*Case Study*

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# Termination of SUNCT with intravenous lignocaine followed by oral mexiletine

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## Abstract

**Background:** The trigeminal autonomic cephalalgias (TACs) are a group of debilitating, pathophysiologically similar headache syndromes characterized by facial pain and autonomic symptoms in areas supplied by the trigeminal nerve. Short-lasting unilateral neuralgiform headache with conjunctival injection and tearing (SUNCT) is among the rarest of the TAC syndromes and can be particularly recalcitrant to treatment.

**Case:** We describe the case of a 50-year old woman with difficult-to-control SUNCT whose pain was completely aborted within hours of commencing intravenous lignocaine therapy and was maintained pain-free after transitioning to oral mexiletine.

**Conclusion:** This is the first report of successful transition from intravenous lignocaine to oral mexiletine in SUNCT, and we suggest that this treatment should be tried early in difficult-to-control SUNCT. This therapy is safe, effective and with minimal side effects if administered in an appropriate manner.

## Keywords

headache, lignocaine, mexiletine, neuralgia, trigeminal autonomic cephalalgias

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## Introduction

The trigeminal autonomic cephalalgias (TACs) are a group of debilitating, pathophysiologically similar headache syndromes characterized by facial pain and autonomic symptoms in areas supplied by the trigeminal nerve.[1] Short-lasting unilateral neuralgiform headache with conjunctival injection and tearing (SUNCT) is among the rarest of the TAC syndromes and can be particularly recalcitrant to treatment.[1] This report describes the first ever case of successful transition from intravenous lignocaine to oral mexiletine therapy in SUNCT.

## Clinical case

A 50-year old woman with episodic SUNCT experienced an increase in headache frequency and intensity over a 4-week period. At 45 years, she had first presented with short-lasting (20–60 s) excruciating, stabbing right-sided retro-orbital pains associated with ipsilateral lacrimation, conjunctival injection and nasal stuffiness. Attacks occurred in a periodic fashion, on average 10 times per day, for 4–6 days followed by 2 weeks of freedom from pain; this lasted 18 months, during which she unsuccessfully trialled many abortive treatments including diclofenac, codeine, tramadol, 100% oxygen and oral and subcutaneous triptans. Preventive treatments including prednisone 60 mg daily, nortriptyline 75 mg daily, topiramate 200 mg daily and sodium valproate 1400 mg daily were ineffective. Bradycardia precluded the use of verapamil. Indomethacin 75 mg three times daily

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produced modest improvement. After 18 months, the pain abated and she remained symptom-free for 5 years.

Her medical history was significant for treated hypertension, depression and previous sinus disease. Neurological examination and brain magnetic resonance imaging were normal.

After 5 years without SUNCT, off treatment, the condition recurred. She required admission to hospital for pain management. Medications on admission included paracetamol 1 g four times daily, indomethacin 75 mg three times daily, atenolol 50 mg daily, bendrofluazide 2.5 mg daily and citalopram 30 mg daily. Her flare of SUNCT was initially treated with intravenous dihydroergotamine (DHE) infusion (total dose 11.25 mg) without effect. Lamotrigine 25 mg daily was added to her medication regimen in addition to prednisone 60 mg daily. Again, these were ineffective. Lamotrigine was slowly up-titrated to 150 mg twice daily.

A decision was made to proceed with intravenous lignocaine infusion at 1 mg/kg/h. Within 4 h, the pain dramatically improved. As she put it, 'tears of SUNCT have been substituted by tears of joy'. The lignocaine infusion was continued for 5 days, during which she remained pain-free; she then successfully transitioned to mexiletine 150 mg twice daily. A recurrence of pain at week 6 was improved by an increase in mexiletine dose to 250 mg twice daily. We plan to continue mexiletine until such time as she achieves a therapeutic lamotrigine blood level, at which point we will attempt to wean mexiletine.

## Discussion

Because of its rarity as a clinical entity, there is little evidence base upon which to approach treatment of SUNCT.[1] SUNCT is a capricious condition prone to variable and unpredictable fluctuations in headache severity and frequency, which makes it difficult to interpret the effectiveness of any particular therapy.[1] At best, treatment response rates are estimated at roughly 62–68%.[2,3] Acute abortive treatment options include non-steroidal anti-inflammatory medications (including indomethacin), paracetamol, 5-HT receptor antagonists (triptans and DHE), intravenous phenytoin and intravenous and intranasal lignocaine.[1–3] Based on the currently available literature and published guidelines, lamotrigine appears to offer the best chance of sustained remission.[1–3] Many other preventive treatments have been studied, some with good effects, including topiramate, gabapentin, beta blockers, carbamazepine and verapamil, but again the uncommonness of the condition often precludes conduction of useful randomized trials.[1–3] Botulinum toxin administration, greater occipital nerve blockade and surgical treatments for SUNCT have also been reported.[1]

Lignocaine is an amide-type local anaesthetic that exerts its effect through blockade of sodium channels in neural tissues, interrupting transmission. The first report of successful use of systemic lignocaine infusion in pain management came in 1943 in burn victims; since that time, its use has extended to both acute and chronic pain syndromes such as intra- and perioperatively, acute radicular pain and chronic neuropathic pain disorders, such as diabetic neuropathy and post-herpetic neuralgia, complex regional pain syndrome and fibromyalgia.[4] Within the headache sphere, there is good evidence of its effectiveness in chronic daily headache syndromes and to some extent in TACs.[2,3,5] In SUNCT, it likely exerts its effect through both modulation of the trigeminal autonomic reflex and attenuation of central (hypothalamic) activation during SUNCT attacks.

Intravenous lignocaine infusions carry a certain mystique that begets an irrational fear of its use. However, the treatment is both easy to administer and relatively safe as long as standard protocols are followed. Depending on the institution, an initial bolus of 1–2 mg/kg may be given followed by infusion of lignocaine at a rate of 1–3 mg/kg/h, though for SUNCT, the initial bolus is rarely required.[6] The drug is predominantly hepatically metabolized, requiring dose adjustments and increased monitoring in any condition reducing hepatic blood flow or hepatic metabolic capacity.[6] Lignocaine has a narrow therapeutic window, with toxic effects occurring at plasma levels slightly above (>5 μg/ml) the therapeutic window (2.5–3.5 μg/ml).[6] Toxicity follows a predictable sequence, beginning with mild central nervous system (CNS) symptoms, such as tongue numbness, metallic taste and tinnitus, followed by severe CNS toxicity (which produces sedation or, paradoxically, euphoria) before progressing to cardiovascular and respiratory collapse. Such a progression mirroring increasing blood levels means that early signs of toxicity can be detected and remedial action can be taken prior to progression to severe events.[6] With continuous infusion, lignocaine reaches steady-state plasma levels after 4–8 h.[6] Serum lignocaine assays are available in many institutions and can help reassure clinicians that levels are within the therapeutic window and/or confirm the diagnosis of lignocaine toxicity. In clinical practice, most toxicity occurs due to medial error, infusion pump misprogramming or failure to attend to signs of early toxicity.[6]

Although a dichotomy of opinion exists regarding the usefulness of intravenous lignocaine as an abortive treatment in SUNCT, some suggest it as an almost miracle cure, reporting response rates approaching 100% for acute attacks.[2,3] Lignocaine offers a number of attractive options. As a sodium channel blocker administered intravenously with a half-life of approximately 30 min, it has a rapid onset of action. It is safe when administered under controlled conditions and also offers the opportunity to switch to an oral treatment in the form of mexiletine upon discontinuation. Phenytoin, a drug with a similar mechanism of action, has been used in the treatment of TACs but has less robust efficacy data and, in our experience, is less effective than intravenous lignocaine for SUNCT.

Mexiletine, a class 1B anti-arrhythmic sodium channel blocker, is essentially an oral analogue of intravenous lignocaine, which has proven efficacy both as a primary agent in the treatment of neuropathic and other painful conditions and as a transition agent upon weaning from intravenous lignocaine. A

response to intravenous lignocaine predicts a response to oral mexiletine.[7,8] Usual doses range from 400 mg/day to 600 mg/day, and it should only be started after discontinuing intravenous lignocaine due to the potential for additive toxicity.[7,8]

Successful use of intravenous lignocaine in aborting SUNCT attacks has been documented in the literature, but previous cases have transitioned to conventional preventive agents, such as lamotrigine, topiramate and so on.[1–3,9,10] Transition to oral mexiletine has not been previously reported in SUNCT, though the process makes intuitive sense and is the standard for many other pain syndromes.

## Conclusion

In this case, intravenous lignocaine immediately terminated SUNCT attacks; transition to oral mexiletine was successful, as was an increase in mexiletine dose in controlling further episodes of pain. We suggest that intravenous lignocaine with transition to oral mexiletine should be tried early in difficult-to-control SUNCT. This therapy is safe, often effective and with minimal side effects if administered in an appropriate manner.

## Clinical implications

- SUNCT can be particularly difficult to treat. At best, 62–68% of patients respond to preventive medications.
- Intravenous lignocaine is an effective abortive treatment for SUNCT.
- Mexiletine is a useful agent for transitioning from intravenous lignocaine to oral preventive treatment in SUNCT.

### Authors' note

Informed consent was obtained from the patient in this case report for submission to the medical literature.

### Declaration of conflicting interests

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