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The Use of a Subanesthetic Infusion of Intravenous Ketamine to Allow Withdrawal of Medically Prescribed Opioids in People with Chronic Pain, Opioid Tolerance and Hyperalgesia: Outcome at 6 Months

To the Editor,

The problems of opioid tolerance [1], hyperalgesia (and other side effects of prescribed opioids), and the difficulties involved with opioid withdrawal, are rapidly becoming an enormous health problem. Ketamine, in addition to the potential to reduce pain for some weeks or months postinfusion [2], has been shown to ameliorate symptoms of opioid withdrawal [3].

Patients with chronic pain taking medically prescribed opioids who had developed opioid-related tolerance and probable hyperalgesia were admitted for 5 days of subanesthetic infusion of ketamine to assist in complete withdrawal of opioids.[1] The aim was to withdraw all opioid medication for a period of at least 2 weeks to allow tolerance to minimize and review progress over 6 months. Note that it is essential for patients and prescribers to realize that the patient's tolerance will return to that of "opioid naïve" patients once opioids have been withdrawn for 2 weeks, i.e., if opioids are restarted it must be at a low dose to avoid risk of overdose.[2]

The patients were not treated as "research subjects" but as individuals—given the interaction between chronic pain, opioid withdrawal, the potential side effects of ketamine, and the selection bias of long-term patients whose opioid treatment was failing, the aim was to see how effective this treatment was in achieving the goal of long-term (in this report 6 months) complete cessation of opioids.

The patients included a man with a large cervical syrinx following insertion of Harrington rods as a child, a woman with relapsing polyarthralgia, several patients with abdominal pain following multiple operations, one patient with arachnoiditis, and patients with ongoing pain having had several back operations—common features included a pain history longer than 5 years, escalating opioid doses with no improvement of pain and function, multiple trials of medications during their illness, and lack of other therapeutic options.

Fifteen consecutive patients were sent a questionnaire 6 months post-ketamine infusion; 11 responded. Eight of the 15 patients had attended pain management programs prior to detoxification. None of the patients had dorsal column stimulators or pumps.

The questionnaire involved patients scoring five questions on an analogue scale from 0 (disagree) through to 5 (strongly agree). Patients were asked whether they had any further comments regarding the treatment, and to give a list of current medications (Table 1).

The responses show that:

- While having the infusion was not pleasant, it was tolerated by most.
- The patients felt better initially.
- Eight of 11 continued to feel better at 2 months.
- At 6 months, three of the patients continued to feel well and were not taking opioids.

Adverse events:

- One patient developed hypomania at completion of the infusion requiring psychiatric consult. Bipolar disorder was thought probable (there was a past history of major depressive disorder). Discharge was delayed by 7 days and outpatient psychiatric follow-up continued for 3 months with normalization of mood.
- One patient developed delirium 24 hours after discharge and presented to A and E twice over 48 hours.

Table 1 Raw data of questionnaire responses

	0	1	2	3	4	5
I found the ketamine infusion easy to tolerate.	1		3	3	1	3
I found that the ketamine infusion significantly reduced my pain.	1	3			4	3
I felt much better in the month after the infusion.	2			1	1	7
I feel much better 6 months after the infusion.	6			1		4
I have remained off morphine like medications.	8			0		3

The delirium resolved fully by 5 days postdischarge without specific treatment. No other cause was found.
- None of these patients required alteration of the protocol because of changes to blood pressure, oversedation, or poorly controlled pain.

In conclusion, the initial response to ketamine reduced with time. This was a patient cohort in distress with few treatment options. We will endeavor to improve patient selection/outcome prediction but this management may have a place for some patients.

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Notes

1. Briefly, the infusion began with 2.5 mL/h of ketamine, incrementally rising to a maximum of 40 mL/h—the protocol allows for alteration to infusion rates pending observation and side effects. Diazepam and buscopan were used to assist in minimizing withdrawal symptoms; paracetamol and physical methods were used to assist with pain control; regular reassurance was also given.

2. "Most opiate overdose deaths occur in people who have just withdrawn or detoxed. Because withdrawal reduces . . . tolerance to the drug, those who have just gone through withdrawal can overdose on a much smaller dose than they used to take". http://www.nlm.nih.gov/medlineplus/ency/article/000949.htm.

References

1 Ballantyne JC, Mao J. Opioid therapy for chronic pain. N Engl J Med 2003;349(20):1943–53.

2 Visser E, Schug SA. The role of ketamine in pain management. Biomed Pharmacother 2006;60:341–8.

3 Jovaisa T, Laurinenas G, Vosylius S, et al. Effects of ketamine on precipitated opioid withdrawal. Medicina (Kaunas) 2006;42(8):625–34.