Trigeminal neuropathic pain (TNP) can be defined as a constant, unilateral facial pain of variable intensity that is nontriggerable and unremitting (1). The patient profile in orofacial pain clinics points to an increasing prevalence of painful traumatic neuropathies affecting the trigeminal nerve and is mirrored in our practice (2). TNP secondary to trauma has been classified as painful traumatic trigeminal neuropathy (PTTN) (3). PTTN occurs because of unintentional injury to the trigeminal system from orofacial trauma, third molar extraction, dental injection, dental implant placement, and maxillofacial surgery (3-5). However, trigeminal neuropathy can also develop from inflammation...
secondary to an infective process including postherpetic neuralgia, recurrent sinus infection, or dental pathologies (tumors, abscess formation) (6). The pain has been reported as constant, dull, boring, or burning in nature with paroxysms that can be spontaneous or evoked (1,7).

Current management of TNP is primarily based on expert opinion and follows the general principles in the management of neuropathic pain (8,9). The recommendations include a 2-pronged strategy involving pharmacologic agents and psychological support. Clinically significant pain relief in patients with neuropathic pain has been defined as 30% reduction in pain at 12 weeks (10,11). It is generally accepted that most patients with TNP fail to achieve this endpoint (2,9). The patients with refractory TNP have limited management options and must endure the devastating effect of the condition on their quality of life (4). Clearly, there appears to be a significant gap in the management of refractory TNP (12).

In the authors’ experience, patients with TNP can also present with clinical features of superficial cervical plexus irritation including periauricular pain and ipsilateral trapezius myofascial pain. We have also observed tenderness over the ipsilateral greater occipital nerve in patients with TNP. There appears to be a significant interplay between the trigeminal nerve system, the greater occipital nerve, and the cervical plexus in this population (13,14).

Peripheral trigeminal nerve blocks have been reported in the management of patients with refractory trigeminal neuralgia and TNP (15,16). In 2013, Nader et al (17) described ultrasound-guided trigeminal nerve block in the pterygopalatine fossa with depot steroids. The technique was successful in blocking the maxillary and mandibular branches while the ophthalmic division was blocked in 50% of cases (17). Intermediate cervical plexus block has been described in the management of periauricular pain, and in refractory cervicothoracic myofascial pain. Greater occipital nerve blocks have been reported to be effective in occipital neuralgia secondary to TNP (13). We embedded these 3 ultrasound-guided blocks in our pathway for managing refractory TNP.

We, the authors, present a novel strategy in the management of refractory TNP. We have performed a longitudinal prospective audit of a novel management protocol and present our observations in 70 patients with TNP over a 4-year period.

Methods

Adult patients presenting with unilateral TNP to the multidisciplinary facial pain clinic at a tertiary university hospital were included in the prospective audit. The team included specialists in pain medicine, maxillofacial surgery, neurology, and clinical psychology.

Patients with trigeminal neuralgia, isolated myofascial pain, burning mouth syndrome, cervicogenic headaches, primary greater occipital neuralgia, bilateral facial pain, or temporomandibular joint dysfunction were excluded.

The prospective audit spanned 4 years (2015–2019). The audit was registered with the Clinical Audit Safety and Effectiveness (CASE 8161), University Hospitals of Leicester NHS Trust, UK. CASE approved analyses and use of the collected data. The patients provided written consent for participation in the audit, for telephone review, for the use of the deidentified data for analyses, and publication in a peer-reviewed journal.

The objective of the audit was to identify an effective and durable treatment for the individual patient and evaluate patient satisfaction with a novel management pathway (Fig. 1). All patients diagnosed with TNP were included in the audit.

Management Pathway of TNP

Step 1a

Diagnosis of TNP was primarily based on the diagnostic criteria described by Benoliel et al (3).

- Criteria A: Constant pain with spontaneous or touch evoked pain predominantly affecting the receptive field of one or more divisions of the trigeminal nerve.
- Criteria B: Develops within 6 months of an identifiable traumatic or inflammatory event to the painful area. Continues for more than 3 months.
- Criteria C: At least one clinically evident neurologic dysfunction: positive sign: hyperalgesia, allodynia, swelling/flushing; negative sign: anesthesia, hypoesthesia.
- Criteria D: Magnetic resonance imaging (MRI) of the head to rule out trigeminal neuralgia (no signs of neurovascular contact, infection, demyelination, or tumor). Neurophysiologic testing was not performed.
- Criteria E: Not attributed to another disorder.
Step 1b  
Presence of clinical signs and symptoms of ipsilateral greater occipital nerve irritation (occipital headache, occipital allodynia, tender occipital nerve).

Step 1c:  
Presence of clinical features of ipsilateral superficial cervical plexus involvement (periauricular pain, tender lesser occipital nerve, trapezius myofascial pain).

Step 2  
Medical management included 2 strategies in parallel.

Step 2a: Pharmacotherapy.  
We based the pharmacologic treatment on a review by O’Connor and Dworkin (18). First-line agents included tricyclic antidepressants (amitriptyline, nortriptyline), gabapentinoids (pregabalin and gabapentin), and topical lidocaine. Second-line agents included tramadol and duloxetine. Lamotrigine was the third-line agent. Patients in this series had seen multiple specialists including dentists; maxillofacial surgeons; ear, nose, and throat surgeons; neurologists; and primary care physicians. They were often trialed on first- and second-line agents. Subsequently, patients were trialed on agents singly and in combination in the doses recommended.

Step 2b: Psychological management.  
All patients were offered psychological therapy. Patients who consented were initially assessed by a clinical psychologist, and if suitable, were offered 6 to 12 therapy sessions. The clinical psychologists involved specialized in chronic pain, including facial pain.
Step 3: Intervventional treatment.
Patients who had failed pharmacologic management were offered the novel interventional treatment.

Failure of medical management was defined as an inability to achieve clinically significant pain relief at 3 months after trialing at least 3 medications singly or in combination for a minimum of 3 months (9). The objective criteria used was Numeric Rating Scale (NRS-11) score of ≥ 7/10 on the “Pain at its worst in the last 24 hours” construct in the Brief Pain Inventory Short Form (BPI-SF) questionnaire at 3 months after trialing medications. This 11-point pain NRS-11 has been found to have the strongest relationship with the pain interference scale (19,20).

We did not include a response to clinical psychology intervention as a criterion because the waiting list for receiving psychological therapy following an initial assessment at our center can reach 12 months.

Intervventional Treatment

- Ultrasound-guided trigeminal nerve block with a mixture of local anaesthetic (1% lidocaine, 6 mL) and depot methylprednisolone (60 mg).
- If the patient presented with clinical signs of greater occipital nerve irritation, they received ultrasound-guided greater occipital nerve block with a mixture of 20 mg depot methylprednisolone and 1 mL 1% lidocaine.
- If the patient presented with clinical features of superficial cervical plexus involvement, they received intermediate cervical plexus block with a mixture of 40 mg depot methylprednisolone and 5 mL 1% lidocaine.

At 12 weeks following the intervention(s) (T1), the patient was reviewed over the telephone by our team.
- If the patient reported over 50% relief at 12 weeks, interventional treatment(s) T1 was repeated in 9 months.
- If the patient reported 30% relief at 12 weeks, interventional treatment(s) T1 was repeated in 6 months.
- Patients who reported no benefit were labeled as nonresponders. They were referred to a tertiary center with a specialist facial pain service.

Patients completed 2 questionnaires (BPI-SF and Hospital Anxiety Depression Scale [HADS]) to record baseline scores before each interventional treatment. Following the intervention, the patient completed questionnaires at 3 months (BPI-SF) and at 6 months (BPI-SF and HADS).

Following IMMPACT recommendations (Initiative on Methods, Measurement, and Pain Assessment in Clinical Trials), a 2-point change (30%–36%) at 3 months posttreatment was considered as successful intervention (21). A 4-point change (> 50%) at 3 months and a 2-point change (30%–36%) at 6 months posttreatment was considered as durable treatment (22).

Interventional treatment failure was defined as return of “pain at its worst in the last 24 hours” to the baseline at 3-month review following the intervention.

Data collected included patient satisfaction with the management pathway, percentage relief with pharmacologic agents and psychological therapy, complications with the interventional treatment, presence of pain elsewhere in the body, ability to maintain gainful employment, and improvement in mood and quality of life.

Technique

The interventional treatment(s) was performed under real-time ultrasound guidance using a linear high-frequency probe and in-plane approach (17,23,24).

Statistical analysis of the results was performed using Stata version 13.1 (StataCorp LLC, College Station, TX) statistical package for Windows (Microsoft Corp., Redmond, WA). The paired t-test was used to compare baseline pain NRS-11 to NRS-11 at each follow-up period (3 months, 6 months). The paired t-test was used for HADS scores at baseline and at 6-month follow-up. Differences were considered significant for \( P < 0.05 \).

Missing data were imputed using the “last-observation-carried-forward” method.

RESULTS

Over the 4-year period, 70 patients with unilateral TNP were referred to our tertiary facial pain medicine clinic based at a university hospital. All patients were included in the audit.

In this cohort of 70 patients with unilateral facial pain, 38 patients (38/70, 54%) had either associated involvement of ipsilateral superficial cervical plexus (10 patients), greater occipital nerve (15 patients), or both ipsilateral greater occipital nerve and the superficial cervical plexus (13 patients).
Interventional Management of TNP

Medical Management

Step 1

All patients reported unilateral constant pain. MRI of the head did not reveal any abnormality. Demographic characteristics, mechanism of injury, and trigeminal division(s) involved are shown in Table 1.

Step 2a: Pharmacologic management.

Thirteen patients reported clinically significant and durable response to pharmacologic management (13/70, 18%). In 5 patients, combination of tricyclic antidepressant and gabapentinoids proved effective. In the remaining 8 patients, monotherapy with nortriptyline (4 patients), gabapentin (3 patients), and lamotrigine (1 patient) was beneficial.

Step 2b: Clinical psychology.

The team assessed all patients. Twenty-seven patients were discharged after an initial assessment. Eighteen patients refused to engage further with clinical psychology. Out of 25 patients who were booked to receive further sessions, 17 patients received further sessions, whereas 8 patients are on the waiting list. Response to psychological therapy is shown in Table 2.

Step 3: Interventional management.

Fifty-seven patients with TNP who had not responded to the pharmacologic management were offered interventional treatment(s). Seven patients refused the intervention (reasons included needle phobia and anxiety of postprocedural flare-up).

The interventional treatment(s) offered included ultrasound-guided trigeminal nerve block (all patients), intermediate cervical plexus block, and/or greater occipital nerve block.

Fifty patients underwent interventional treatment(s). Forty-two patients (42/50, 84%) reported clinically significant pain relief at the 3-month review (Table 3).

Durable on-going relief at 6 months was reported by over half of the patients (Fig. 2).

Interventional treatment(s) failed to provide any relief in 8 patients (8/50, 16%); they were referred to another tertiary center.

Other Outcomes

Patient satisfaction with the TNP management pathway was high with 75% of patients reporting the pathway as excellent or good (53/75).

<table>
<thead>
<tr>
<th>Demographics</th>
<th>Patients with Trigeminal Neuropathic Pain (N = 70)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years (mean ± SD)</td>
<td>51.8 ± 16.2</td>
</tr>
<tr>
<td>Gender, N (%)</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>18 (26%)</td>
</tr>
<tr>
<td>Female</td>
<td>52 (74%)</td>
</tr>
<tr>
<td>Duration, years (median (P25, P75))</td>
<td>3 (1, 4)</td>
</tr>
<tr>
<td>Employment, N (%)</td>
<td></td>
</tr>
<tr>
<td>Employed</td>
<td>45 (64%)</td>
</tr>
<tr>
<td>Unemployed</td>
<td>9 (13%)</td>
</tr>
<tr>
<td>Retired</td>
<td>16 (23%)</td>
</tr>
<tr>
<td>Satisfaction, N (%)</td>
<td></td>
</tr>
<tr>
<td>Excellent</td>
<td>33 (47%)</td>
</tr>
<tr>
<td>Good</td>
<td>20 (29%)</td>
</tr>
<tr>
<td>Fair</td>
<td>8 (11%)</td>
</tr>
<tr>
<td>Poor</td>
<td>3 (4%)</td>
</tr>
<tr>
<td>Not Available</td>
<td>6 (9%)</td>
</tr>
<tr>
<td>Trigeminal Nerve Division, N (%)</td>
<td></td>
</tr>
<tr>
<td>I + II</td>
<td>11 (16%)</td>
</tr>
<tr>
<td>II</td>
<td>31 (44%)</td>
</tr>
<tr>
<td>II + III</td>
<td>20 (29%)</td>
</tr>
<tr>
<td>III</td>
<td>8 (11%)</td>
</tr>
<tr>
<td>Background Pathology, N (%)</td>
<td></td>
</tr>
<tr>
<td>Dental Surgery</td>
<td>23 (33%)</td>
</tr>
<tr>
<td>Dental Infection</td>
<td>14 (20%)</td>
</tr>
<tr>
<td>Maxillofacial surgery</td>
<td>6 (8%)</td>
</tr>
<tr>
<td>Physical trauma</td>
<td>16 (23%)</td>
</tr>
<tr>
<td>Sinus infection + surgery</td>
<td>5 (7%)</td>
</tr>
<tr>
<td>PHN</td>
<td>2 (3%)</td>
</tr>
<tr>
<td>Unclear</td>
<td>4 (6%)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Response to Therapy</th>
<th>Patients with Trigeminal Neuropathic Pain (N = 70)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Psychological Therapy, N (%)</td>
<td></td>
</tr>
<tr>
<td>No benefit</td>
<td>12 (17%)</td>
</tr>
<tr>
<td>20-30% benefit</td>
<td>29 (42%)</td>
</tr>
<tr>
<td>&gt; 40% benefit</td>
<td>3 (4%)</td>
</tr>
<tr>
<td>On waiting list</td>
<td>8 (11%)</td>
</tr>
<tr>
<td>Refused to engage</td>
<td>18 (26%)</td>
</tr>
</tbody>
</table>
There was significant improvement reported in anxiety and depression scores following the interventional treatment (Table 3).

Sixteen patients (16/70) had retired from gainful employment. In the remaining 54 patients, 45 patients (83%, 45/54) reported that they could maintain gainful employment as a result of effective management of their facial pain.

Complications recorded during the 4-year audit period included steroid-induced hot flushes (1 patient), transient nightmares (2 patients), and postprocedural flare-up in pain lasting more than 1 week (2 patients).

Missing data imputed using “last-observation-carried-forward” methods were used in 2 patients.

Table 3. ‘Worst Pain at 24 hours’ scores and HADS scores at baseline and at 6 months post nerve block(s) with steroids.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Baseline Mean ± SD</th>
<th>6-month Mean ± SD</th>
<th>Change from Baseline Mean (95% CI)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>HADS</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anxiety (N=43)</td>
<td>9.8 ± 4.40</td>
<td>7.4 ± 3.80</td>
<td>-2.4 (-3.3, -1.6)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Depression (N=43)</td>
<td>10.3 ± 4.5</td>
<td>7.5 ± 4.10</td>
<td>-2.8 (-3.9, -1.8)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Pain Scores</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Steroids (3 months) (N=50)</td>
<td>8.8 ± 1.3</td>
<td>5.1 ± 2.7</td>
<td>-3.7 (-4.5, -2.9)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Steroid (6 months) (N=50)</td>
<td>8.8 ± 1.3</td>
<td>6.7 ± 2.2</td>
<td>-2.1 (-2.7, -1.5)</td>
<td>&lt; 0.001</td>
</tr>
</tbody>
</table>

Fig 2. “Worst pain score at 24 hours” baseline, 3 months, and 6 months for patients with refractory TNP who received ultrasound-guided nerve block(s) with steroid (N = 50).

**Discussion**

TNP presents with a constant unremitting unilateral facial pain that is often refractory to standard management (8,9). Our report shows that a novel management pathway in patients with refractory TNP can provide significant and durable pain relief thereby improving function, mood, and the ability to maintain gainful employment. Over 75% of the patients who received interventional treatment reported clinically significant pain relief at 3 months, and 54% of patients had durable pain relief lasting over 6 months. Over half of our patients with unilateral facial pain reported associated ipsilateral symptoms of greater occipital nerve irritation, trapezius myofascial pain, or both.

The novel strategy involved targeting the trigeminal nerves, the greater occipital nerve, and the cervical plexus in patients with refractory unilateral TNP. There appears to be a significant interplay between these 3 nerve systems. Jürgens et al (13) have reported on the benefit of occipital nerve block in patients with TNP (13). In our cohort, 54% of patients with unilateral facial pain due to TNP had associated symptoms relating to greater occipital nerve and cervical plexus. Animal experimental studies and human empiric evidence demonstrates neurophysiologic and structural convergence of cervical sensory and muscle afferent inputs onto the trigeminal subnucleus.
caudalis nociceptive and nonnociceptive neurons. There is evidence to suggest that a strong connectivity exists between trigeminal and cervical motor and sensory responses (14,25). Superficial cervical plexus involvement in TNP can present as periauricular pain and trapezius myofascial pain (24,26). Trapezius muscle receives sensory innervation from the cervical plexus (27). We have shown that intermediate cervical plexus block with depot steroids can alleviate refractory trapezius myofascial pain (24).

The novel strategy could be relevant as the treatment success with current recommendation in this population is dismal (9). It is accepted that the response to pharmacologic therapy is often inadequate in patients with TNP, occipital neuralgia, and trapezius myofascial pain (9,28,29). In our cohort, the reasons for poor response to medical management included patient refusal to trial medications, inability to tolerate medications, nonengagement with psychological therapy, and failure of pharmacologic treatment. Antineuropathic medications can impede daily activities, including gainful employment, resulting in poor compliance. Treatment success in our population with pharmacologic management was 18% and is in concordance with the literature (9,30). It has been reported that 1 in 3 patients abandon pharmacologic treatment (30). Recent controversies surrounding the safety (suicidal ideation), addiction, and misuse potential of antineuropathic agents, including tricyclic agents, gabapentinoids, and opioids, has been a factor that has affected patient compliance in our cohort.

Cognitive behavioral therapy has been reported to have a limited benefit in chronic neuropathic pain (31). However, psychological therapy appears to have a role in the management of TNP (2,32). Therapy models offered included cognitive behavioral therapy, acceptance and commitment therapy, compassion focused therapy, and relaxation and mindfulness techniques. In our cohort, patients who engaged with therapy reported benefits from both an initial assessment and subsequent therapy (Table 2). Nonengagement with therapy was a maker for treatment failure.

Although various modalities of invasive and semi-invasive neuromodulation techniques have been reported in the management of painful TNP, these therapies are limited to highly specialized tertiary centers (33,34). Surgery remains an option in a small subset of patients with traumatic nerve injury (4).

Ultrasound-guided trigeminal nerve block in the pterygopalatine fossa primarily targets the maxillary and mandibular divisions of the trigeminal nerve. These 2 divisions make up for a majority of cases with TNP. It is a fairly safe intervention, as the needle does not enter the cranium, thus avoiding potential side effects of the traditional fluoroscopy-guided trigeminal ganglion block through the foramen ovale. It does not require sedation or general anesthesia. In approximately 50% cases, the ophthalmic division is blocked (17). In our cohort, only 16% (11/70) had associated involvement of the ophthalmic division.

It is now increasingly recognized that trauma to the trigeminal nerves can result in persistent neuropathic pain. Conditions that were previously diagnosed as unilateral atypical facial pain and atypical odontalgia could be subsets of TNP (7). Features of neuropathic pain are usually present including tingling, numbness, and burning pain. Pain is moderate to severe in intensity associated with sensory dysfunction. Neurophysiological testing reveals that these patients have peripheral and central sensitization and nociceptive features (35).

We present a prospective audit into a structured pathway in the management of refractory TNP. The primary objective was to identify the optimal treatment for the individual patient diagnosed with refractory TNP. TNP was diagnosed using the diagnostic criteria described by Benoliel et al (3). In our experience, traditional management of TNP based on expert opinion is insufficient in providing clinically significant pain relief. In this audit, patients reported improvement in pain intensity and mood. Patient satisfaction with the TNP management pathway was high. We recommend trialing an ultrasound-guided trigeminal nerve block at the pterygopalatine fossa with steroids in patients with TNP refractory to standard management. It is a simple, low-risk intervention that has the potential to provide long-term pain relief and improvement in quality of life in combination with pharmacologic and psychological therapies. We would also recommend obtaining a detailed history and clinical examination to diagnose concurrent greater occipital nerve tenderness and trapezius myofascial pain. In our experience, both conditions respond poorly to antineuropathic agents and often require nerve blocks with steroids to provide clinically significant pain relief.

Fifteen patients in this series failed to respond to the novel management pathway. This included 7 patients who refused to trial the interventional treatment(s), and 8 patients who did not respond to the interventional treatment(s). The factors predicating poor response in our cohort include inability to accept
a diagnosis of TNP, severe psychological distress, failure to engage with psychological therapy, and pain at other sites.

The limitations include an open-label, nonrandomized observational design in a limited cohort of patients from a single center. Neurophysiological testing was not performed.

**Conclusions**

Tailoring treatment for individual patients should remain a priority in pain medicine. Practice-based evidence as reported here could have some significance in enhancing the management of a refractory condition that has the potential to cause significant disruption in quality of life.

**Acknowledgements**

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**Authors’ Contributions**

GN: Design, performed the interventions, and drafting the manuscript; LS: Design, drafting manuscript; BR: Data collection and drafting the manuscript.

**References**


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