

MUCH HAS BEEN LEARNED ABOUT KETAMINE infusions since my article published in the Spring 2006 *RSDSA Review* that provided an overview of ketamine infusion therapy.¹ Since initiating outpatient ketamine infusion protocols in my office in the Fall 2004, I have treated close to 100 patients. All of them had a diagnosis of complex regional pain syndrome (CRPS), had been seen by

to shut off the N-methyl-D-aspartate (NMDA) receptors in the brain over time, as opposed to at a single session. Our experience shows that single doses of ketamine do little to improve the patient's condition, while repeated doses of ketamine have worked very well to relieve sympathetic dysfunction. Using protocols established by Robert J. Schwartzman, MD, at Hahnemann

both. Research is ongoing at the Drexel University College of Medicine, using a double-blind placebo-controlled study to determine the efficacy of ketamine for CRPS², and the preliminary results have been extremely promising.

There has been limited use of inpatient ketamine infusion therapy. This protocol consists of a five-day treatment with slowly-accelerating dosage, usually reaching a maximum of 40 mg to 50 mg per hour over a four- to five-day time frame, with gradual weaning on the fifth day. Obviously, an accelerated dose of ketamine can be given in this fashion, leading to higher blood levels and further improvement. This does not preclude the necessity of outpatient "boosters" at varying intervals following the patient's discharge from the hospital.

Update on Low-dose Ketamine Infusions

By Philip Getson, DO



numerous physicians, and had undergone a variety of treatments, including medical therapy, physical therapy, occupational therapy, sympathetic blocks, spinal cord stimulators, and intrathecal pumps, before beginning ketamine infusions. In all cases, the syndrome was out of control, and we decided to try intravenous ketamine.

Physicians have different protocols for the administration of ketamine, but we have learned over these last four and a half years that the **quantity** of ketamine is less important than the **duration** of the treatment regarding the ability

University Hospital in Philadelphia, with whom I have collaborated on many cases, all patients begin with a 10-day "start-up" of ketamine followed by accelerating doses. The average maximum dose is 200 mg to 250 mg ketamine per treatment, infused intravenously over a four-hour time frame. In addition to ketamine, other medications, including midazolam HCl (Versed[®]), ondansetron HCl (Zofran[®]), alprazolam (Xanax[®]), diazepam (Valium[®]), and butalbital (Fioricet[®]), are used as needed for symptom relief. Vital signs are monitored electronically, while the patient's condition is overseen by an infusion nurse. Detailed information is taken regarding allodynia, response to general pain, sweating, flushing, etc.

Over this four and a half-year time frame, we have concluded that ketamine is currently the best available outpatient treatment for refractory and difficult cases of CRPS. Between 66% and 80% of patients have shown an overall improvement, which is measured by an increase in functional capability, decrease in medication, or a combination of

Ketamine therapy has provided significant success not only in the reduction of pain, allodynia, and other well-recognized forms of sympathetic dysfunction, but also for improving patients who suffer from the sequelae of CRPS, such as neurogenic bladder, gastropoiesis, and neurodermatitis, the most common dermatologic manifestation of CRPS. The beneficial effects of ketamine have proved far reaching.

Ketamine in the Literature

There have been many articles written regarding ketamine. The 2003 review article by Hocking and Cousins³ suggests that "the efficacy for ketamine for treatment of chronic pain is moderate to weak." Clearly our statistics and experience have shown this not to be the case.

In the June 2007, *Pain: Clinical Updates* from the International Association for the Study of Pain (IASP)⁴, it was suggested that "complex regional pain syndrome may respond to intravenous ketamine, topical ketamine ointment, or epidural

infusion.” Our ongoing treatments have shown that the word “may” for intravenous ketamine should be replaced by “do,” as it is clear that CRPS does respond to intravenous ketamine infusion. However, I have not found topical ketamine ointment or epidural infusion to be particularly helpful at this point in time.

A 2005 Goldberg et al study⁵ suggested mixed results with outpatient ketamine, but again, ongoing treatments and sheer numbers of patients have suggested that

modalities of treatment have been tried and failed, we have been successful in obtaining insurance authorization from many insurers. Aetna US Healthcare is reviewing the payment of this treatment, as they are currently the only major insurer denying payment.

Unfortunately, this is not a “cure.” Currently, patients who have been labeled “cured” all received high-level comatose doses of ketamine in either Germany or Mexico. However, the low-

I advise women of childbearing age to stop ketamine therapy 30 days before conception, although there is no indication of greater residual risk than with any other medication. Finally, it should be noted that no patients have been eliminated from the treatment protocols due to unmanageable side effects.

As with any therapeutic measure, more information will be necessary and will be obtained over time. We continue to make adjustments in the protocols in an effort to produce better outcomes.

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In cases where all “conventional” modalities of treatment have been tried and failed, we have been successful in obtaining insurance authorization from many insurers.

their original data, on a small patient population, was incorrect. It is entirely possible that their patient population was too small, or the dosage of ketamine too low, as their maximum outpatient dose was 100 mg ketamine.

All of this notwithstanding, it is clear that the infusions are helpful. My 2006 article¹ maximized the outpatient dose at 100 mg ketamine, and currently, we are at 2 to 2.5 times that dose with an inherent safety factor being maintained. Certainly some patients suffer side effects to include mild hallucinations (which are extremely rare), nausea, headache, and anxiety. All of these are dose related and easily controlled by adjunctive medication.

Outcomes

It is clear that patients with CRPS who have received ketamine have made significant strides in a positive direction. Insurers have been more understanding regarding payment for ketamine. In cases where all “conventional”

dose outpatient infusions are clearly beneficial and should be considered in individuals whose treatment with more “conventional” modalities has caused limited improvement.

A comprehensive ketamine treatment program must include other treatment modalities. A good diet, exercise, physical and occupational therapy, and an overall attempt at a healthier lifestyle all play a positive role in improving the patient’s health. All of these modalities, and a reduction of pain medications, specifically opioids, should be incorporated into the overall treatment regimen.

We have been treating individuals of all ages. Recently a 14-year-old boy in Michigan underwent hospital-based infusion, followed by outpatient treatment using our established protocols. Reportedly, the treatment was approximately 80% to 90% successful in diminishing his pain and helping him to recover a more normal lifestyle.

References

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