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Developing a Ketamine Infusion Protocol to Treat Complex Regional Pain Syndrome

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Executive Summary

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Introduction of the Problem

Patients who suffer from complex regional pain syndrome (CRPS) live with a disorder that causes severe pain, which is often chronic and resistant to conventional therapy (Correll, Maleki, Gracely, Muir, & Harbut, 2004). One treatment that has shown to be effective in reducing pain scores in patients with chronic CRPS is a multiple day infusion of ketamine (Sigtermans et al., 2009). Developing a protocol for the treatment of CRPS with ketamine infusions can reduce pain scores in patients with CRPS.

Literature Review

Only two randomized controlled trials (RCTs) evaluating intravenous ketamine for CRPS have been conducted. Sigtermans et al. (2009) conducted a double-blind randomized placebo-controlled parallel-group trial in which sixty CRPS patients received a 4.2-day intravenous infusion of ketamine or placebo titrated to effect and showed that the patient group given ketamine had significantly lower pain scores than the placebo group. The lowest pain score was at the end of the first week, ketamine 2.68 ± 0.51 and placebo 5.45 ± 0.48 (Sigtermans et al., 2009, p. 304).

Schwartzman et al. (2009) performed a double-blind placebo controlled study evaluating intravenous ketamine for treating pain from CRPS and found that intravenous ketamine administered in an outpatient setting resulted in statistically significant ($p < 0.05$) reductions in multiple pain parameters. The patients treated with ketamine had a 27% decrease in pain scores, while the placebo group saw a 2% decrease. The patients

were given a four hour infusion on an outpatient basis for ten days, with a maximum infusion rate of 0.35mg/kg/hr not to exceed 25mg/hr; clonidine and versed to deal with potential side effects; and were followed for three months post-treatment (Schwartzman et al., 2009). Additional RCTs are needed to further study the effectiveness of using intravenous ketamine to treat CRPS.

A systematic review performed by Azari et al. (2012) yielded seven observational studies and nine case reports examining intravenous ketamine for CRPS. The nine case reports show that ketamine is effective in treating the pain of CRPS, although unsuccessful trials may be underreported, which makes it difficult to assess the efficacy of this treatment by examining case reports (Azari et al., 2012). Correll et al. (2004) performed a retrospective analysis of 33 patients receiving ketamine infusions to treat pain associated with CRPS. 54% of the patients were pain free three months after a single infusion and 31% remained that way six months post-infusion. Further, 58% of 12 patients who received a repeat infusion had retained their pain relief at one year post-infusion, and 33% were pain free greater than three years post-infusion (Correll et al., 2004). Additionally, one prospective study showed significant reduction in pain scores following 4-hour infusions performed for 10 consecutive days, as well as the benefit of increased mobility in the affected limb (Azari et al., 2012; Schwartzman, Alexander, & Grothusen, 2014).

There appears to be no consensus on dosing or duration of intravenous ketamine infusions to treat CRPS. Durations reported varied from a few hours up to ten days, doses varied from 0.35mcg/kg/hr to a high dose of 7mg/kg/hr, and titration techniques varied from set intervals to titrating to effect of analgesia or feeling of inebriation (Azari

et al., 2012). Side effects include feelings of inebriation, dizziness, nausea, headache, lightheadedness, hallucinations, psychotomimetic effects, hypertension, and elevated liver enzymes (Connolly et al., 2015; Correll et al., 2004). All side effects were reported to resolve upon termination of ketamine infusion; there were no cognitive side effect at six weeks post-treatment, any elevated liver enzymes returned to baseline within two months, and hallucinations or psychotomimetic effects were largely controlled with the concurrent administration of intravenous midazolam (Azari et al., 2012; Connolly et al., 2015). A potential side effect is neurotoxicity from prolonged ketamine infusion, as evidenced in the brains of rats that develop Olney's lesions. This potential side effect can be prevented by concurrent administration of clonidine, and Olney's lesions have never been documented in a human (Schwartzman et al., 2014).

IRB information

The institutional review board at Southern Illinois University Edwardsville determined that this project was not considered research and therefore did not require review by the board.

Project Methods

Setting and sample population. The project setting was the pain clinic at Passavant Area Hospital in Jacksonville, Illinois. The providers include Certified Registered Nurse Anesthetists (CRNAs), anesthesiologists, Registered Nurses (RNs) in the pain clinic, and pharmacy staff.

The implementation of this project was carried out through an inservice for anesthesia providers at Passavant Area Hospital in Jacksonville, IL. The presentation was then evaluated using a short survey, which was filled out by the audience

anonymously. The audience included four Certified Registered Nurse Anesthetists and one Physician Anesthesiologist. All five individuals returned a completed survey. The survey consists of five questions on a Likert scale ranging from 1 (strongly disagree) to 5 (strongly agree). The survey assessed if this project was informative, if it improved the audience's understanding of CRPS, if it helped them to understand the concept of using ketamine to treat CRPS, the contraindications and side effects, and if the project helped them to feel comfortable implementing a ketamine infusion protocol at their workplace.

For the questions on the survey numbered 1 through 5, the responses were 4.6, 4.4, 4.8, 4.6, and 4.4, respectively. Based upon the responses, it is reasonable to assume that this project was effective in educating anesthesia providers on the topic of using ketamine infusions to treat CRPS. The protocol can be changed to fit the needs and constraints of a facility.

Purpose and goals. To promote the use of ketamine to treat patients with CRPS.

To provide alternative options for treatment of CRPS.

To educate providers in the use of an evidence-based protocol for the administration of ketamine to treat CRPS.

Resources/supports and risks/threats. Potential benefits of project: anesthesia providers at Passavant Area Hospital will have a better understanding of risks and benefits in the administration of ketamine to treat CRPS patients, and the potential for a new service to be provided for the patients in the community suffering from CRPS. Weaknesses and threats include: the protocol may be denied by the administration of the hospital and the staff may fail to properly utilize the protocol.

Impact on Practice

The immediate impact at the clinical site was the anesthesia staff being more informed on the use of ketamine to treat CRPS. The predicted long-term impact is that the clinical site starts to offer the service and that patients suffering from CRPS gain relief from their disease. This project can be replicated easily by modifying the protocol to match a facilities needs and constraints and by presenting it to the anesthesia staff. This project can be expanded upon by collecting data on the actual administration of the protocol and evaluating its effectiveness.

Conclusions

This project shows that presenting a protocol via an educational presentation can effectively convey the concept of using ketamine infusions to treat CRPS. A literature review reveals the need for more studies evaluating the effectiveness of such a protocol, and this project can be expanded upon to strengthen the body of evidence available to practitioners.

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