Use of ketamine for acute suicidal ideation in a patient with chronic pain on prescribed cannabinoids

Daniel Bigman, Sindhura Kunaparaju, Bradford Bobrin

SUMMARY
Ketamine is a standard anaesthetic drug that has been studied as a possible treatment for acute suicidal ideation. Aside to the potential psychotropic effects of ketamine, a Cochrane review reported that available studies suggest a modest effect of ketamine for chronic pain months to years after surgical intervention. We present a patient with acute suicidal ideation who required immediate inpatient psychiatric admission in the setting of concurrent chronic pain on cannabinoids which could not be prescribed within our inpatient hospital setting. This presented a clinical dilemma to rapidly reverse the patient’s suicidality while substituting the patient’s prescribed cannabinoid products with an alternative pain regimen. Since there is emerging support in the use of ketamine in suicidality and chronic pain, we administered ketamine while withholding cannabinoid products and found evidence to support its use in rapid reversal of suicidal ideation and temporary chronic pain relief.

BACKGROUND
There is emerging evidence that glutamatergic system dysfunction might play an important role in the pathophysiology of bipolar depression. Ketamine is a dissociative anaesthetic that produces analgesia and amnesia. Its contemporary use can have a variety of side effects; agitation, hallucinations, hypertension or emergence of other excitement symptoms. In comparison to bipolar depression, there is greater evidence that long-term treatment of chronic pain with ketamine will cause prolonged pain relief. Of importance is that no effect on functionality or on depressive symptoms was observed. Still, although ketamine treatment is linked to a variety of side effects, we feel that benefits outweigh the risks in specific patient populations and further research is needed to address the use of ketamine in suicidality and chronic pain.

CASE PRESENTATION
JM is a 46-year-old African-American man with a self-reported history of bipolar disorder, chronic shoulder pain on prescribed cannabinoids, who presents to the emergency department with suicidal ideation. The patient states that he has been having progressed depressed mood over the past week and started to have suicidal ideation for a few days. He endorsed a plan of drinking bleach or any toxic liquid he could purchase in the grocery store. These thoughts were associated with insomnia, decreased appetite, feelings of hopelessness and helplessness. He states that over the past 2 days, he has noticed increased anxiety associated with ‘shadows’ which have been occurring more frequently in the evening. He reports medication non-compliance in the past 3–4 weeks; quetiapine 400 mg at bedtime and bupropion SR 150 mg twice daily. He states that he got into a verbal altercation with his girlfriend after she found out about his ‘infidelities’ and was kicked out of their home in Delaware. He decided to seek shelter with his aunt in New Jersey. He reports a long psychiatric history with initial 3-week inpatient hospitalisation in his mid-late twenties for decreased need for sleep, impulsive financial spending and hypersexual behaviour. He has experienced elated mood which cycles with periods of depression every few months. He reports a history of two suicide attempts; first in his 20s for overdose of pills and second 2 years ago when he ingested bleach and was subsequently hospitalised. The patient’s medical history is significant for a gunshot wound to his right shoulder which required emergent surgical stabilisation. He subsequently underwent over a dozen reconstructive surgeries to his right shoulder. The patient reports an allergy to aspirin and non-steroidal anti-inflammatory drugs and chart review is notable for anaphylaxis during a previous hospitalisation after the administration of ketorolac. He was ultimately prescribed medicinal marijuana through the state of Delaware for his debilitating chronic shoulder pain. He denied any history of substance dependence with tobacco, alcohol, opiate, benzodiazepines, cocaine or hallucinogens. To note, the patient’s quetiapine and bupropion prescriptions were confirmed at his local pharmacy in Delaware and marijuana card validated through the state of Delaware. In addition, the patient’s aunt provided collateral information which corroborated the patient’s presenting history.

The patient appeared in no apparent distress, normal posture, wearing a hospital gown, thin with no obvious skin lesions. There is obvious right shoulder atrophy and asymmetry with at least six visible scars throughout the anterior shoulder extending to the posterior shoulder blades and upper back. The right shoulder is in fixed position with no range of motion. There is some hypersensitivity to the surgical scars. There are no signs of erythema, fluctuance, effusion or discharge. The patient has a steady gait. The rest of the musculoskeletal examination is with normal range, no rigidity or spasticity. The patient is cooperative and engaged with the examination. The patient
OUTCOME AND FOLLOW-UP
On day 2 of admission, the patient had a dramatic improvement in mood with resolution of his suicidality. In addition, the patient stated that his chronic shoulder pain was controlled with decreased feeling of the dull throbbing pain. By day 3 of the patient’s hospital course, he was doing well, slept throughout the night, increased appetite and participating in group therapy with complete resolution of his suicidal ideation and depressed mood. The patient was discharged on day 3 with instructions to follow-up with his psychiatrist in 1–2 weeks after he completed the quetiapine titration to home dose of 400 mg at bedtime. At 30-day follow-up, the patient reports to be doing well, tolerating his home medications; quetiapine 400 mg at bedtime and bupropion SR 150 mg daily. Denied any depressed mood, suicidal ideation, perceptual disturbances, increased anxiety, decreased need for sleep, insomnia, loss of appetite or other complaints. Chronic pain was described similar to presentation with a pain severity of 2–3/10. PHQ-9 depression questionnaire score of 2. In addition, he reported that 4 days post discharge, he did not use any prescribed marijuana due to tolerable chronic pain. The patient claims to be in the process of undergoing an evaluation for intravenous ketamine infusion in hopes of discontinuing medicinal cannabinoid products.

DISCUSSION
A Cochrane, Google Scholar and PubMed search yielded no literature to indicate the use of ketamine for concurrent suicidal ideation and chronic pain. We present a patient with complex psychiatric and pain concerns; acute suicidality due to bipolar depression secondary to his recent medication non-compliance and chronic shoulder pain on prescribed cannabinoid products which could not be prescribed while the patient was admitted to the inpatient psychiatric unit due to formulary issues and being a non-smoking facility. The patient agreed for voluntary admission for escalation of psychiatric care. However, the patient was averse to receiving any opioids for his chronic pain in fear of random drug screening that would be given by his medical marijuana prescriber. Thus, an effort was made for rapid reversal of the patient’s mood, with anticipation for discharge so the patient could return to self-administration of prescribed cannabinoids. Other alternative pain management options were considered such as non-narcotic medication for neuropathic pain. This was not feasible since gabapentin, pregabalin or antiepileptic drugs need weeks of therapeutic titration. In addition, we thought of rapid re-initiation of the patient’s home dose of quetiapine 400 mg at bedtime but were paused by the package insert recommendations to re-titrator at 50–100 mg/day since this patient had discontinued therapy for in the past 3–4 weeks. The patient’s home dose of bupropion 300 mg/day was also retarded at starting dose of 150 mg as per package insert recommendations.

While administration of ketamine intravenous or intramuscular remains off label in the use for chronic pain and acute on chronic episodes of neuropathic pain, there is widespread literature supporting its use of continuous intravenous infusion with initial dosing of 0.5 mg/kg.

In addition, there is an increasing data suggesting the use of single-dose, intravenous administration of ketamine (0.2–0.5 mg/kg) for the reversal of suicidal ideation while reporting reversal as early as 40 min postadministration and sustained effects lasting up to 7–10 days. There has also been case reports indicating similar outcomes with intramuscular administration.

The patient demonstrated questionable impulse control, fair insight and fair judgment. The patient agreed to a trial of ketamine for acute stabilisation of his bipolar depression secondary to his recent medication non-compliance and chronic shoulder pain on prescribed cannabinoid products which could not be prescribed while the patient was admitted to the inpatient psychiatric unit due to formulary issues and being a non-smoking facility. The patient agreed for voluntary admission for escalation of psychiatric care. However, the patient was averse to receiving any opioids for his chronic pain in fear of random drug screening that would be given by his medical marijuana prescriber. Thus, an effort was made for rapid reversal of the patient’s mood, with anticipation for discharge so the patient could return to self-administration of prescribed cannabinoids. Other alternative pain management options were considered such as non-narcotic medication for neuropathic pain. This was not feasible since gabapentin, pregabalin or antiepileptic drugs need weeks of therapeutic titration. In addition, we thought of rapid re-initiation of the patient’s home dose of quetiapine 400 mg at bedtime but were paused by the package insert recommendations to re-titrator at 50–100 mg/day since this patient had discontinued therapy for in the past 3–4 weeks. The patient’s home dose of bupropion 300 mg/day was also retarded at starting dose of 150 mg as per package insert recommendations.

While administration of ketamine intravenous or intramuscular remains off label in the use for chronic pain and acute on chronic episodes of neuropathic pain, there is widespread literature supporting its use of continuous intravenous infusion with initial dosing of 0.5 mg/kg. In addition, there is an increasing data suggesting the use of single-dose, intravenous administration of ketamine (0.2–0.5 mg/kg) for the reversal of suicidal ideation while reporting reversal as early as 40 min postadministration and sustained effects lasting up to 7–10 days. There has also been case reports indicating similar outcomes with intramuscular administration.

The patient displays normal psychomotor activity, appropriate eye contact and normal speech. Reports depressed mood with appropriate and congruent sad affect. His thought content was with suicidal ideations with plans to overdose on toxic liquids. He denies any homicidal ideation or delusions. His thought process is linear, clear and coherent. The patient is alert and awake to person, place and time. He denies any active perceptual disturbances. His memory, concentration, abstraction, language and vocabulary are grossly normal. His intelligence is noted to be average. The patient complained of chronic dull throbbing pain with occasional burning sensation to his right shoulder with a severity of 5/10.

INVESTIGATIONS
Medical screening labs were ordered and yielded the following: urine screen positive for tetrahydrocannabinoids and negative for phencyclidine, benzodiazepines, cocaine metabolites, amphetamines, opiates, barbiturates, methadone and ethanol; white cell count 8.38x10⁹/μL, haemoglobin 14.8 g/dL, haematocrit 43 %, platelet count 321x10⁹/μL, Na 140 mmol/L, K 3.9 mmol/L, Cl 101 mmol/L, CO₂ 24 mmol/L, blood urea nitrogen 13 mg/dL, Cr 0.93 mg/dL, glucose 88 mg/dL, alkaline phosphatase 111, total bilirubin 0.2 mg/dL, direct bilirubin <0.2 mg/dL, alanine aminotransferase 16 U/L, aspartate aminotransferase 15 U/L, albumin 4.2 g/dL, protein 6.7 g/dL, and thyroid-stimulating hormone 2.64 uIU/mL.

Chest radiograph (posterioranterior, lateral): no acute cardio-pulmonary disease.

Right shoulder radiograph (two view): right shoulder images demonstrate surgical arthrodesis of the glenohumeral joint with two cannulated screws, unchanged in appearance from prior exam. Impression: stable appearance of the right shoulder post arthrodesis.

Patient Health Questionnaire (PHQ-9) for depression: 21 (severe).

TREATMENT
The patient was agreeable for a voluntary psychiatric admission for re-initiation of his psychotropics and monitoring his progress due to safety concerns. The patient reported smoking prescribed medical marijuana every 2 days for his chronic shoulder pain for the past 2 years. Last use was one day prior to admission. However, the patient expressed concern to not being able to smoke during his inpatient course. The patient refused oral acetaminophen or opiates, reporting a history of poor palliation of his chronic pain. In addition, the patient was averse to receiving prescription opiates due to random drug testing that the marijuana prescriber would use to screen. Efforts to contact the medical marijuana prescriber were unsuccessful. Ultimately, the patient agreed to a trial of ketamine for acute stabilisation of his suicidal ideation and temporary pain control while admitted to the inpatient psychiatric unit.

The patient was administered ketamine 30 mg intramuscularly based on a 0.5 mg/kg dosing. The patient was monitored in the Emergency Department with ongoing pulse oximeter and vitals every 15 min for 1 hour. The patient tolerated the administration and was subsequently medically cleared for inpatient psychiatric admission. The patient endorsed to 3–4 weeks of medication non-compliance and a plan was agreed to re-start quetiapine and bupropion the following morning at 50 mg and 150 mg, respectively. The patient complained of chronic dull throbbing pain with occasional burning sensation to his right shoulder with a severity of 5/10.
decision to administer ketamine intramuscular was due to knowledge that the patient would be admitted to the inpatient psychiatry unit in which intravenous access is restricted due to safety concerns. We saw significant improvement in clinical appearance and noted PHQ-9 scores before and after ketamine administration. In addition, the patient’s pain was controlled without the need of alternative pain management intervention during the hospital course.

**Learning points**

- Administration of ketamine while withholding cannabinoid products can be considered for temporary management of chronic pain.
- Administration of ketamine for acute suicidal ideation can be considered for rapid reversal of suicidal ideation.
- Administration of ketamine for patients presenting with suicidal ideation and chronic pain may benefit due to its potential dual treatment of symptomatology.
- Further research is needed to address the use of ketamine in suicidality and chronic pain.

**Contributors**

DB designed data collection tools, monitored data collection for the whole study, wrote the statistical analysis plan, cleaned and analysed the data, and drafted and revised the paper. He is the guarantor. SK, analysed the data and drafted and revised the paper. BB analysed the data and drafted and revised the paper. He is the guarantor. SK, analysed the data and drafted and revised the paper.

**Competing interests**

None declared.

**Patient consent**

Obtained.

**Provenance and peer review**

Not commissioned; externally peer reviewed.

**Open Access**

This is an Open Access article distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: http://creativecommons.org/licenses/by-nc/4.0/

© BMJ Publishing Group Ltd (unless otherwise stated in the text of the article) 2017. All rights reserved. No commercial use is permitted unless otherwise expressly granted.

**REFERENCES**