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Evaluating the impact of trigeminal neuralgia.

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Abstract

There is a lack of prospective systematic studies on the clinical characteristics of pain in trigeminal neuralgia (TN) as well as its 'psychosocial burden'.

Patients with idiopathic TN were categorised into three sub-types (n = 225). Group 1 (n= 155, 68.9%) had TN without concomitant pain, Group 2 (n=32, 14.2%) had TN with intermittent concomitant pain and Group 3 (n=39, 16.9%) had TN with autonomic symptoms. We tested two hypotheses: (i) that different pain profiles would be associated with the different groups; (2) that the severe pain associated with TN would impact negatively on activities of daily living and thereby result in disability as defined by the World Health Organisation. A different pain profile was found across the groups. We obtained unequivocal evidence that TN causes disability with up to 45% of patients being absent from usual daily activities 15 days or more in the past 6 months. On the Hospital Anxiety and Depression Scale, 35.7% patients had mild to severe depression and over 50% were anxious. The Pain Catastrophizing Scale showed that 78% of patients had considerable negative thoughts with scores > 20 and a mean score of 36.4. Prior to referral only 54% had been prescribed carbamazepine whilst opioids had been prescribed in 14.6% of the patients. Prior to referral over 80% had already been to one specialist centre which had not provided appropriate management. Patients with TN report varied characteristics but all result in some degree of psychosocial disability especially before adequate therapy is attained.

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1. Introduction

Trigeminal neuralgia (TN) is defined by the International Association for the Study of Pain (IASP) as "a sudden, unilateral, severe brief stabbing recurrent pain in the distribution of one or more branches of the fifth cranial nerve" [19]. The disorder is often misdiagnosed, being commonly confused with toothache or temporomandibular disorders, with reports of patients undergoing unnecessary, aggressive and irreversible dental treatments before obtaining a correct diagnosis [6,29;30]. The estimated misdiagnosis by general practitioners could be as high as 48% which led to a 'neurologist validated' diagnosis incidence rate of 12.6 per 100,000 person years in the Netherlands [11].

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Although a relatively rare condition, the impact on the lives of patients is profound [1], [31]. Allsop et al [1] provided a qualitative study suggesting TN places a large burden on patients and TN is known to be associated with severe pain [16]. Nevertheless, there are few studies that have determined the impact of the pain on the lives of the affected individuals. This is highly problematic as it prevents proper evaluation of the health economics associated with existing treatment for these patients. In turn, this prevents evaluation of alternative treatment regimens. We hypothesised that the pain associated with TN would cause a high degree of disability (as defined by the World Health Organisation, WHO) within the population. The framework described in the WHO's international classification of functioning, disability and health (ICF) outlines how impairment (e.g. pain) relates to disability. The ICF identifies three levels: the body function and structure level; the activity level and the participation level (WHO 2001). The ICF framework suggests that a functional deficit does not automatically result in an activity limitation or participation restriction. Rather, these different levels are proposed to interact with each other in a complex manner (mediated by personal and family factors). There are three studies that support the general idea that the pain associated with TN will lead to disability. Tolle et al [24] found a significant impact of TN on activities of daily living in their study of 82 patients, mean pain interference of 3.6$\pm$2.4 . Wu et al [27] reported that TN was associated with increased depression 2.2%, anxiety 1.8% and sleep disturbance 1.2% in a retrospective study of 3273 TN patients compared to controls 13,092 based on health insurance claims databases. Mačianskytė et al [17] identified disability, anxiety and depression in 30 to 47% of 30 TN patients.

The aim of the current study was to collect detailed clinical characteristics from patients attending a TN clinic. We wished to determine the burden of TN at the point of referral to the specialist centre. Our goal was explore differences between three groups of patients. Group 1 - Type 1 or 'classical' without concomitant persistent pain, irrespective of neurovascular compression findings; Group 2 - Type 2 with intermittent concomitant pain often associated with 'after-pain' following an attack [21] ; Group 3 - TN with autonomic symptoms which are either present consistently or intermittently. We wanted to explore whether these different classifications produced different pain profiles (thereby supporting the clinical utility of this categorisation).

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2. Material and Methods

2.1 *Study subjects*

We enrolled 237 consecutively consenting patients with TN (and its variants - short-lasting unilateral neuralgiform headache attacks with autonomic system symptoms (SUNA) or short-lasting unilateral neuralgiform headache attacks with conjunctival injection and tearing (SUNCT)) into a cohort study between April 2007 and December 2015. The patients were all attending a national Facial Pain Unit within a London teaching hospital. Patients with multiple sclerosis or tumour related TN (n = 12) were excluded but those who had undergone previous surgery for TN were included if their pain was the same as pre-operatively. The resulting cohort (n = 225) undertook a baseline assessment that comprised both physician measures and patient-completed questionnaires.

2.2 Ethics approval

The project had ethical approval and all patients were provided with an information sheet and gave written consent according to the Declaration of Helsinki. The study was approved by South East Research Ethics Committee REC Reference Number 07/MRE01/38.

2.3 Patient history of TN

Basic demographic data including ethnicity and social status were recorded. A note was made regarding the specialists seen prior to attendance. The medical history was ascertained from the primary care physician (GP) and particular note was made of conditions associated with TN and the presence of headaches, migraines and other chronic pain. All current and past treatments for TN were recorded including maximum doses and, where possible, efficacy and tolerability. Patients were asked about any history of bruxism (teeth grinding), jaw clenching habits and jaw clicking. Examination included a gross cranial nerve examination and sensory testing with light touch, cotton wool and pin-prick. The muscles of mastication were examined for tender spots to determine if a musculoskeletal temporomandibular disorder was present and an oral examination was done.

A history of the patient's experience was collected: duration; onset, including whether this was acute and memorable (i.e. could they remember the circumstances of the first attack); length of attacks; whether these were single stabs, a series of stabs in quick succession or more continuous 'saw tooth' [5]; whether any 'after pain' remained and its duration and characteristics; remission periods and their length; provoking factors (including whether attacks were only evoked or could be spontaneous). The pain location for the third division

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was noted and whether this remained only in the lower part of the face ie. Pre-auricular area down to the mental area or extended to the temporal region.

2.4 Patient questionnaires

Pain ascertainment

Patients completed the following questionnaires at their first visit: The Brief Pain Inventory [4,13] which uses a Lickert (1-10) scale to determine pain intensity and quality of life (an extended one was introduced later); The Graded Chronic Pain Scale (GGPS) [26] which uses a Lickert (1-4) scale to determine pain over last six months; The McGill pain questionnaire, where users select words that best describe their pain [18]; The Pain Catastrophizing Scale (PCS) [23] to assess catastrophizing (scores > 20 deemed 'significant').

Depression and anxiety ascertainment

The Hospital Anxiety and Depression scale (HAD) [32] scores > 8 significant replaced the DAPOS to assess depression which was used for the first year only; plus two NICE questions to screen for depression [22].

Data collection

Each patient was assigned a unique study ID number. A standardised data extraction form and simple UCLH/ University of Leeds TN patient data base was developed to facilitate the data collection. The patient data were transferred from the paper case report form into the TN database (quality of inputting audited). Patients were followed up via routine clinical consultations and self-completed questionnaires. All patients were seen by one clinician (JZ), with 58 (26%) also seen by a headache neurologist to independently validate the diagnosis. All patients had an MRI to exclude a symptomatic cause and identify potential neurovascular compression, some of which had been done prior to referral. Patients were managed according to the Facial Pain Unit protocol, similar to the recently published Danish protocol [9]. Questionnaires were collected at each routine visit.

2.5 Statistical Analysis

A case series analysis was performed. Summary statistics were used to describe the sample: means and standard deviations were provided for continuous variables and frequency distributions for categorical variables. One-way ANOVAs were used for continuous

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outcomes and chi-squared tests were used for categorical outcomes (significance level set at 5%). Pain severity was categorized as mild, moderate, or severe.

3. Results

A total of 237 patients were referred to the clinic between 2007 and 2015. Twelve of these patients (5.1%) had TN secondary to other causes and were excluded from further analysis. Nine of these 12 patients (6 women and 3 men) had multiple sclerosis before the onset of their TN, three had tumours.. The remainder (n = 225) were divided into three groups: Group 1 TN (n= 155) had TN without concomitant pain, Group 2 TNC (n=32) had TN with at least some concomitant pain and Group 3 TNA (n=38) had TN with autonomic system symptoms. Group 3 contained 13 patients that could be classified as SUNA/SUNCT with the rest having only intermittent autonomic symptoms. The 23 patients who had had previous surgery fell within Group 1 (n = 15), Group 2 (n = 3) and Group 3 (n = 5, with 3 patients having SUNA). Table 1 provides details of type of surgery they had and its effect.

[TABLE 1 AROUND HERE]

3.1 Baseline characteristics

The baseline demographic and clinical characteristics of the 225 patients are presented in Table 2. The mean (SD) age was 60.9 (12.5) years, and the median age [IQR] at first attack was 57.0 [46.0, 65.0] years. The median duration of TN was 4.0 [2.0, 7.0] years. There were no statistically significant differences in symptom duration or age between the three groups. There was a predominance of females (63.6%) within the population. There was a bias towards a higher socioeconomic position within the population, with over 70% of the patients having an index of multiple deprivation of 3 or less (1 = least deprived and 5 = most deprived). Two thirds of the patients (63.7%) had managerial or professional occupations according to the standard occupational classification (Office for National Statistics 2010).

[TABLE 2 AROUND HERE]

A family history of TN was reported by 13 (5.8%) of the patients. Nearly half of the patients (45.7%) were referred to the clinic by a primary care medical practitioner (GP), a fifth were referred by a dentist with the rest referred by specialists. There was not a statistically higher

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incidence of lower facial pain in those referred by a dentist. Prior to referral, the majority of the patients had already consulted a GP (80.0%) or dentist (71.6%). Many had used secondary dental (42.2%) or medical (58.7%) services and 32.5% had seen two or more dental or medical specialists. One hundred and fifteen patients (87.1%) had seen a neurosurgeon or neurologist or both.

3.2 Medical history and oral health

A quarter of patients had headaches and 44 had migraines or migraines with tension type headache (10 of these were in Group 3). Patients in all groups had a similar incidence of hypertension (37.3%) and other cardiovascular diseases (12.4%) and those proportions were lower than the population prevalence (hypertension 52.0% and cardiovascular disease 22%) of similar age (table 3). Fifty four patients (24.0%) reported bruxism but the frequency was not different between groups. The quality of oral hygiene was evenly distributed among poor (31.5%), moderate (28.9%) and good (31.5%) quality for 108 patients who were examined. Two hundred and eleven patients had partial/full dentition and only 24 (14.3%) patients had little conservation but all had evidence of some dental treatment. Oral health was not associated either with the duration of TN or pain severity.

[TABLE 3 AROUND HERE]

3.3 Pain characteristics

The pain locations for Group 1 (n = 155) and Group 2 (n = 32) were similar in all trigeminal divisions. In contrast, those patients in Group 3 (n = 38) had a significantly lower proportion of pain in the first division of the trigeminal nerve and third division (0% and 10.3%) but a higher proportion of pain in the second division (Table 4). Right-sided TN (65.6%) was twice as prevalent as left-sided TN (32.5%), while 1.9% of the patients had bilateral TN. All patients had extra-oral pain but 79.9% also reported intra-oral pain (whereas 68.6% reported only extra-oral pain) across all type of TN.

[TABLE 4 AROUND HERE]

Patients reported a variety of different types of attacks. The predominant type of attack was a single stab for all groups but a series of stabs was also frequently reported in Group 1 (36.4%) and Group 2 (31.3%) and patients would also report having a combination of these

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types. Pain severity was similar across the three types of TN. Less than 5% of patients in Group 1 and 3 could not recall the circumstances of the first attack while a fifth of Group 2 (79.3%) could not remember the circumstances (p-value = 0.001).

The pain frequency in TN is high with over 90% reporting daily pain attacks though only a small proportion reported attacks on an hourly basis. Very few patients reported attacks lasting more than a few minutes but 62% of Group 2 reported a prolonged after-pain.

Remission periods were reported consistently across the groups but were least likely to be in Group 3. Overall, the remission duration decreased with time. Nearly all patients had spontaneous pain but all had pain provoked by light touch on the face or intra-orally. A large proportion of patients across all TN types (30-60%; p-value = 0.05) could be provoked by cold wind or bodily movement. Four patients had attacks that could be provoked by noise or light and one patient had attacks that could be provoked by alcohol. Group 3 reported the most ipsilateral autonomic features (p-value = <0.001) and the most common ones were tearing, nasal stuffiness, redness of the cheek or eye, and these were all statistically different from the other groups (p-value <0.001) (see table 3). These were not observed but reported several times at follow ups.

The McGill pain questionnaire was fully completed by 193 of the 225 patients (85.8%). The words were analysed by sensory type (1-10), affective type (11-15), evaluative type (16) and miscellaneous type (17-20). The sensory words most commonly used by patients across all Groups were ‘shooting’ (84.5%), followed by ‘sharp’ (72.5%) and ‘stabbing’ (55.4%). More than 50% of patients choose a word from ‘fearful’, ‘frightful’ or ‘terrifying’. The evaluative and miscellaneous words most commonly chosen in all TN categories were ‘unbearable’ (45.1%) and ‘piercing’ (45.1%).

3.4 Treatment

Pharmacological management of TN was the most commonly reported treatment modality for TN. All patients received at least one medication for their facial pain before referral. A quarter of the patients (27.6%) had two medications while nearly half (46.7%) had used three or more medications. Prior to referral, the most frequently prescribed drug was carbamazepine (including retard type) 122/225 (54.2%) which also caused significant side

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effects. Opioids had been prescribed in 14.6% of the patients. Over 75% were put on anticonvulsants after the first consultation as shown in figure 1.

[FIGURE 1 AROUND HERE]

3.5 Impact of pain

Pain had a significant impact on health status, including functioning and well-being across all TN groups as shown in Table 4. On the NICE questions, 106/216 (49.1%) felt depressed and 101/216 (47.6%) had little pleasure in life. This correlated with the HAD results where 75/210 (35.7%) patients had mild to severe depression. More than 50% were anxious as indexed by the HAD. The Pain Catastrophizing Scale (PCS) showed that a significant proportion of patients with TN had considerable negative thoughts about their pain: 146/188 (77.7%) patients had a PCS score of 20 and over with a mean score of 36.4 (95% CI: 34.9-37.9).

Completion of the CGPS questionnaire (grading pain in the past 6 months) achieved 175/225 (77.8%) respondents. Ninety five of these patients (54.3%) had high and moderately or severely limiting disability (Grade III and IV). 89/198 (44.9%) patients were absent from usual daily activities (work, school or housework) 15 days or more in the past 6 months because of the facial pain. The CGPS was significantly associated with HAD -Anxiety ($p < 0.001$) and HAD -Depression ($p < 0.001$) using Pearson's Chi-square test, table 5.

[TABLE 5 AROUND HERE]

On the Brief Pain Inventory (BPI)–Facial, reporting pain intensity and impact in the week prior to assessment, two thirds (66.3%) of patients reported moderate (score of 4-7) or severe (score of 7-10) overall pain within the prior 24 hours and the mean overall Pain Severity Index scores for 194 patients was 3.9 (95% CI: 3.6-4.3), indicating a mild to moderate level of pain. The pain severity was significantly associated with HAD-Depression ($p = 0.022$) but not HAD -Anxiety ($p = 0.163$) using Pearson's Chi-square test table 6.

[TABLE 6 AROUND HERE]

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The mean pain interference on the BPI was higher (mean = 4.9) when the facial domains were assessed. The pain interference was more salient for 110 patients who also reported pain interference on seven face related daily activities (mean 4.9, 95% CI: 4.3-5.5). Pain severity significantly affected general activity, mood and enjoyment of life (Figure 2). Sleep was affected for those with severe pain, with thirty five patients reporting that pain affected their sleep. Pain severely interfered with all daily activities, especially activities involving the face (such as eating a meal, brushing or flossing teeth and eating hard food like apples) as seen in Figure 3.

[FIGURE 2 AND 3 AROUND HERE]

4. Discussion

The reported research represents the largest and most comprehensive biopsychosocial prospective study on TN that has been conducted to date.

4.1. Population characteristics

The study involved a population of patients with TN who attended a specialist clinic. In this regard, the population may not be representative of the general TN population (as less severe cases may not end up at such a specialist clinic). Indeed, the average socioeconomic position of the population was skewed away from the greatest levels of deprivation. It seems likely that TN (like most other diseases including multiple sclerosis) would be over represented in lower socioeconomic positions. Thus, the population reported within this paper are probably overrepresented with those who could utilise social capital to attend the clinic. Patients access many health care professionals prior to referral to a specialist clinic. These clinics can provide appropriate treatment but over 37% of those visiting a dentist get dental treatment which is often irreversible (such as root canal treatments and extractions) which contribute to the burden [16]. Garvan and Siegfried [6] reported that in their series of 140 patients 67 patients had 680 teeth extracted. Patients with only intraoral pain may obtain continuing care from dental practitioners and not be referred whereas patients in Group 3 may be more complex and less responsive to carbamazepine and so referred in earlier. Repeated consultations and inappropriate use of medications (despite numerous guidelines) add to the economic costs to the providers and the patients.

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4.2 TN variants

The participants were considered as falling within one of three groups. Group 1 had TN without concomitant pain, Group 2 had TN with concomitant pain and Group 3 had TN with autonomic symptoms. We hypothesised that the different groups would show disparate pain profiles. There were clear differences between the groups. Group 3 were more likely to have a lower proportion of pain in the lower part of the face and had prominent autonomic symptoms. Groups 1 and 2 were more likely to experience a series of stabbing pains, with Group 2 more likely to experience a prolonged after-pain and were less likely to recall the circumstances of their first attack. We observed in our cohort that 68.4% had TN without concomitant pain and 14.2% had TN with at least some concomitant pain and 30% had attacks lasting minutes rather than seconds – this was a distinctive difference to the Maarbjerg et al [15] cohort who had 49% with concomitant pain. This might be explained by differing clinical referral processes to a specialist headache neurology clinic compared to ours , a specialist facial pain clinic within a dental school[15]. Haviv et al [8] hypothesised that length of individual pain attacks correlates to presence of background pain - a similar finding to this cohort. They reported that 87% of those with attack duration of over 2 minutes (n= 20) had background pain whereas this was 30% in those with shorter attacks. Bowsher [3] reported that 50% of 50 patients who had prior surgery reported longer attack duration but, in the present study, the 10.2% who had undergone surgery were not significantly different from the rest of the population (except for having consulted more specialists).

In agreement with other studies, our work shows that autonomic features are often present and this is reflected in emerging data showing that SUNCT, SUNA and TN may be variants of the same disorder [12,25]. Patients did report some altered sensation and this was highest in Group 2. This may be of importance as a recent study has suggested that classical TN (Group 1) may have sub-clinical hypoesthesia whereas those with concomitant pain (Group 2) were more likely to have more clinically detectable sensory changes but all had sensory changes not just on the side of pain but also on the opposite side and in other parts of the body suggesting central sensitisation [28]. What still needs to be established is whether patients move between the different groups during the course of disorder.

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4.3 Clinical characteristics

This study has provided useful information on the clinical characteristics of TN patients. Our results concur with a large UK population study that showed greater prevalence in women and a higher occurrence of right-sided symptoms and pain in second and third divisions that is consistent with the somatology relationship of sensory fibres in the trigeminal nerve Hall et al [7]. The study has highlighted that pain in the third division may only involve the lower branches and not the temporal branches does not always extend to the entire third division and is often present only in the lower division as proposed by Henderson [10] who suggests a mouth –ear zone and nose-orbit zone. Other features, including the McGill pain descriptors, are similar to other studies reporting on phenotypic features [3,8,16] and highlights the frequent use of words like "fearful" and "terrifying". Fear could be a driver for the spontaneous pain rather than evoked pain as shown in a small fMRI study done with patients with classical TN, where patients were told that their pain would be triggered during the examination [20].

4.4 Management

Pharmacological management is the most commonly used treatment modality for patients with TN. The anticonvulsant class (particularly carbamazepine) is considered the gold standard treatment [30]. It is clear though that a wide range of drugs are being provided to TN patients and over 75% have used more than one drug prior to referral with 21% having used four or more. The prescribed drugs include opioids despite the lack of any evidence that these drugs are effective in TN. Despite all the guideline recommendations only 54% of the patients were or had used carbamazepine which agrees with Hall et al's [7] survey of primary care management of TN (where the figure was 58%). An additional 37 patients were prescribed this drug after their attendance at the clinic and other non-effective drugs were stopped. This suggests that large numbers of TN patients outside specialist clinics are not being provided with the optimal drug regime which adds to the burden of their disease. The effectiveness of carbamazepine/retard was witnessed by the fact that 91.8% of the patients taking this drug reported that it was partially or completely effective. Unfortunately, 42.8% of these patients reported significant side effects which is to be expected as all these drugs result in side effects - especially cognitive side effects [2].

4.5 Burden of disease

The results of the present study provide further empirical evidence that patients with TN suffer considerable pain and disability – even when prescribed the optimal drug regimen. We hypothesised that the high levels of pain would produce disability as defined by the WHO's

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International Classification of Disability. The data showed unambiguously that patients with TN experience considerable activity limitation and the limitation is particularly pronounced with activities that involve the face (e.g. eating a hard piece of food, such as an apple). Moreover, there was a relationship between pain and the ability of the patients to participate. We found evidence that over 50% of the patients had to take significant time off work which has a significant economic impact as the median age for the start of the TN is 57 and over 50% are still in employment. This has never previously been reported. The disability experienced by patients with TN is consistent with the high levels of anxiety and depression recorded within this population. Fear, unpredictability of the pain attacks and lack of confidence in dealing with flare ups results in high catastrophizing scores.

The quantitative data in the present study are consistent with the qualitative data reported in Allsop et al [1]. The overall picture suggests a population who have a high chance of experiencing excruciating pain, leading to activity limitation and participation restriction. These findings suggest that patients with TN should be offered psychological support –this is not routinely provided at present. A multidisciplinary approach for pain management (including, for example, Cognitive Behavioural Therapy) can be effective for pain control, developing coping skills and restoration of functional status. It is important that patients with TN are provided with an individualised pain management programme that is not limited to pharmacological or surgical interventions alone.

5. Conclusions

We conclude that patients with TN are experiencing a poor quality of life even when being treated with the optimal drug regimen. This suggests an urgent need to evaluate alternative treatment pathways (such as newer medications, psychological support, earlier surgical interventions and access to newer surgical innovations such stereotactic radiosurgery, neuromodulation). For example, Lee et al [14] have suggested that surgical management can significantly improve quality of life in patients with TN when assessed using the Brief Pain Inventory –Facial. The data presented in the current manuscript provides a starting point for evaluations of the true health burden and cost of TN.

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Legends for Figures

Figure 1. Medication type prescribed before and after referral. Legend: sky blue-Antibiotics, red-Anticonvulsant, grey-Antidepressants, orange-Analgesics, blue-OTC Analgesics, black-Opioids, dark blue-Others

Figure 2. Association between Pain Severity and Interference on Health Status Domains and general daily activities. Legend: sky blue-Mild (1-3), orange-Moderate (4-6), grey-Severe (7-10). * means $p < 0.001$.

Figure 3 Association between Pain Severity and Interference on Health Status Domains and general daily activities including facial status. Legend: sky blue-Mild (1-3), orange-Moderate (4-6), grey-Severe (7-10). * means $p < 0.001$.

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Table 1 Surgery type and effectiveness for 23 patients

	Effectiveness (n)		
Surgery type	**Complete**	**Partial**	**No effect**
Gamma Knife	3	0	0
Glycerol	4	5	2
MVD	5	5	0
Peripheral	1	0	1
RFT	3	0	2

Note: some patients had multiple surgeries

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Table 2 Characteristics for 225 TN patients.

Characteristic	Value (n = 225)
Age in years, mean (SD)	60.9 (12.5)
Age at first attack, median [IQR]	57.0 [46.0, 65.0]
Duration of TN in years, median [IQR]	4.0 [2.0, 7.0]
Female	143 (63.6)
Ethnicity	
Asian	25 (11.0)
Caucasian	189 (83.5)
Others	12 (5.5)
Index of multiple deprivation	
1 (least deprived)	64 (28.4)
2	47 (20.9)
3	47 (20.9)
4	42 (18.7)
5(most deprived)	25 (11.1)
Profession classification	
Higher managerial, administrative and professional occupations	28 (12.6)
Intermediate occupations	52 (23.3)
Lower managerial, administrative and professional occupations	62 (27.8)
Lower supervisory and technical	10 (4.5)

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occupations	
Routine occupations	18 (8.1)
Semi-routine occupations	34 (15.2)
Small employers and own account workers	7 (3.1)
Unemployed	12 (5.4)
Employment status	
Employed full time	82 (36.6)
Employed part time	21 (9.4)
Full time homemaker	13 (5.8)
Retired	96 (42.9)
Unemployed	12 (5.4)
Referrer to specialist clinic	
Dentist	46 (20.6)
GP	102 (45.7)
Specialist	75 (33.6)
Family history of TN	13 (5.8)
Previous services used	
GP	180 (80.0)
Dentist	161 (71.6)
Dental Service	95 (42.2)
Dental Specialist	29 (12.9)
Oral Surgeon	74 (32.9)

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Dental Procedures	17 (7.6)
Medical Service	132 (58.7)
ENT surgeon	13 (5.8)
Neurosurgeon	43 (19.1)
Neurologist	83 (36.9)
Physician	23 (10.2)
Psychiatrist	1 (0.4)
Psychologist	2 (0.9)
Pain Specialist	14 (6.2)
Other medical procedures	34 (15.1)
No. of secondary dental or medical services	
0	40 (17.8)
1	112 (49.8)
2	53 (23.6)
3+	20 (8.9)

Note: values are presented as frequency (%) unless specified.

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Table 3 Associated factors and medical history stratified by the type of TN

Associate factors and medical history	Group 1 TN n = 155	Group 2 TNC n = 32	Group 3 TNA n = 38	P-trend
Altered sensation or numbness	39 (25.3)	12 (40.0)	11 (28.9)	0.258
Any autonomics unilateral	86 (55.5)	17 (53.1)	38 (100.0)	<0.001
Swelling face	19 (12.3)	3 (10.0)	12 (31.6)	0.009
Redness of the face	14 (9.1)	2 (6.7)	13 (34.2)	<0.001
Nasal stuffiness/runny	17 (11.0)	4 (13.3)	23 (60.5)	<0.001
Eye redness	6 (3.9)	1 (3.3)	12 (31.6)	<0.001
Eye tearing	18 (11.7)	7 (23.3)	22 (57.9)	<0.001
Oedema eyelid	4 (2.6)	1 (3.3)	7 (18.4)	<0.001
Earache	13 (8.4)	1 (3.3)	3 (7.9)	0.628
Fullness ears	8 (5.2)	3 (10.0)	6 (15.8)	0.080
Headaches	37 (24.0)	6 (20.0)	10 (26.3)	0.829
Migraines	17 (11.0)	3 (10.0)	7 (18.4)	0.426
Migraines + TTH	12 (7.7)	1 (3.1)	3 (7.9)	0.638

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Bruxism	36 (23.7)	8 (26.7)	10 (26.3)	0.906
Medical history				
Hypertension	57 (36.8)	14 (43.8)	13 (34.2)	0.690
CVS	19 (12.3)	4 (12.5)	5 (13.2)	0.989
Diabetes	10 (6.5)	2 (6.2)	0 (0.0)	0.276
Deafness	17 (11.0)	1 (3.3)	2 (5.3)	0.272
Ringing ears	18 (11.7)	0 (0.0)	2 (5.3)	0.083
Other chronic pain	33 (21.3)	9 (28.1)	8 (21.1)	0.686
Neck pain	15 (9.9)	4 (13.3)	4 (10.5)	0.857
Back pain	23 (15.1)	5 (17.2)	5 (13.2)	0.898
Previous surgery TN	15 (9.7)	3 (9.4)	5 (13.2)	0.806

Note: values are presented as frequency (%); P-trend represents comparison across three groups.

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Table 4 Pain characteristic stratified by the type of TN

Pain characteristic	Group 1 TN n = 155	Group 2 TNC n = 32	Group 3 TNA n = 38	P-trend
V1	3 (1.9)	0 (0)	0 (0)	0.496
V2	35 (22.7)	6 (18.8)	13 (33.3)	0.289
V3	52 (33.8)	14 (43.8)	4 (10.3)	0.005
V1 + V2	8 (5.2)	4 (12.5)	9 (23.1)	0.002
V2 + V3	46 (29.9)	7 (21.9)	9 (23.1)	0.516
V1 + V2 + V3	9 (5.8)	1 (3.1)	4 (10.3)	0.438
Right	101 (65.6)	18 (56.2)	30 (76.9)	0.720
Left	50 (32.5)	13 (40.6)	9 (23.1)	0.106
Bilateral	3 (1.9)	1 (3.1)	0 (0.0)	0.587
Intra oral	123 (79.9)	26 (81.2)	34 (87.2)	0.578
Extra oral	83 (68.6)	17 (65.4)	22 (62.9)	0.802
Predominant type of attack				0.116
Single stab	71 (46.1)	11 (34.4)	18 (46.2)	
Series of stabs	56 (36.4)	10 (31.3)	9 (23.1)	

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Saw tooth	8 (5.2)	6 (18.8)	4 (10.3)	
Single stab + Series of stabs	19 (12.3)	5 (15.6)	8 (20.5)	
Pain severity, median [IQR]				
Worse	10.0 [8.0, 10.0]	9.0 [7.0, 10. 0]	10.0 [8.0, 10.0]	0.715
Average	5.0 [3.0, 7.0]	6.0 [4.0, 8.0]	5.0 [3.0, 7.0]	0.298
Least	0.0 [0.0, 3.0]	2.0 [0.0, 6.0]	2.0 [0.0, 5.0]	0.043
Circumstances				0.001
Acute	48 (34.0)	10 (34.5)	11 (30.6)	
Memorable	60 (42.6)	4 (13.8)	20 (55.6)	
Slow to develop	27 (19.1)	9 (31.0)	4 (11.1)	
Cannot remember	6 (4.3)	6 (20.7)	1 (2.8)	
Frequency of pain attack				0.865
Hourly	11 (8.7)	1 (4.0)	2 (6.2)	
Daily	115 (91.3)	24 (96.0)	30 (93.8)	
Duration of attacks				0.872
Seconds	105 (69.5)	20 (66.7)	24 (61.5)	
Minutes	42 (27.8)	9 (30.0)	13 (33.3)	

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1-4 hours	4 (2.6)	1 (3.3)	2 (5.1)	
Pain after main attack	50 (36.0)	20 (62.5)	17 (45.9)	0.020
Length of remission				0.385
None	12 (9.0)	2 (6.7)	6 (17.1)	
Days	16 (11.9)	1 (3.3)	3 (8.6)	
Weeks	70 (52.2)	14 (46.7)	16 (45.7)	
Months	23 (17.2)	6 (20.0)	5 (14.3)	
Years	13 (9.7)	7 (23.3)	5 (14.3)	
Remission period change				0.470
No change	42 (31.6)	5 (19.2)	14 (37.8)	
Shorter	84 (63.2)	18 (69.2)	21 (56.8)	
Longer	7 (5.3)	3 (11.5)	2 (5.4)	
Provoking factors				
Spontaneous pain	151 (98.1)	32 (100.0)	38 (97.4)	0.690
Provoked by light touch	143 (92.9)	29 (90.6)	39 (100.0)	0.187
Provoked by other factors				
Cold wind/weather	80 (51.9)	10 (31.2)	23 (59.0)	0.050

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Bodily movement	65 (42.2)	12 (37.5)	24 (61.5)	0.063
Noise or light	3 (1.9)	0 (0.0)	1 (2.6)	0.690
Alcohol	1 (0.6)	0 (0.0)	0 (0.0)	0.793
McGill pain questionnaire				
Number of words chosen (mean ± sd)	10.3 ± 3.8	12.2 ± 3.9	12.3 ± 2.8	0.003
Pain rating index (mean ± sd)	27.7 ± 12.1	32.8 ± 14.4	31.9 ± 8.4	0.044
Sensory groups	Shooting (110)	Shooting (24)	Shooting (29)	
	Sharp (93)	Sharp (21)	Sharp (26)	
	Stabbing (73)	Stabbing (14)	Stabbing (20)	
Affective	Vicious (43)	Terrifying (8)	Wretched (13)	
	Terrifying (39)	Fearful (6)	Fearful (12)	
Evaluative	Unbearable (58)	Unbearable (16)	Unbearable (13)	
Miscellaneous	Piercing (57)	Piercing (14)	Piercing (16)	
HAD-Anxiety				
Nil	72 (53.3)	16 (59.3)	8 (22.2)	
Mild	29 (21.5)	3 (11.1)	18 (50.0)	0.001
Severe	34 (25.2)	8 (29.6)	10 (27.8)	

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HAD-Depression				
Nil	95 (69.3)	19 (70.4)	16 (44.4)	
Mild	21 (15.3)	5 (18.5)	8 (22.2)	0.047
Severe	21 (15.3)	3 (11.1)	12 (33.3)	
Brief pain inventory, median [IQR]				
Pain severity index	3.50 [2.00, 5.25]	3.50 [2.25, 6.25]	5.00 [3.25, 6.31]	0.090
Pain interference-general daily life	2.71 [1.14, 5.29]	3.14 [0.57, 4.57]	3.29 [1.71, 6.00]	0.380
Pain interference-facial status	4.57 [2.07, 7.14]	7.00 [2.43, 7.86]	5.93 [2.21, 7.71]	0.349

Note: values are presented as frequency (%) unless specified; P-trend represents comparison across three group

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Table 5 Association between HAD-anxiety and depression and graded chronic pain scale in patients with trigeminal neuralgia and its variants.

	Graded chronic pain scale			
HAD-Anxiety	Grade 1	Grade 2	Grade 3	Grade 4
Nil	19	30	13	19
Mild	2	17	5	17
Severe	1	5	7	25
HAD- Depression				
Nil	18	41	19	26
Mild	3	5	3	16
Severe	1	6	5	19

Pearson's Chi-square test: p-value < 0.001

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Table 6 Association between HAD-anxiety and depression and Brief Pain Inventory (BPI) pain severity in patients with trigeminal neuralgia and its variants.

	BPI pain severity			
HAD-Anxiety*	No pain/ not reported	Mild	Moderate	Severe
Nil	12	29	33	11
Mild	3	12	21	10
Severe	1	14	20	12
HAD- Depression**				
Nil	12	42	41	17
Mild	3	6	22	5
Severe	2	8	11	11

*Pearson's Chi-square test: p-value = 0.163 **Pearson's Chi-square test: p-value = 0.022

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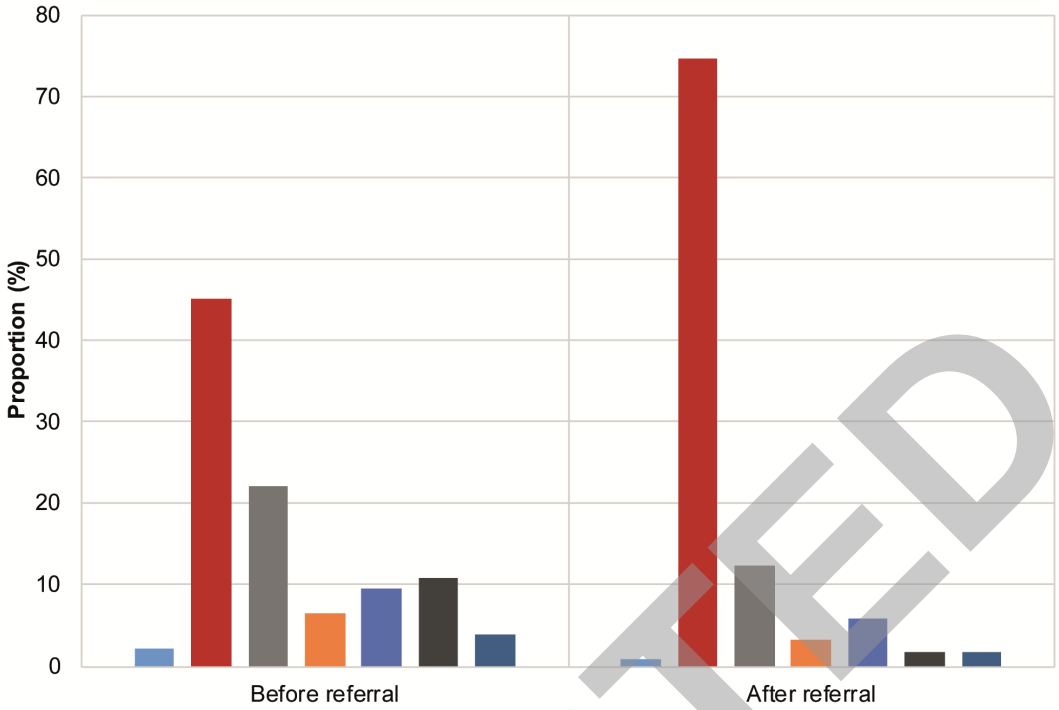

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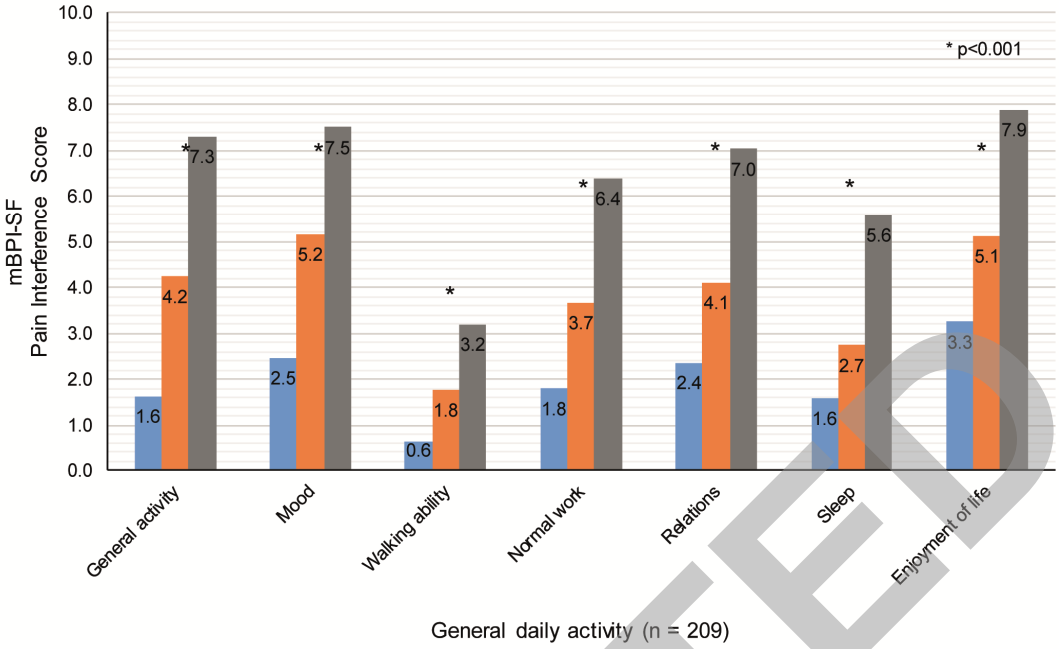

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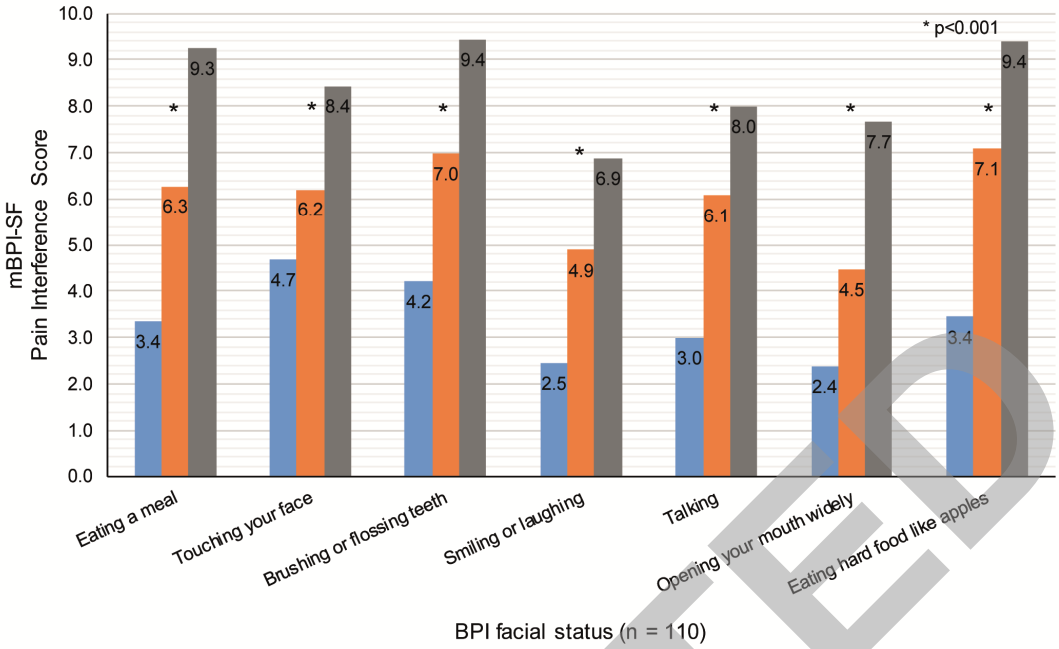

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