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## CASE REPORT

## Acute suicidal ideations responsive to hydromorphone

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## SUMMARY

A 72-year-old woman with suicidal ideations for the first time was seen for a follow-up medical visit. Patient diagnosed with bipolar disorder II, chronic complex pain and other complex medical issues. Patient was on long-standing chronic opioid agonist therapy. Patient was prescribed oral hydromorphone to supplement her chronic opioid regimen. Within 24 hours, the patient reported no further suicidal ideations and there were no reported complications. The case provides impetus for further study as to what interventions work best for patients who present with acute suicidal ideations. The case acknowledges cultural issues and implicit biases that can influence medical care and perceptions thereof. Implicit biases may be particularly apparent as they relate to mental health concerns and the use of substances that are susceptible to abuse. The most important clinical lesson reminder may be the importance of adequate documentation and discussion be provided when one prescribes an opioid in a novel way in a special clinical context.

## BACKGROUND

The incidence and prevalence of acute suicidal ideations are significant. Their aetiology is complex and may have multiple contributing factors.<sup>1</sup> Is the patient seriously depressed? Does the patient suffer from pain or other devastating or debilitating illness? Does the patient no longer want to be a burden on family, friends or their larger community?

The common uncertainty as to the aetiology of acute suicidal ideations contributes to the challenges associated with determining the best clinical response. In the state of Washington, there are Designated Mental Health Professionals who are legally responsible to sort out the immediacy and severity of suicidal risk. Financial and other access issues influence their recommendations. Non-clinical variables, in addition to the strictly clinical ones, often influence whether further evaluation, hospitalisation or emergency treatment is mandated.

Clinicians are familiar with the rudiments of suicide risk assessments: presence of a specific plan, means, presence of active steps, history of previous attempts and so on. Other factors worthy of consideration include the patient's medical history and comorbid conditions, accessible resources, laws, financial issues, social factors, 'death with dignity' concerns, and so on. The complexity of considerations and the paucity of relevant clinical trials to

guide care all help to explain the potential clinical challenges in managing acute suicidal ideations.

Although cases of acute suicidal ideations are prevalent, this case is unique in the author's 38-year medical career. This provides further reason to not attribute causality between the intervention provided and outcomes observed. The case does though provide impetus for further study into what interventions may work best for acute suicidal ideations. The case also supports the value of long-standing therapeutic relationships and individualised patient care. It alerts us to possible cultural issues and implicit biases that influence medical models, beliefs and ultimately the delivery of medical care.<sup>2-7</sup> Implicit biases are particularly apparent as they relate to mental health concerns, substance use disorders and the use of psychoactive substances.

The literature involving clinical trials on suicidal ideations is relatively sparse. In 2015, there was a randomised clinical trial looking at intravenous ketamine in the context of suicidal ideations. The results were promising.<sup>8</sup> The authors provide a more formal review of the literature and stated: 'Despite the devastating costs of suicidal behavior to individuals, families and society, very few biological treatments for acute suicidality exist.'

More pertinent to this specific case, there was a randomised controlled trial which evaluated the use of ultralow dose buprenorphine as an efficacious and time-limited treatment for suicidal ideations. It involved a group of patients known to have an opioid use disorder.<sup>8</sup> The article reviewed some of the challenges in effective management of acute suicidal ideations and stresses the need for further research. The authors also recognise the indications for longer follow-up studies that better establish safety, dosing and appropriate patient populations for various treatments.

Different opioids have unique properties, and buprenorphine is known to influence the kappa receptors in addition to the mu receptors. As a partial agonist, buprenorphine's actions on mu receptors is uncommon among opioids. Nonetheless, based on the established effects of opioids on mu receptors,<sup>9-12</sup> a subset of patients have significantly higher affect, particularly when opioid serum levels are abruptly rising.

To evaluate the potential benefits of prescribing opioids to patients with acute suicidal ideations, the design and implementation of a clinical trial is challenging. Clinical trials require explicit inclusion and exclusion criteria. These criteria, the cost of clinical



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trials, and potential ethical and cultural concerns contribute to the challenges. Clinical trials that would comprehensively address and compare interventions for acute suicidal ideations are understandably lacking and not likely to occur soon.

Will a common underlying physiology for suicidal ideations be found? There are likely multiple aetiologies for this complex phenomenon. Until further study and understandings unfold, one is advised to use sound physiological, pharmacological, as well as established behavioural principles.

### CASE PRESENTATION

A 72-year-old married woman reported acute suicidal ideations during a routine follow-up appointment. The setting was a specialised pain management and addiction medicine practice. She was known to the attending physician for decades. The patient had long-term chronic complex pain (migraines, fibromyalgia, etc) and had a bipolar 2 diagnosis. Her bipolar condition was diagnosed when the patient was in her early 50s. The patient had never reported or remembered having had suicidal ideations.

Patient had bariatric surgery approximately 5 years beforehand. Complications from the bariatric surgery included adhesions, ongoing abdominal pain, nausea, anorexia, hypoproteinaemia, progressive weight loss and overall failure to thrive. Despite the best of conservative nutritional support, the patient's failure to thrive warranted consideration of parenteral nutrition.

These medical concerns were in addition to family stressors and other situational stressors. Patient also continued to have pain scores of about 5 out of 10. Patient struggled with moderate recurrent depression over a large part of her adult life.

At the time she presented, patient was prescribed both methadone 30 mg/day in divided doses and a fentanyl patch at 25 µg/hour. The patches had been prescribed to limit concerns of malabsorption and unstable opioid levels. The patient was also taking 5 mg/day of diazepam. The 5 mg daily dose had been recently reduced from a previous established dose of 10 mg/day. The diazepam had been prescribed for anxiety, poor sleep, and nausea the patient commonly experienced following her bariatric surgery.

Patient was also on a regimen of mood regulators including valproic acid, escitalopram and low dose oral ketamine. She took a variety of supplements and was getting extensive behavioural support. Of note, the patient's medical regimen had been relatively stable for a month or more prior to the onset of suicidal ideations. Patient never had any adherence issues related to her medical regimen. Her husband was willing and able to help oversee and dispense medications as indicated.

The patient's dose of opioids was reduced several months previously because of symptoms associated with feeling 'loopy' and poor memory. Because there was no clear aetiology for these symptoms, it was hypothesised absorption and assimilation concerns were contributing to the changes in mentation. Might her digestive issues relate to significant changes in methadone levels as well as other medication levels? Patient's methadone dose was lowered from 60 to 40 mg/day and then to 30 mg/day. Her fentanyl patch had been reduced from 50 to 25 µg/hour. Following these dose reductions, her mental symptoms did improve. The cognitive complaints may have related to the use and dose of opioids, but the differential is significant and includes depression, malnutrition, poor sleep and even low blood sugar. Indeed, after this first episode of suicidal ideations the patient was hospitalised to rule out a stroke. Her symptoms were eventually attributed to hypoglycaemia.

### Prescription

Patient agreed to a trial of a rapid increase in her dose of opioids. The patient knew the prescription for oral hydromorphone was intended to help not only with her pain but to improve her affect and hopefully limit her wanting to die. In addition to the neurophysiological principles discussed below, this patient had already experienced significant benefit from opioids for both her pain management and mood regulation.

The patient received, in addition to her other prescribed medications, a small prescription for hydromorphone (Dilaudid) 2 mg by mouth three times a day as a trial. Within 24 hours, she was dramatically better and suicidal ideations were gone. She reported feeling even better than before she started to have the suicidal ideations. The hydromorphone was soon thereafter tapered, and patient continued to stabilise and improve on her previous regimen.

### TREATMENT

See Case presentation section for details.

### OUTCOME AND FOLLOW-UP

As dramatic and rapid as this patient's recovery was, other sequelae from the intervention warrant review. The patient's primary care provider, a family physician, received patient's progress notes and had concerns about the opioids prescribed to the patient. As a result, the author was reported to the Medical Quality Assurance Commission of Washington State. An extensive investigation was undertaken for alleged unprofessional conduct related to prescribing opioids for depression. The psychiatrist who reviewed the records was concerned about the safety of my prescribing. The psychiatrist was critical that my chart notes lacked a full discussion of the risks and benefits for the 'off-label' use of hydromorphone for depression. In contrast to the therapeutic intent to bring the patient out of a depressed state, the reviewer was concerned because hydromorphone has the potential of triggering a hypomanic episode.<sup>10</sup> Afterwards, the patient has been maintained on stable levels of opioids. No further episodes of suicidal ideations have been reported more than a year out.

Our ability to work with the primary care provider was strained based on the likelihood he reported me to the Medical Quality Assurance Commission. As a result, I chose to become a non-prescribing consultant.

### DISCUSSION

The author is unaware of other comparable case reports regarding acute suicidal ideations responding to hydromorphone. For the sake of brevity, this case report leaves out many details of the patient's complex medical record and history. The patient had a dramatic and favourable response following the first dose of hydromorphone. Suicidal ideations often subside naturally with time, but such dramatic turnarounds as in this case are not common. There is commonly a lack of resources to safely and effectively address acute suicidal ideations. This lack of resources is commonly worse in more rural areas, as was the case here.

A potential dopamine and endogenous opioid deficiency was hypothesised as an important contributor to her acute suicidal ideations.<sup>8-17</sup> Both acupuncture (endorphin release) and methadone had been previously effective in helping to stabilise the patient's mood, manage pain and improve overall mood and functioning. The patient's malnutrition could have contributed to less tyrosine being absorbed, as well as other nutrients being

assimilated less. The lack of absorbed tyrosine may have further compromised dopamine levels.

Relative lower levels of dopamine could also have been present based on the patient's recent and significant reduction in opioid doses. As noted above, the reduction was based on concerns of potential toxicity related to absorption fluctuations in her gut. The patient satisfied Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM IV) criteria for having opiate dependence. This diagnosis is consistent with higher daily morphine equivalents being indicated for optimal outcomes.<sup>18</sup> This patient's long-standing use of opioids was also consistent with significant tolerance to opioids. Her diazepam dose was also stable and at a relatively low dose. These considerations made the possible benefits from a sudden increase in opioids safer than would typically be the case. Speaking to the safety of the hydromorphone prescription, the per cent increase in daily morphine equivalents was approximately 10%–20% depending on Morphine Equivalent Dose (MED) conversion tables used. Distinct differences in the risks associated with short-term and long-term opioid use are confirmed. Furthermore, once tolerance is well established, the risks of adding extra opioids is significantly less.<sup>19</sup>

### Clinical pharmacological considerations

Opioids act as analgesics and have potent anti-anxiety effects. They may also for some increase a sense of well-being.<sup>9–17</sup> Some patients appear genetically more susceptible to the mood elevating and 'energising' effects of opioids. This susceptibility is associated with a greater risk for developing an opioid use disorder. Furthermore, mood elevation and hedonic properties are prominent when opioid serum levels are rising quickly.

Hydromorphone was chosen because it has a high affinity for the mu receptor and when taken orally it often translates into rapid rises in serum levels. Stable levels of opioids, such as seen with a long-term user of methadone generally are not associated with any measurable cognitive defects. As noted in the Background section, extensive laboratory and clinical evidence has supported the role of dopamine in depression and affect regulation.<sup>9–17</sup> Dopamine's role in the nucleus accumbens speaks to its essential role in anticipating reward. Might opioids have a role for antidoting the hopelessness associated with severe depression or acute suicidal ideations? Serious concerns about overdoses and interactions with other medications are highly justified if one were to attempt to treat with hydromorphone the typical patient with acute suicidal ideations.

### Societal/cultural factors

A striking aspect of this case report is the reaction it caused in colleagues. There is common misunderstandings about the risks associated with long-term opioid use. The risks are commonly underappreciated and exaggerated. Colleagues who are unaware of pertinent variables that attenuate risk are understandably likely to exaggerate the risks of opioids. There are also implicit biases associated with chronic opioid use.<sup>2–7</sup> Many, even outside of the addiction field, commonly speak to unjustified moral considerations and stigmas associated with opioid use.<sup>19–23</sup>

There are additional cultural taboos in using addictive and psychoactive substances, especially when they are prescribed outside of Food and Drug Administration (FDA)-approved indications. Our American culture may be the best example of stringent opioid control as reflected in the immense authority

provided to the Drug Enforcement Agency. As a testimony to our cultural proclivities regarding substances and their misuse, less than a hundred years ago, through a constitutional amendment, Americans prohibited alcohol use.

Some colleagues consider FDA off-label prescribing as unduly risky. This belief is held even though the FDA itself formally recognises the inherent limits of its 'guidelines'. The FDA off-label use of substances is professionally indicated, particularly when safer or more efficacious approaches are not readily available or working.<sup>24</sup> The professional liabilities are significant for an American physician who uses a scheduled drug for an off-label use. This is true whether they are being prescribed also for approved indications. In this case, in addition to the acute suicidal ideations, the patient suffered from chronic complex pain and an opioid use disorder.

Opioid prescriptions carry risks both for patients and their communities. The largest liabilities in this case were arguably though not the traditional ones. The professional liabilities arguably related to cultural factors were significant to the prescriber, as they often are for patients. *When using addictive substances in novel ways, the need for adequate documentation and discussion of risks and benefits is warranted.*

### CONCLUSION

A formal clinical trial to validate a potential role of opioids in managing suicidal ideations would be helpful. There is likely a subgroup of patients, as was the case here, who would greatly benefit particularly if associated risks were minor. Formal studies to assess and help better acknowledge the stigma and prejudices associated with chronic opioid agonist therapy would likely enhance professional objectivity.

### Patient's perspective

I am grateful for the care received. I hope this case helps others. As a published expert of Charles S Peirce's philosophical writings, I also appreciate the role of abductive reasoning in the care received.

### Learning points

- ▶ Further clinical studies are indicated to improve outcomes for both acute and chronic suicidal ideations.
- ▶ Based on the clinical pharmacology of opioids, there is probably a subset of patients whose suicidal ideations could be safely and effectively treated by an opioid.
- ▶ Cultural determinants influence professional medical opinions and care.
- ▶ Individualised care supported by a well-established therapeutic relationship can greatly contribute to safe and effective medical care.
- ▶ Clinicians who prescribe addictive substances for novel uses must be prepared for misunderstandings and concerns when the documentation or discussion of risks and benefits is not considered adequate.

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