notable that this is the only case in which IV morphine was given as part of the pre-flight sedation.

Effect on mental state

There were no cases identified where agitation or psychiatric symptoms were deemed to have worsened as a result of ketamine administration. All of the cases in which agitation was manifest after retrieval had significant agitation prior to retrieval. One patient had three retrievals alone during the study period, which coincided with cessation of his chronic injectable depot antipsychotic medication regimen. Once this regimen was restarted, this patient did not require any further inpatient treatment. Of the three transfers, two required ketamine, whereas midazolam alone was sufficient in the third. There was no discernible difference in amount of sedation, agitation or overall clinical impression during the 72hours post transfer in this patient whether or not ketamine was used.

Discussion

The use of ketamine as a sedating agent for the acutely disturbed patient with a psychiatric diagnosis in the aeromedical setting has not been reported or previously described. However, ketamine has been viewed as being capable of triggering acute agitation and frank psychoses and therefore contraindicated in patients with known or suspected psychotic disorders. Ketamine is structurally similar to the drug phencyclidine, which was used as an anaesthetic agent

in the early 1960's but then withdrawn from use due to post-operative psychosis (3). As both ketamine and phencyclidine are NMDA receptor antagonists there have been theoretical concerns that ketamine may exacerbate psychosis in patients with schizophrenia. Indeed, ketamine has been used in low doses in normal patients to produce brief psychotic-like symptoms (4). However, studies investigating ketamine challenge in patients with schizophrenia have not found long term adverse effects or ketamine induced relapse of psychosis (5). Its use as emergency sedation for acute agitation has been described in the military setting for injured battlefield soldiers (6). There are also case reports of its use in the emergency department setting and prehospital setting for acutely intoxicated, delirious patients (7, 8). Standard first line sedating agents for acute undifferentiated agitation in the emergency department and acute mental health unit setting are a benzodiazepine and a sedating antipsychotic (1). When such measures fail, the usual approach is repeated doses of the same agents and in extreme circumstances, seclusion is used. Whilst this works well in the hospital setting, its validity and practicality in the aeromedical setting has never been ascertained or evaluated.

Wheeler and Wong of the British Columbian Air Ambulance Program describe one standard method of sedation for air transport patients, requiring at least 3 intramuscular injections one hour prior to flight. In their protocol a key element of safety is the right to refuse transport by the escorting flight paramedic if sedation effect is deemed to be inadequate (9). Whilst intubation and ventilation is not formally recognised or recommended in any mental health transport guidelines within the state of Queensland, we are aware it is a widespread practice across Australia where transport times from remote locations are prolonged (averaging 2-3 hrs or more in some locations). Our study raises the possibility of an alternative which balances the need for sedation against the complexities of general anaesthesia and tracheal intubation.

The benefits of avoiding intubation as a method of restraint are multiple. Intubation purely for combativeness in the trauma patient group has been shown to lead to higher rates of hospital pneumonia and longer lengths of stay (10). Emergency rapid sequence induction in an uncooperative patient outside of the ideal environment of an operating theatre or ED resuscitation area are not to be underestimated. Simple safety measures such as pre-oxygenation, monitoring, patient positioning and access to difficult intubation equipment are difficult if not impossible. Tracheal intubation requiring general anaesthetic drugs carries significant risks and should not be undertaken for non critical care reasons unless there are clear benefits. When dealing with a vulnerable group such as involuntary status patients the legal principle of minimal restraint should be adhered to. Further, when a psychiatric patient is intubated for transport, difficulties frequently arise as to where and when to extubate the patient at their destination. It is invariably the emergency department of the receiving hospital which has limited resources and is not at all the peaceful, non stimulating environment that the agitated patient requires.

We have reviewed the main adverse effects of ketamine sedation, being risk of aspiration from vomiting, abnormal cardio respiratory events and worsening agitation and psychiatric symptoms. Our review of 18 patients over 3 years showed a single incidence of vomiting, with no aspiration and some mild blood pressure abnormalities that spontaneously resolved without treatment. The unique ability of ketamine to preserve upper airway reflexes and maintain spontaneous respirations in standard dosing range meant that with the one vomit that occurred, there was no need for intervention. No airway manoeuvres were required at all nor was any ventilatory assistance. The practice, of using opioids in addition to other sedatives in the non ventilated patient, should be flagged as requiring extra precaution and is not recommended by the authors. The 12 year old patient requiring transport (one of only two patients who did not have a diagnosis of a psychotic disorder) only responded to IV ketamine sedation after multiple first line agents had failed. Indeed in this case, standard sedation appeared to have worsened the agitation in a setting in which both police and family were involved with obvious distress for the latter. In this paediatric group it could be argued that ketamine carries better evidence to support its use as paediatric sedation in the emergency setting than other sedatives (11). The authors believe that when benzodiazepine and antipsychotic medications have been administered and fail to adequately control acute agitation, ketamine sedation is a safe and effective strategy for managing agitation of psychiatric patients requiring aeromedical transport and it should reduce the need to resort to tracheal intubation and general anaesthesia in this setting. As a result of this study the RFDS QLD aeromedical service in conjunction with authors EH, BG and PS, has developed formal retrieval sedation guidelines for use of ketamine including a formal anaesthetic assessment process that incorporates review of fasting status, airway examination and targeted sedation levels using a validated sedation scoring system. A prospective audit of these formal guidelines is planned.

Study limitations

The dataset is small. The accuracy of records in a retrospective chart review can always lead to incomplete data collection and so compromise interpretation of results. The psychiatrists involved in the study were not blinded to the sedation used and were aware of the new technique being tried.

Conclusions

Ketamine sedation is effective and safe in agitated patients with a psychiatric diagnosis in the aeromedical setting and does not lead to worsening agitation during transport in the subsequent 72 hr period.

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