

CURRENT THERAPEUTIC RESEARCH

VOLUME 71, NUMBER 6, DECEMBER 2010

Letter to the Editor

Dear Dr. Walson:

With great interest we read the paper by Kang et al¹ on the analgesic effects of ketamine infusion therapy in Korean patients with neuropathic pain.

Since 1994, various articles based on case reports, pilot studies, and clinical trials have documented the value and tolerability of ketamine for the treatment of neuropathic pain states.²

Due to its unique mechanism of action, ketamine is a highly interesting drug for treatment-resistant neuropathic pain syndromes, administered via various routes. Long periods of decreased pain can be triggered by relatively short courses of infusion. Dutch anesthesiologists found that complex regional pain syndrome type 1 (CRPS-1) patients with severe pain treated for 4 days with a continuous infusion of low-dose S-ketamine (N = 30) had a clinically relevant and statistically significant reduction in pain lasting for up to 11 weeks compared with patients receiving placebo ($P < 0.001$). However, one of the troublesome clinical aspects of treatment using intravenous ketamine is the reemergence of pain after some weeks and, therefore, the necessity to readminister treatment.³

Various topical racemic ketamine formulations, such as gels, ointments, and creams, in a dose range from 0.25% to 10.0%, have been compounded, and the efficacy and tolerability has been documented in a number of papers.⁴⁻⁷ In a 2009 double-blind, placebo-controlled, crossover study, ketamine 10% in pluronic lecithin organogel was associated with alleviating allodynia in CRPS-1 patients without detectable blood levels of ketamine.⁸ This might suggest a topical mechanism of action, or a suboptimal dose regimen.

In our clinic, we gained experience prescribing 10% racemic ketamine cream in CRPS-1 patients with treatment-refractory pain. Anecdotally, we have noted significant pain reduction with this intervention without additional adverse effects, including without negative effects on blood pressure. Well-designed studies evaluating the use of a topical 10% ketamine cream are necessary, as such treatment may be more easily tolerated and less expensive than ketamine infusion therapy.

Jan M. Keppel Hesselink, MD, MSc, PhD
David J. Kopsky, MD
Institute for Neuropathic Pain
Soest, The Netherlands

REFERENCES

1. Kang JG, Lee CJ, Kim TH, et al. Analgesic effects of ketamine infusion therapy in Korean patients with neuropathic pain: A 2-week, open-label, uncontrolled study. *Curr Ther Res Clin Exp*. 2010;71:93-104.
2. Backonja M, Arndt G, Gombar KA, et al. Response of chronic neuropathic pain syndromes to ketamine: A preliminary study. *Pain*. 1994;56:51-57.

3. Sigtermans MJ, van Hilten JJ, Bauer MC, et al. Ketamine produces effective and long-term pain relief in patients with Complex Regional Pain Syndrome Type 1. *Pain*. 2009;145:304–311.
4. Gammaitoni A, Gallagher RM, Welz-Bosna M. Topical ketamine gel: Possible role in treating neuropathic pain. *Pain Med*. 2000;1:97–100.
5. Quan D, Wellish M, Gilden DH. Topical ketamine treatment of postherpetic neuralgia. *Neurology*. 2003;60:1391–1392.
6. Ushida T, Tani T, Kanbara T, et al. Analgesic effects of ketamine ointment in patients with CRPS type 1. *Reg Anesth Pain Med*. 2002;27:524–528.
7. Crowley KL, Flores JA, Hughes CN, et al. Clinical application of ketamine ointment in the treatment of sympathetically maintained pain. *IJPC*. 1998;2:122–127.
8. Finch PM, Knudsen L, Drummond PD. Reduction of allodynia in patients with complex regional pain syndrome: A double-blind placebo-controlled trial of topical ketamine. *Pain*. 2009;146:18–25.