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Gratis

Case Report

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Safe Administration of Subanesthetic Ketamine Infusions in a Heart Transplant Patient

Douglas Ardekani[1], Louis Tsichlis[1], Prabhneet Pannu[2] and Bal Nandra[3]

[1]Chicago College of Osteopathic Medicine, Midwestern University, Downers Grove, IL, USA
[2]Aureus University School of Medicine, Oranjestad, Aruba
[3]Ketamine Centers of Chicago, Chicago, IL, USA

***Correspondence:** Louis Tsichlis, Chicago College of Osteopathic Medicine, Midwestern University, Downers Grove, IL, USA, E-mail: ltsichlis93@midwestern.edu

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Abstract

The method of treating bipolar disorder through subanesthetic ketamine infusions is becoming increasingly common. Particularly, patients with bipolar disorder who are refractory to other forms of mood stabilizing treatment are seeking the alternative avenue ketamine provides. Several factors exist, however, that act to hinder patients from seeking this avenue of treatment, the first of which being ketamine's hallucinogenic properties. Another factor that may hinder a patient's decision in seeking ketamine treatment is its sympathomimetic effect in stimulating adrenergic receptors while inhibiting muscarinic receptors. Due to this effect, a seeming contraindication exists in patients with underlying heart conditions. Although this seeming contraindication exists, successful treatment of bipolar disorder symptoms in a patient with previous heart transplant in this case report demonstrated ketamine's potential to be administered safely in patients with underlying heart conditions.

Introduction

Bipolar disorder is a mood disorder characterized by episodes of mania, hypomania, and major depression. Studies have shown that the clinic course of bipolar disorder is predominated by depressive symptoms [1]. The management of both pathologic mood elevation and depression in these patients often creates complicated management with pharmacotherapy. Ketamine is a widely used dissociative anesthetic that mainly acts as a non-competitive antagonist at glutamatergic NMDA receptors of nerve cells. It possesses a well-documented safety profile, allowing it to have a wide spectrum of clinical applications. Although ketamine is documented as a safe and effective tool in the setting of anesthesia, pain management and in the treatment of numerous mental illnesses, contraindications are thought to exist in patients with cardiovascular conditions [2]. This is due to ketamine's additional mechanism of action in stimulating alpha and beta adrenergic receptors while inhibiting muscarinic acetylcholine receptors. This leads to increased cardiac excitability as heart rate, cardiac output and myocardial oxygen demands increase through autonomic nerve stimulation [3]. In another study testing the alterations of adrenergic mechanisms by ketamine on epinephrine-induced arrhythmia, it was thought that ketamine may also act to increase arrhythmogenic potential of the heart when coupled with epinephrine [4]. The question that remains is whether the increase in cardiac excitability is safe in patients with critical conditions such as the heart transplant patient in this study. Additionally, this study gives us evidence that ketamine does not increase arrhythmogenic potential when coupled with epinephrine. This is supported by the subject patient's concurrent use of prescription serotonin-norepinephrine reuptake inhibitor during the

ketamine infusions without any consequences on heart rate. The purpose of this study was to illustrate that ketamine's cardiovascular effects pose no significant risk on heart transplant patients and that it is indeed safe to use on this group clinically.

Case Study

A 63-year-old married Caucasian man presented to our clinic seeking treatment for bipolar depression. He has a history of hypertension, five myocardial infarctions requiring triple bypass surgery and heart transplant done in 2003. Other history includes bipolar depression which was diagnosed 25-30 years ago and is currently being managed medically with a mood stabilizer (valproic acid) and a serotonin-norepinephrine reuptake inhibitor (levomilnacipran). Throughout his course of managing this condition, he has not had sufficient relief as he has been admitted to the psychiatric ward twice and has also had multiple therapist interventions. Patient additionally described many side effects from the medications such as tremors and unstable gait. These undesirable factors inevitably led him to seek an alternative direction in treating his condition through ketamine infusion therapy.

Treatment protocol at our clinic includes six infusions over a 1.5 - 2 week period with no change in regular medications. This is followed by maintenance infusions for which timing is dependent on recurrence of patient symptoms. Infusions take place over the course of approximately one hour with the patient's vital signs and tolerance to infusion being monitored every 15 minutes over this period. The patient was started on a ketamine dose of 0.4 mg/kg, and incrementally increased as tolerated. Our patient's progress was tracked with self-reported scores with the Beck's Depression Inventory, Beck's Anxiety Inventory, Concise Health Risk Tracking - Self Report (CHRT-SR), and the Quick Inventory of Depressive Symptomatology (QIDS-SR16). The staff administered these inventories prior to each treatment with interpretation as follows:

QIDS: Scale 1-27. 1-5 = no depression, 6-10 = mild depression, 11-15= moderate depression, 16-20= severe depression, 21-27 = very severe depression

Beck's Depression Inventory: Scale 1-40+. 1-10 = normal, 11-16 = mild mood disturbance, 17-20 = borderline depression, 21-30 = moderate depression, 31-40 = severe depression, 40+ = extreme depression

Beck's Anxiety Inventory: Scale 1-36+. 0-21 = low anxiety, 22-35 = moderate anxiety, 36+ = potentially concerning levels of anxiety

CHRT-SR: Three digit score representing patient's propensity (first digit), impulsivity (second digit) and suicide risk (third digit).

Results

Table 1: Depression and Anxiety Ratings over six treatments.

Date	QIDS	Rating	Beck Depression	Rating	Beck Anxiety	Rating	CHRT-SR
11/25/19	20	Severe	30	Moderate	41	High	24-3-3
12/3/19							
12/5/19	8	Mild					2/2/2000
12/10/19	7	Mild	9	Normal	19	Low	3/1/2000
12/12/19	11	Moderate					13-5-0
12/20/19	10	Mild	12	Mild mood disturbance	25	Moderate	11/4/2000

Table 2: Vital Signs - Treatment 1 (11/25/19).

Time	HR	BP	RR	O_2 Saturation
Baseline - 12:45	105	162/107	18	94
12:55	105		18	94
13:05	103	170/97	18	92
13:15	101	176/91	18	96
13:25	100	169/91	18	97
13:35	98	167/90	18	98
13:45	97	166/93	18	97

Table 3: Vital Signs - Treatment 2 (12/03/19).

Time	HR	BP	RR	O_2 Saturation
Baseline - 10:00	106	163/87	18	94
10:15	105	155/86	18	93
10:30	103	169/94	18	94
10:45	99	152/90	18	94
11:00	96	153/84	18	94
11:15	95	168/100	18	94

Table 4: Vital Signs - Treatment 3 (12/05/19).

Time	HR	BP	RR	O_2 Saturation
Baseline - 9:40	106	175/95	18	96
9:55	109	169/100	18	96
10:10	109	169/96	18	96
10:25	105	160/88	18	95
10:40	106	165/82	18	95

Table 5: Vital Signs - Treatment 4 (12/10/19).

Time	HR	BP	RR	O_2 Saturation
Baseline - 9:35	103	183/104	18	96
9:50	104	183/111	18	96
10:05	103	182/100	18	96
10:20	102	176/108	18	96

Table 6: Vital Signs - Treatment 5 (12/12/19).

Time	HR	BP	RR	O_2 Saturation
Baseline - 9:40	107	163/92	18	96
9:55	107	168/102	18	95
10:10	107	173/101	18	95
10:25	105	166/105	18	95

Table 7: Vital Signs - Treatment 6 (12/20/19).

Time	HR	BP	RR	O_2 Saturation
Baseline - 9:55	101	182/101	18	97
10:10	100	172/100	18	91
10:25	100	169/101	18	89
10:40	104	171/101	18	94

Discussion

The results of our patient's treatment regimen show that IV ketamine therapy is a viable option for heart transplant patients despite this medication's sympathomimetic properties. Our patient tolerated treatment and suffered no adverse events, contrary to the belief that ketamine is contraindicated in patients with heart conditions. Also of note, this patient's drug regimen was held constant throughout the course of his treatment with us. Included in his regimen are drugs used to treat his bipolar depressive disorder such as the antidepressant levomilnacipran. As a serotonin-norepinephrine reuptake inhibitor, this drug functions to increase the availability of serotonin and the catecholaminergic norepinephrine. The results in this study show that the clinical use of ketamine when coupled with catecholamines such as norepinephrine does not pose an increased arrhythmogenic risk, as previously thought [4]. Overall, this study provides a new avenue for treating heart transplant patients with depression, anxiety, PTSD, bipolar disorder, and chronic pain among other conditions.

Our patient showed significant progress with decreases in Beck's Depression Inventory, Beck's Anxiety Inventory, CHRT and QIDS questionnaires in addition to verbal reports indicating improvement in mood. QIDS screening displayed a decrease from severe score of 20 to a mild score of 10 by the end of the six treatments. Similarly, Beck's Depression Inventory screening decreased from a moderate score of 20 to a score of 12 indicating mild mood disturbance at the end of treatments. Prior to the patient's fourth treatment, Beck's Depression Inventory reached a treatment low of 9 which represents a normal result. Beck's Anxiety Inventory also indicated a significant alleviation of symptoms throughout treatment with an initial high anxiety score (41) improving to moderate anxiety (25) at the end of treatment. A treatment low was also reached on the Anxiety Inventory prior to the fourth treatment indicating low anxiety levels. The patient also verbally reports no exacerbation of symptoms of mania. Additionally, as documented in tables 1-7 there were no concerning changes in the patient's vitals including heart rate, blood pressure, and oxygen saturation throughout treatment. Thus, our studies suggest that subanesthetic doses of ketamine can be safely used to treat heart transplant patients for a variety of conditions. The current study is limited by a limited sample size. Future studies with subjects similar to the patient evaluated in this case will be used to further our findings.

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