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Ketamine Infusion for Pain Management in a Case of Thoracic Outlet Syndrome

Ronald J Corbee*

Department of Clinical Sciences, Faculty of Veterinary Medicine, Utrecht University, the Netherlands

*Corresponding author: Ronald J Corbee, Department of Clinical Sciences, Faculty of Veterinary Medicine, Utrecht University, Yalelaan 108, 3584CM Utrecht, the Netherlands.

Tel: +31-30-2539411; E-mail: r.j.corbee@uu.nl

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Abstract

This case report presents the successful use of ketamine infusion therapy as pain relief for a patient with bilateral neurogenic Thoracic Outlet Syndrome (TOS) combined with arterial TOS after bilateral first rib resection surgery. The patient did not respond well to medical management due to limited effects and severe side effects. However, surgical treatment resulted in temporary relief. After ketamine infusion, quality of life has improved considerably because of increased functional capacity and decreased pain sensation. However, the clinical signs of arterial TOS remained. Additional prospective and standardized studies are needed to confirm if ketamine infusion is a good option for pain management in refractory cases of TOS.

Introduction

Thoracic outlet syndrome (TOS) is a complex disorder resulting from the compression of nerves and/or blood vessels in the thoracic outlet region [1]. The incidence of neurogenic TOS (NTOS) is estimated to be between 2 and 3 cases per 100,000 people per year, and that of venous TOS (VTOS) between 0.5 and 1 per 100,000 people per year, arterial TOS (ATOS) being sporadic [2]. The symptoms of TOS include neuropathic pain, numbness, and paresthesia in the fingers, as well as an upper-extremity weakness [1]. Furthermore, patients may wake up at night with pain, paresthesia, or tingling or get up with headache and neck hardness in the morning. Most probably, they are doing actions that will aggravate the symptoms in the cervicoscapular area during sleep [3]. Many patients with TOS symptoms are relieved by conservative treatment such as rehabilitation therapy, exercise, and activity modification. Recovery rates are reported to be 50%–90% [3]. Oral pain medications can be used to relieve neuropathic pain, such as NSAIDs, benzodiazepines [4], nortriptyline [5], pregabalin [6], gabapentin [7], and amitriptyline [5]. If the patients do not respond to these conservative treatments, surgical treatment, such as first rib and/or cervical rib resection, may be considered with a reported success rate of 89% [8]. If surgical treatment does not result in sufficient pain relief, there are no other options rather than getting back to physiotherapy as well as different combinations of pain medication. Ketamine infusion therapy can be an alternative treatment option to manage neuropathic pain associated with TOS in refractory cases. This treatment was successfully prescribed in patients with complex regional pain syndrome [9]. The analgesic effect of ketamine can be explained by N-methyl-D-aspartate (NMDA)-receptor antagonism. This case report presents the successful use of ketamine infusion therapy as pain relief for a patient with bilateral NTOS combined with

ATOS after bilateral first rib resection surgery.

Case Presentation

Interestingly, the patient was diagnosed with cheiralgia paresthetica of the left thumb 15 years prior to presentation with TOS symptoms, which might have been the first clinical sign of TOS in this case. No treatment was prescribed. Two years after the cheiralgia diagnosis, the patient was diagnosed with epicondylalgia of the right elbow was diagnosed, and diclofenac 50 mg TID was prescribed along with physiotherapy. The patient was involved in a car accident almost four years thereafter and complained of neck pain. A side complaint was the occasional numbness of his fingers. The Spurling test was positive on the left side. No treatment was prescribed, but the use of ibuprofen or paracetamol was permitted. Complaints worsened over time, so a neurologist was consulted four years after the car accident. Physiotherapy was prescribed but turned out to be unsuccessful. Two years later, a neurologist consulted again with an additional complaint of numbness and loss of strength when stretching the arms, which is the start of the case description.

A 46-year-old man (body weight 82 kg (181 lbs.), body height 1 m 88 (6 foot 2)) visited the general practitioner with a 6-year history of pain in the neck-shoulder region, with the additional complaint of numbness and loss of strength when stretching the arms, as well as pain and tingling in the hands and lower arms. His symptoms also aggravated when his head was rotated sideways. The complaints also affected his sleep, as they woke him up, either due to pain in the neck-shoulder region or due to numbness in either of his arms. He has been working as an operator at a production plant for animal food (i.e., concentrates for livestock) and was still able to have normal activities of daily living until he visited the general practitioner at 46 years of age. He was unable to do his work because of his inability to perform repeatable actions due to pain and numbness, as well as loss of strength when he had to maintain the force for a prolonged period of time. This was especially the case when he had to raise his hands above his shoulders. Sensory nerve conduction studies revealed the presence of NTOS because of partial loss of the sensory nerve action potential of the medial antebrachial cutaneous nerve, combined with numbness and sensory loss. Hoffman Tromner test and Adson test were positive bilaterally. Angiography performed at 180° shoulder abduction revealed complete obstruction of both the axillary and the subclavian artery on the left and right arm. At rest, there was a normal flow, confirming the presence of ATOS. Mensendieck and physiotherapy combined with ibuprofen and/or paracetamol did not give any improvement in clinical signs, after which surgical options were discussed with a vascular surgeon. First rib resection was performed on both sides one year after another, which resulted in clinical improvement for 2.5 years, but thereafter clinical signs worsened (i.e., pain, numbness, and sleeping problems). Radiographs of the shoulder regions at that time did not reveal abnormalities. Further evaluation with MRI and/or surgery to remove scar tissue was not recommended because of the low success rate and the increased risk of side effects (e.g., pneumothorax and permanent nerve damage). Therefore, medical treatment with nortriptyline was introduced, starting with 10 mg SID and gradually increasing up to 25 mg BID, resulting in partial relief of the complaints.

Nortriptyline also gave side effects (blurred vision, dry mouth, feeling light-headed), and for that reason, a referral to the pain clinic was made. Amitriptyline 25 mg TID and pregabalin 150 mg BID were prescribed, with limited effect, and therefore paracetamol was added up to 1,000 mg Q4h. This made the patient more comfortable, but the patient was also experiencing several side effects, such as sweating, being absent, falling asleep earlier than usual, and depression. These side effects are known for pregabalin (i.e., sweating due to psychomotor hyperactivity, being absent, falling asleep earlier than usual, and depression due to somnolence). Nerve blocks were deemed unsuccessful, so medical treatment was the only effective treatment. Because the side effects worsened over time (i.e., getting more and more depressed), it was decided (after consulting the general practitioner) to gradually reduce medication use to zero and ask for a second opinion at a different pain clinic. After discussions with several anesthesiologists, the patient was offered the possibility of ketamine infusion. Possible outcomes, risks, and side effects were discussed with the patient. After giving his consent, the first in-hospital treatment consisted of an anxiolytic dosage of midazolam (2-4 mg intravenous push), followed by a ketamine (Ketanest-S® 5 mg/mL) IV bolus of 0.6 mg/kg, continued with 1 mL/h (i.e., 0.06 mg/kg per h) continuous rate infusion (CRI) for 24h [10]. This resulted in immediate improvement of clinical signs, as the neurogenic pain was relieved; however, now the clinical signs due to the ATOS became more overt as the patient was sleeping much better and kept on being in one position for a prolonged duration of time resulting in numbness of the arm. However, these symptoms were less severe than the neurogenic pain due to NTOS. After two months, the patient did not experience any effect anymore, as all clinical signs returned. The next treatment was done four months later. Then the patient was administered 0.9 mg/kg initial bolus, followed by 1.5 mL/h (i.e., 0.09 mg/kg per h) CRI for 24h. This initially resulted in some slight side effects of ketamine (hallucinations) during the 24h hospitalization period but gave good pain relief for four months, according to the patient. The next five treatments were done at 5-month intervals (delays because of a shortage of staff due to the ongoing COVID pandemic) with the same dosage and did not result in side effects anymore but did result in pain relief for about four months. The patient's liver enzymes were checked every other treatment and were not affected by ketamine infusion therapy. Despite the pain relief, the activities of daily living were still impaired due to the mechanical obstruction (i.e., NTOS and ATOS), but the overall quality of life improved considerably.

Discussion

TOS is considered to be a congenital disorder, but clinical signs usually present after trauma, which is in agreement with this case, as there were some possible early clinical signs present, but clinical signs were obvious after a car accident [11].

A book chapter on thoracic outlet syndrome describes ketamine infusion as a possible treatment option for NTOS. However, the effects of ketamine infusion for this particular indication have, according to the author's knowledge, not yet been described [12].

Ketamine infusion therapy for chronic pain management in cases of complex regional pain syndrome is proven to be effective in the short term with an immediate pain relief event rate of 69% (95% confidence interval (CI) 53%–84%) and 58% (41%–75%) at 1 month–3 months after treatment [9], which is similar to the observations in this case report. Common adverse effects reported include anxiety, dysphoria, nightmares, hallucinations, insomnia, euphoria, agitation, blurred vision, and sedation [9]. However, the patient, in this case report only experiencing hallucinations once after being administered a bolus of 0.9 mg/kg for the first time. Elevation of liver enzymes has also been reported, and the event rate of hepatotoxicity from ketamine infusion is reported to be 1.9% [9], which has not been reported during the ketamine infusion treatments that the patient has received up till now.

The patient responded well to an initial ketamine bolus of 0.9 mg/kg, followed by 0.09 mg/kg CRI for 24h. Higher dosages were not used in this patient because of the side effects seen at the first administration of the higher dosage bolus (i.e., 0.9 mg/kg). Suggested dosages and treatment protocols for ketamine infusion therapy for the treatment of chronic pain vary widely.

The patient's quality of life has improved considerably because of increased functional capacity and decreased pain sensation, as has also been described in patients with complex regional pain syndrome on ketamine infusion therapy [13]. However, due to vascular obstruction associated with ATOS, he still has signs of loss of strength, numbness, tingling, and swollen hands with discoloration [14]. This can partially be relieved by a change of stature and motion, but it still affects sleep every now and then. Exercise, but also normal movements (e.g., walking the dog, carrying a shopping bag, and cleaning) worsen these clinical signs, so, unfortunately, normal life is still affected.

Conclusion

This patient with chronic neurogenic pain due to TOS, which was refractory to conservative and surgical treatment, did benefit from ketamine infusion therapy. However, additional prospective and standardized studies are needed to confirm if ketamine infusion is a good option for pain management in refractory cases of TOS.

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I would like to thank my husband for giving me full access to his medical history. Furthermore, I would like to thank anesthesiologist Drs. P. de Witte, for prescribing ketamine infusion to my husband, as it has markedly improved my husband's quality of life (as well as mine).

Patient consent statement: The patient is the life partner of the author and has given permission to publish this case report. This case report is written by a partner and scientist with medical background perspective.

Conflict of Interest

The author declares no potential conflicts of interest with respect to the research, authorship, and/or publication of this article. Informed consent was obtained for this publication.

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