

## Low-Dose Sublingual Ketamine for Chronic Pain or Depression

By Lucinda Grande, MD

Formerly depressed chronic pain patients have found themselves doing jumping jacks in the living room, hauling heavy garden hoses, washing windows, polishing the leather seats in their car, and renewing an interest in reading which they hadn't had for years. Two people told me they felt like they could go out and run a marathon. Neither one did it, though - one was on dialysis for kidney failure and the other had bad arthritis in both knees.

These are experiences of my patients using a very low dose of oral ketamine for chronic pain. Patients who use it for depression (with or without pain) can feel relief within a few hours. While some patients do not get symptom relief or have unacceptable side effects, most patients are very happy with it.

**Background:** Ketamine is a drug used most commonly as an intravenous anesthetic for human and veterinary surgery. It was developed in 1962 and was first used for American soldiers injured in Viet Nam. At high doses it puts people into a dreamlike, semi-conscious state where they can undergo surgery without feeling any pain. The dose I usually prescribe for chronic pain is about 2% of that used for anesthesia.

**Opioids.** Ketamine seems to have particular benefit for people who have had exposure to high dose opioid medications, either recently or a long time ago. I believe this is because it reverses the exaggerated experience of pain that occurs in people who use opioid drugs frequently, especially at high doses. Nerve cells that have repeatedly been exposed to opioids become over-excitably, responding more quickly and powerfully to a painful stimulus. Ketamine quiets down these over-excited nerve cells.

**Depression.** There are now quite a few articles published in the psychiatric journals about high dose intravenous ketamine being used to rapidly reverse depression in patients that didn't improve with other treatments. Mood is lifted often within hours. I have not seen any published reports of low dose oral ketamine used stably for long periods for treatment of depression - but a number of my own patients have experienced this.

**Reversal of Stress.** Yale scientists recently did some experiments that show that ketamine's remarkable effect on depression seems to be a result of its action inside nerve cells. It unleashes a cascade of chemicals which results immediately in new connections to other nerve cells. This same cascade of chemicals is known to be clogged up by stresses of all kinds. It seems that ketamine may be reversing some of the destructive effects of stressful events that have occurred over a lifetime throughout the brain and spinal cord. I suspect that this same action inside nerve cells may be part of the reason ketamine is so helpful for chronic pain, which is often suffered by people who have had severe life stressors.

**Oral or Sublingual Use.** While intravenous ketamine can only be given to patients in the hospital under the direction of an anesthesiologist, the drug can be used safely by patients either in or out of the hospital when swallowed or placed under the tongue. It has to be specially prepared by a compounding pharmacy, as it is currently not made by drug companies in a form for oral or sublingual use.

**Dosing.** For chronic pain and depression, I usually start people at a dose equal to about 1/20<sup>th</sup> of the normal anesthetic dose. It is taken once or twice daily and increased to achieve maximum benefit. Those who benefit start feeling the results after a few hours, and feel continuing improvement over days to weeks. I had one patient who immediately had complete relief of her decades-long hand pain 30 minutes after swallowing the first dose, but this was very unusual. People should not expect immediate relief - it seems to act more over time.

**Precautions.** Ultra-low dose ketamine is safe for people with any medical condition except uncontrolled high blood pressure or heart rhythm problems, high intracranial pressure (usually only an issue for patients in the hospital), severe glaucoma, or psychosis such as in schizophrenia. The only side effect to be expected from ketamine is hallucinations or a feeling of unreality, but that normally doesn't occur at this extremely low dose. Lowering the dose or the number of doses each day seems to take care of that.

Effects from long-term daily use of low-dose ketamine are unknown. Among long-term high-dose recreational users, some individuals developed bladder problems including ulcers. Individual people may have their own unique side effects, but there is no reason to expect anything really dangerous or life threatening, especially in comparison with opioid pain medicines, which slow or stop breathing and were responsible for the deaths of about 20,000 people in the U.S. in 2016. If someone swallowed a week's supply of ketamine at once, as with many other prescription medications, they would likely end up in the hospital or worse. Please don't try that.

Please do not drive a motor vehicle for the first hour after you take a dose, until you have experience at that dose level. If you are currently on a high dose opioid medication, it would be wise to reduce the opioid dose when starting ketamine. You may become more sedated than usual from the opioid when the high dose is no longer needed for pain.

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