

MAY 16, 2017

## Survey on IV Ketamine for CRPS Underscores Need for Consensus Protocols



San Diego—A survey of IV ketamine infusion regimens for the treatment of complex regional pain syndrome (CRPS) highlights what many clinicians have observed anecdotally—namely, the need for consensus protocols when using ketamine to manage CRPS pain.

According to the study’s authors, protocols varied widely by provider and institution, and data on adverse events in both outpatient and inpatient settings were “extremely limited.”

“Data from this study demonstrated significant respondent variability of treatment regimens utilizing IV ketamine for the treatment of CRPS in both adult and pediatric populations in outpatient and inpatient settings,” said Jijun Xu, MD, PhD, an anesthesiologist specializing in pain management at the Cleveland Clinic, in Ohio. “Clearly, there is a need to develop treatment protocol standards.”

As Dr. Xu reported at the American Society of Regional Anesthesia and Pain Medicine’s 2016 Annual Pain Meeting (abstract 2918), IV ketamine has been used increasingly to treat CRPS, but no standardized treatment protocol currently exists (*CNS Drugs* 2012;26:215-228; *Anesth Analg* 2016;122:843-856).

As an initial step toward developing a consensus recommendation, Dr. Xu and colleagues looked to obtain data about the various treatment protocols being used around the world. “We want to improve the quality of care and communication in the treatment of CRPS,” Dr. Xu said.

**CRPS Treatment With IV Ketamine** Between July and August 2016, the researchers distributed the questionnaire to a list of international providers using SurveyMonkey, an online survey service. Targeted respondents included medical practitioners with expertise in the treatment of CRPS patients with IV ketamine.

The survey addressed respondent demographics, diagnostic criteria, treatment volume, IV ketamine infusion protocol for adult and pediatric patients in both outpatient and inpatient settings, outcome measure utilization and adverse effects of treatment.

The researchers collected data from 313 respondents from eight countries. Practice specialties included anesthesiology (n=56), physical medicine and rehabilitation (n=8), orthopedics (n=6), neurology (n=5), psychiatry (n=1) and other specialties (n=28).

According to Dr. Xu, the mode of the infusion duration was four hours in the adult outpatient setting. The mode for the number of sessions was three for induction and two for “boosters.” The mode for frequency of repeat outpatient adult infusions was monthly. The mode for frequency of sessions in a round of outpatient adult treatment was daily.

As expected, Dr. Xu said, the range of IV ketamine infusion dose was “very variable” in the adult outpatient setting (n=37), from 0.3 to 10 mg/kg per session to 50 to 2,000 mg per session.

In the adult inpatient setting (n=8), the range of dose was 0.35 to 5 mg/kg per session and 40 to 600 mg per session.

### **Few Data on Pediatrics**

The researchers received very few responses for pediatric questionnaires, especially in the inpatient setting, Dr. Xu reported.

The range of IV ketamine infusion dose in the outpatient pediatric setting (n=3) was 0.35 to 1.4 mg/kg per session and 400 to 1,000 mg per session.

Finally, the incidence of adverse events in either outpatient or inpatient settings was predominantly “not applicable” or “less than 5%.” Providers who responded, however, indicated that hallucinations, vomiting and headache were the most common side effects of treatment.

Dr. Xu’s team is continuing to analyze the data for a correlation between infusion times or days and patient outcomes.

“Based on these results, we’ve tried to generate a possible consensus protocol so that in the future, when we design a study, we can compare outcomes between centers,” Dr. Xu said.

Charles Berde, MD, PhD, division chief of pain medicine and pain treatment service at Boston Children’s Hospital and professor of pediatric anesthesia at Harvard Medical School, in Boston, said his institution has been reluctant to use ketamine infusions as routine pediatric care because “most children with CRPS can be made better by conservative treatment and because literature support is lacking.”

Dr. Berde said, “Our center has treated 1,400 pediatric CRPS patients in the last 30 years, and we don’t use this much. We do overwhelmingly cognitive-behavioral therapy, physical therapy, desensitization, and for really refractory patients or patients with dystonia, short-term peripheral perineural infusions. We use ketamine infusions for people with cancer.”

He added, “I think it ought to be studied. It’s an interesting, complicated therapy that needs more research.”

—Chase Doyle