

Intravenous Ketamine Usage in Treatment of Refractory Neuropathic Testicular Pain

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Background

- Chronic orchialgia is defined as 3 months of intermittent or constant testicular pain
- Accounts for 2.5-5% of all urological consults, representing a significant source of urological pain
- Classified as:
 - Nociceptive: dull, aching pain; associated with an organic cause
 - Neuropathic: burning, hyperesthesia/hypoesthesia, radiating
- Frequently worked up with ultrasonography and urinalysis and culture for organic causes
- Between 25-50% of cases without a specific etiology and considered idiopathic chronic orchialgia; thought to be of neuropathic origin
- No established guidelines for treatment for pain of idiopathic origin
- Neuropathic pain is theorized to be the result of peripheral or central sensitization of neural pathways
- Ketamine exerts its anesthetic and psychomimetic effects via multiple pathways
 - Noncompetitive antagonist of phencyclidine binding site of *N*-methyl-D-aspartate (NMDA) receptors in the CNS
 - NMDA has a role in cognition, chronic pain, opioid tolerance and mood regulation; principal receptor in central sensitization
 - Possible role for ketamine “resetting” the CNS and reversing effects of central sensitization in neuropathic pain
- Consensus guidelines on usage of intravenous ketamine for chronic pain stratify recommendations by condition and provide guidance to assess for successful response to therapy
 - Moderate evidence to suggest effectiveness in CRPS; weak evidence for other neuropathic conditions
 - Recommended infusion rate of 0.5-2.0 mg/kg/hr with a minimum dosage of 80 mg
 - Positive responses to treatment include ≥30% reduction in pain score or comparable measures

Case Report

The patient is a 68-year-old male with a history of chronic back pain, HIV, and diabetes presenting with a 5-year history of chronic testicular pain. An ultrasound of the testes when patient first presented to his urologist was notable for bilateral hydrocele. The pain was described as a 9/10 on the Visual Analogue Scale (VAS) with intermittent throbbing in the testicles that spread to the abdomen when at its most severe; the patient experienced limited pain relief with the lifting of the scrotum. He was initially treated conservatively with doxycycline and ciprofloxacin for 2 weeks with only partial improvement in pain. Subsequently, multiple treatment modalities were attempted, but the pain remained refractory to acetaminophen, NSAIDs, and opioids. The patient was then referred to the pain management service for a workup of refractory pain, suspected to be of neuropathic origin. A trial of gabapentin 600 mg TID was attempted. At the 2 month follow up, the patient reported no improvement in pain, and his urologist did not believe that surgical interventions would be of any benefit. Given the lack of response to conversative management, the patient was offered a potential spermatic cord block or ketamine infusion as an alternative. The patient preferred a trial with ketamine infusion prior to the more invasive block. A single ketamine infusion (0.5 mg/kg) was provided over one hour. At the 6-week follow up, the patient reported a 40% reduction in pain (VAS 5/10) with continued gabapentin usage and no additional side effects.

Step	Details & Considerations
Assessment	History, exam, rule out acute/reversible causes, imaging (including scrotal ultrasound), urinalysis, psych eval
First-line	Physical support (scrotal elevation), NSAIDs, antibiotics, anticonvulsants (gabapentin, pregabalin), antidepressants, pelvic floor therapy
Second-line	Regional blocks (including spermatic cord block, pudendal nerve block, ilioinguinal nerve block), psychological counseling
Third-line	Targeted interventions (epididymectomy, varicocelectomy, vasectomy reversal), microsurgical denervation of the spermatic cord, orchiectomy

Figure 1: Systematic approach to neuropathic testicular pain

Methods

Risks, benefits, and alternatives to the treatment were discussed with the patient, and the patient demonstrated understanding and wished to proceed. The patient was brought to the infusion area and placed in a prone position. Routine monitors were applied, including heart rate, ECG, respiratory rate, pulse ox, and blood pressure. An IV was placed and connected to an Ivenix infusion pump. The patient was given 1 mg of midazolam prior to the initiation of ketamine infusion. A total of 40 mg of ketamine (0.5 mg/kg) was prepared in 250 ccs of normal saline, and the infusion was administered through the infusion pump. Vitals were monitored throughout the course of the infusion. The infusion lasted one hour. After the infusion was completed, the patient was monitored for an additional 30 minutes until sedation wore off.

Conclusions

- Here, we demonstrate that ketamine may prove an effective adjunct in treatment of chronic orchialgia when other treatment modalities have been exhausted, with pain relief of 40% post-infusion with continued with gabapentin usage
- Currently, there are no established guidelines regarding the treatment of neuropathic chronic orchialgia
- Estimated success rates for the treatment of chronic orchialgia with conservative measures are no more than 15%, necessitating more invasive measures, including local blocks and possible surgical intervention
- When surgical interventions are not possible, the next steps in treatment are unclear; although evidence for the efficacy of intravenous ketamine in treatment of neuropathic conditions is limited, the results of this case suggest further research into its use as adjunctive therapy may be merited

References

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