Clinical Case Reports

Ketamine as a potential option in the treatment of short-lasting unilateral neuralgiform headache attacks with conjunctival injection and tearing

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ABSTRACT

A number of treatment options have been used over the years in short-lasting unilateral neuralgiform headache attacks with conjunctival injection and tearing (SUNCT) with variable results. The most common preventive treatments include carbamazepine, lamotrigine, indomethacin, gabapentin and topiramate. Ketamine is being increasingly used in the treatment of neuropathic pain. The parentral formulations are generally used as oral preparations have poor bioavailability. Recently, ketamine lozenges have been shown to have sufficiently high bioavailability to support their use as a preventive treatment in a number of conditions causing intractable neuropathic pain. We report a 58-year-old man whose symptoms of SUNCT were not responsive to conventional preventive treatments but responded well to a subcutaneous, sub-anaesthetic ketamine infusion and subsequently, sublingual ketamine lozenges.

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INTRODUCTION

Short-lasting unilateral neuralgiform headache attacks with conjunctival injection and tearing (SUNCT) is a form of a trigeminal autonomic cephalgia. These predominately occur in men, with around 50 years as the mean age of onset. [1] The attacks are strictly unilateral, especially around the ocular region of the face. Most attacks are moderate-to-severe in intensity and have a stabbing, burning or electrical shock-like character. The mean duration of each paroxysm is 10–120 seconds. During acute episodes, the frequency of attacks may vary from one attack per day to more than 30 attacks per hour. The attacks generally tend to occur during the day rather than at night.[1]

Prominent, ipsilateral conjunctival injection and lacrimation accompany the attacks, which is pathognomonic for the condition. Nasal congestion and rhinorrhoea can also occur. The attacks can be triggered by stimulation of trigeminal innervated areas but can also occur from stimulation of extra-trigeminal areas. The attacks can also occur spontaneously.[2]

A SUNCT-like picture has been described in some patients with either intra-axial or extra-axial posterior fossa lesions, mostly vascular malformations. In the vast majority of cases of SUNCT, however, the aetiology and pathogenesis are unknown.[3,4]

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THE CASE

A 58-year-old man developed sharp, stabbing and burning pain in the right ocular region of the face associated with tearing and redness of his right eye in 2009. He had associated swelling of the right eye and drooping without rhinorrhoea or nasal congestion. Each episode of pain would last for about 30–40 seconds and resolve spontaneously. Over the years, the pain increased in severity and frequency, and he tried a number of preventive treatments including gabapentin, pregabalin, amitriptyline, phenytoin and lamotrigine.

By 2015, he was experiencing approximately 100 attacks of pain per day. He presented to his local hospital and was given an indomethacin suppository which rendered him pain free. He then commenced oral indomethacin tablets, 50 mg three times per day, but this resulted in bleeding gums and was subsequently stopped. Phenytoin was also stopped as this too caused gum problems.

He was started on tapentadol SR 50 mg at night with some improvement in pain, but he was still experiencing between 50 and 100 attacks of pain per day. A lignocaine infusion was started, but this only resulted in 1 hour of pain relief.

Subsequently, he was started on a subcutaneous, sub-anaesthetic ketamine infusion, which resulted in complete relief of symptoms by day 3, with the dose increased slowly up to 6 mg/hour. He did not experience any of the side-effects associated with ketamine, such as dizziness, light headedness, tiredness, sedation, headaches or hallucinations. This probably was related to the relatively low dose required to obtain symptom relief. The ketamine infusion was continued for another 3 days at 6 mg/hour. He remained pain-free, so the infusion was stopped, and he was started on sublingual ketamine lozenges at a dose of 25 mg three times a day.

He was discharged on tapentadol SR 50 mg twice per day, pregabalin 150 mg twice per day, amitriptyline 10 mg at night, clonazepam 0.5 mg at night, lamotrigine 25 mg twice per day and ketamine lozenges 25 mg twice per day.

For the next 3 months, he did not have any spontaneous episodes of pain. He was able to talk without difficulty and did not have any increased sensitivity to touch over the face. He was even able to return to work. He was then weaned off pregabalin and then tapentadol SR and eventually lamotrigine. He noticed a slight recurrence in pain, which improved with increasing ketamine lozenges to 25 mg four-times per day.

Since being on ketamine lozenges, he has been completely pain-free and commented that he has 'said goodbye to SUNCT'. Over time, he has managed to reduce the dose of the ketamine lozenge to 25 mg twice a day. He has also stopped amitriptyline and clonazepam.

DISCUSSION

SUNCT can be a disabling condition that can result in intractable pain. The most widely used treatments during acute attacks include lignocaine infusions[5] or prednisone.[6] There have been some reports of response to supraorbital, infraorbital and greater occipital nerve blocks and even occipital nerve stimulation.[7] The most common preventive treatments include carbamazepine, lamotrigine, indomethacin, gabapentin and topiramate.[8]

Traditionally, ketamine has been used as a general dissociative anaesthetic agent for short diagnostic and surgical procedures.[9] Ketamine, however, exhibits analgesic actions at many sites, both

centrally and peripherally. It is predominately a non-competitive N-methyl-D-aspartate (NMDA) receptor antagonist but also has effects on kainate, gamma-aminobutyric acid receptors, alpha-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid, inhibition of voltage-gated Na+ and K+ channels and serotonin and dopamine reuptake.[10]

Ketamine reduces NMDA-mediated nociceptive responses in dorsal horn neurons by binding to the phencyclidine site of the NMDA receptor-gated ion channel. Ketamine can minimise excessively painful responses.[11]

Sublingual ketamine formulations are not currently commercially available but can be formulated by compounding pharmacists. Studies have shown that the bioavailability of the sublingual formulation is superior to an oral formulation, 40% compared to 20%. There is substantial metabolism to norketamine, which possesses analgesic activity, from both routes. The mean norketamine/ketamine area under the plasma concentration-time curve from baseline-to-8 hours ratios was 5 and 2.1 after sublingual and oral administration, respectively.[12]

A study in 2016 showed that sublingual ketamine lozenges offer a promising therapeutic option for long-term relief of chronic non-malignant pain. Ketamine lozenges have been shown to have acceptable storage stability, and the sublingual bioavailability is sufficiently high and reproducible to support its use in this context.[13]

Subcutaneous, sub-anaesthetic ketamine infusions are generally well tolerated and in particular, less cardiotoxic compared to the conventionally used lignocaine infusion. Once response occurs, ketamine lozenges can be used as preventive treatment, whereas lignocaine does not have a suitable oral alternative.

As there are increasing reports of ketamine lozenges being used in the treatment of intractable neuropathic pain, a commercially available form of the lozenge with adequate licensing and formulation controls in place is needed.

To the best of my knowledge, this is the first report in the literature of a case of SUNCT responding well to ketamine.

Conflicts of interest. None declared

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