Does increasing the duration of low dose outpatient ketamine infusion improve outcomes in chronic neuropathic pain? A pilot study under patients undergoing repeat ketamine infusions.

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INTRODUCTION

Ketamine, an N-methyl-d-aspartic-acid (NMDA) receptor antagonist, has re-emerged in the anesthesiologist’s arsenal as a drug with diverse utility in pain management. The drug has also proven effective in the treatment of depression, PTSD, asthma and peripheral pain (1). Outpatient ketamine infusions have been shown to provide relief in patients with chronic neuropathic pain (2) by blocking central NMDA receptors and by preventing central sensitization and hyperalgesia (3, 4). Long-term benefits will require further study given ketamine’s psychotropic effects and abuse potential (1). At our institution, patients have demonstrated improvement in mood and ambulation after treatment with four-hour ketamine infusion at subanesthetic doses. In this pilot study, we compared four and five-hour outpatient ketamine infusions in the same patient to determine if a longer duration of infusion or a higher daily ketamine dose improved pain scores and quality of life (QOL) outcomes.

MATERIALS AND METHODS

With IRB approval, we examined QOL outcome measurements in patients treated at the George Washington University Spine and Pain Center with subanesthetic ketamine infusions. Patients included in our study initially received three consecutive days of four-hour ketamine infusions followed by three consecutive days of five-hour ketamine infusions several months later. The ketamine doses ranged from 0.2mg/kg/hr to 1mg/kg/hr. At both four and five-hour infusion sessions, patients completed a Brief Pain Inventory (Figure 1) to assess the impact of chronic pain on their quality of life (overall daily pain score, general activity, walking, work, relationships with others, sleep, and enjoyment of life). This survey was completed both before receiving ketamine infusion and two to four weeks after ketamine infusion in follow-up. The patients ranked the impact of pain on QOL from a scale of zero (no impact) to ten (severe impact). Overall change in QOL both before and after treatment was evaluated. Four covariates (age, sex, race, and pre-treatment score) were used in order to evaluate any change in QOL due to demographics. To compare scores between four and five-hour infusion sessions, a paired two-tailed t-test and multivariate generalized estimating equations were used.

RESULTS

Ten patients underwent three consecutive days of four and five-hour ketamine infusions. In all cases (every day and for both timing strategies), pain score fell significantly from pre-infusion to post-infusion. This result remained significant after adjusting for patient covariates (p<0.005). Overall, our results showed that patients undergoing four-hour ketamine infusion had higher pain scores compared to patients undergoing five-hour ketamine infusion. This result was statistically significant (p<0.05). In addition, we found that pain scores were higher on day 1 and 2 compared to day 3. This result was also statistically significant (p<0.001 and p=0.055 for day 1 and 2 respectively). However, our results comparing pain reduction in the four vs. five-hour infusion were not statistically significant (p=0.27), indicating that the pre vs. post-infusion pain reduction was similar in patients receiving four and five-hour ketamine infusion. Similarly, although patients reported greater improvement in certain QOL outcomes (level of activity, mood, work, relationships and sleep) after five-hour infusion compared to four-hour infusion, these results were also not statistically significant. Finally, no adverse side effects were reported other than mild nausea and headache in some patients.

DISCUSSION AND CONCLUSION

This study demonstrates that ketamine infusion leads to a reduction in pain, consistent with previous studies that have shown that patients with chronic pain syndromes experience an improvement in their pain with ketamine infusion. In addition, patients reported improvement in activity level, mood, work, relationships and sleep after ketamine infusion. Increasing the duration of the infusion allowed a higher total daily dose of ketamine while keeping the infusion rate at subanesthetic levels. However, our study did not show a significant difference in pain score reduction pre vs. post-infusion when comparing four and five-hour ketamine infusions. It is possible that the effects of ketamine may not be entirely dependent on total daily doses. Our study is a pilot project limited by a small number of subjects. Studying a larger patient population may be helpful in determining whether an increase in the total daily dose of ketamine significantly improves outcomes in chronic neuropathic pain.

REFERENCES