Associations Between Chronic Pain and Depressive Symptoms in Patients With Trigeminal Neuralgia

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Key words: *trigeminal neuralgia; chronic pain; depression.*

Summary. *Trigeminal neuralgia (TN) is a rare neuropathic disorder with an excruciating facial pain. The unpredictable pain attacks may result in anxiety and depression.*

The aim of this study was to determine and to evaluate the level of chronic facial pain and its association with the appearance of anxiety and depression.

Materials and Methods. A total of 30 patients with TN and chronic facial pain (group A, 25 women and 5 men; mean age, 64.2±3.2 years) and 30 with atypical facial pain (group B, 26 women and 4 men; mean age, 64.8±1.9 years) were examined. A standardized diagnostic protocol was applied to all of them, which consisted of the following: 1) demographic data and estimation of overall pain on a visual analog scale; and 2) evaluation of emotional status using the Sheehan Disability Scale, Covi's Anxiety Scale, and Beck Depression Inventory.

Results. The intensity of facial pain was much higher in the group A than the group B (89.7±2.5 versus 44.0±2.9, P<0.0001). Besides, the group A reported increased scores on the disability and anxiety symptom scales (17.4±1.3 and 9.7±0.3 vs. 6.4±0.7 and 3.6±0.1, respectively, P<0.0001). Severe (46.7%) or moderate (30%) levels of depression were documented in the majority of patients in the group A, while the group B did not show depressive symptoms (P<0.0001).

Conclusions. Patients with TN and chronic facial pain had a significantly higher level of pain perception, and they presented the higher level for anxiety and depression than those with atypical facial pain. A multidisciplinary approach is needed for the additional assessment of emotional status of patients in order to improve the efficacy of treatment and patients' quality of life.

Introduction

The International Association for the Study of Pain (IASP) defines trigeminal neuralgia (TN), also known as "tic douloureux," which means "painful spasm," as a severe unilateral paroxysmal facial pain in the distribution of one or more of the branches of the fifth cranial nerve (1). TN, which affects the trigeminal nerve, may have a multifactorial etiology (2). Although compression of the nerve root is the most commonly reported cause of the disorder, most cases are idiopathic (3). The pain can be triggered by touching the face, brushing teeth, chewing, or even by talking and is commonly described as sudden, severe, or electric shock-like. Each pain episode generally lasts only a few seconds and occurs irregularly. However, the sudden attacks of pain may be repeated one after the other. The patient is usually asymptomatic between paroxysms, but dull background pain may persist in some cases (4, 5). Pain-free periods may last for several months or years.

TN is rare, and therefore, the statistical data concerning this disease are scarce. Mostly, TN affects the older individuals, perhaps because their tolerance to pain declines with age. The peak onset of the disorder occurs between the age of 50 and 70 years, and the early literature suggests a higher prevalence in women (60%) than men (2, 6). On the other hand, the other studies have found no sex difference and have shown variability in the prevalence across the age groups (7). More recently, due to changing lifestyle and occupations, pain disorders are becoming more prevalent in the younger populations, since there is an increase in work-related injuries in, for example, information technology industry, leading to persistent pain syndromes. However, the disorder can also occur in children (8). The youngest child reported to have TN was only a 1-year-old infant (8). Patients with multiple sclerosis may develop TN as a secondary symptom, but this happens quite rare (in 1% of cases) (9).

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TN is often considered to be one of the most painful conditions observed in medicine and is accompanied by severe limitations in the patient's quality of life (10). Chronic pain is one of the main causes of physical and psychological distress (11). The rates of depression in the patients with facial pain are higher and cause intense suffering and anxiety (12). However, different orofacial pains may induce variable levels of anxiety and depression (13–15). The mechanisms leading to the development of chronic facial pain not related to dentoalveolar or musculoligamental disorder are not well understood. Understanding the psychological processes that underlie the development of a chronic pain problem is important in order to improve prevention and treatment (16). To date, however, there are inconsistent data, which difficult to interpret, whether depression is more severe in TN patients with chronic facial pain. Thus, the aim of this study was to determine and evaluate the level of chronic facial pain and its associations with anxiety and depression in TN patients.

Materials and Methods

Study Population. This study was conducted in the Department of Maxillofacial Surgery, Hospital of the Lithuanian University of Health Sciences, and carried out in accordance with the institutional guidelines confirmed by the local Ethics Committee. All patients were older than 18 years; all of them agreed to participate in the anonymous study and gave verbal informed consent. All patients selected for the study had pain in the region of the trigeminal nerve and were divided into 2 groups according the presence or absence of chronic facial pain as the main complaint: group A comprised 30 patients (25 women and 5 men; mean age, 64.2±3.2 years; range, 29 to 100 years) with TN and chronic facial pain. Chronicity was defined as TN with persistent, dull background facial pain with superimposed, typical neuralgic, paroxysmal TN attacks. The group B comprised 30 patients (26 women and 4 men; mean age, 64.87±1.88 years; range, 36 to 84 years) with atypical facial pain, i.e., without chronic pain and without history of neurological or psychiatric disorders. The exclusion criteria for both groups were previous diagnoses of psychosis, dementia, delirium, which could compromise data collection. No patients withdrew during the period of the study.

Procedures. In the first part of the study, all targeted patients completed a self-administrated questionnaire (Table 1). It consisted of an interview on demographic data (age, gender, body weight, education level, marital status, etc.) and systematic evaluation of pain, based on the following criteria: pain perception (location, intensity, duration, etc.), self-reported symptoms (orofacial pain), limitations of daily activity, medical history, and self-evaluation of overall pain on a visual analog scale (VAS) (17) to measure the intensity of pain. The guidelines of the Lithuanian Ministry of Health (No. V-608, 26/08/2004) suggest the following interpretation of the levels of pain severity (in mm): minimal (0–9), mild (10–39), moderate (40–59), severe (60–89), and excruciating or severest (90–100). Patients were asked to indicate the severity of their pain by placing marks on a 100-mm line, where 0 indicated no pain and 100 indicated pain as severe as the patient could imagine.

In the second part of the study, clinical examination was performed: the evaluation of emotional status by using the Sheehan Disability Scale (SDS),

Table 1. Demographic Data and VAS Scores of Patients With Trigeminal Neuralgia and Chronic Facial Pain (Group A) and With Atypical Facial Pain (Group B)

Characteristic	Group A n=30	Group B n=30	*P*
Age, mean±SEM (range), years	64.20±3.20 (29–100)	64.87±1.88 (36–84)	0.858*
Women, n (%)	25 (83.3)	26 (86.7)	0.718**
Men, n (%)	5 (16.7)	4 (13.3)	
Body mass index, mean±SEM, kg/m^2	26.45±1.19	25.14±0.58	0.813***
Educational level, n (%)			0.191**
No education	8 (26.7)	3 (10)	
Secondary education	16 (53.3)	22 (73.7)	
Higher education	6 (20)	5 (16.7)	
Marital status, n (%)			0.386**
Single	1 (3.4)	4 (13.3)	
Married	23 (79.3)	23 (76.7)	
Widower	5 (17.2)	3 (10)	
VAS, mean±SEM, score	89.7±2.47	44.0±2.98	<0.0001***

VAS, visual analog scale: pain was assessed by assigning scores from 0 (no pain) to 100 (the severest pain imaginable). Means were compared using the Student *t* test (*), chi-square (χ^2) test (**), and Mann-Whitney *U* test (***).

Covi's Anxiety Scale (CAS), and Beck Depression Inventory (BDI) was performed.

The SDS was used as a measure of global functioning (18). This scale assesses the patient's functional impairment in 3 domains: work/school, social life/leisure activities, and family life/home responsibilities. Response categories for each of the three items range from 0 to 10, with higher values indicating greater disruption in the respective area of life. The total score is obtained by summing up the first 3 items (work, social life, and family life) and ranges from 0 (no disability) to 30 (extreme disability). The SDS global functioning scores ($\geqslant$5) were associated with impairment due to illness (19).

The CAS was used to evaluate the severity of anxiety (20). This self-administered scale consists of three items, which are rated on 5-point Likert scales, and ranges from 1 (never happens or is never present) to 5 (always happens or is always present). The items explore verbal communication, behavior, and secondary complaints. The total score represents the sum of all items and ranges from 3 to 15. A score greater than 9 indicates significant anxiety.

The BDI was also used to assess the severity of depressive symptoms (19). The BDI contains 21 items, each with a series of 4 statements. The statements describe the severity of symptoms from absent or mild (a score of 0) to severe (a score of 3). The scores of depression severity were obtained by summing up the scores of the items endorsed from each item set. The total score ranges from 0 to 63, with higher scores indicating greater symptom severity. The most recent guidelines suggest the following interpretation of the severity scores: minimal (0–9), mild (10–16), moderate (17–29), and severe (30–63) (21).

Statistical Analysis. Statistical analysis was performed using the Statistical Package for Social Sciences (SPSS/w13.0). Mean and standard errors of the mean (SEM) were used to describe continuous data. The normality of the distributions of continuous variables from the self-reported facial pain intensity and VAS, SDS, CAS, and BDI levels was verified using the Kolmogorov-Smirnov test. Differences between two independent groups were determined using the Mann-Whitney *U* test. The Student *t* test was used for comparisons, when appropriate. Nonnormally distributed data were compared using nonparametric statistics. Interdependence of qualitative attributes was evaluated by applying the precise chi-square (χ^2) criterion (for small samples) and asymptotic χ^2 criterion. Depending on the sample size, the comparison of probabilities was performed by applying the precise Fisher criterion and normal approximation criterion. The relationship of separate risk factors (i.e., anxiety and depression) in dependence on pain severity was analyzed using unvaried logistic regression techniques. Odds ratios (OR) and their 95% confidence intervals (CI) were calculated. Correlation analysis was performed using the Spearman rank correlation. Two-tailed *P* values of less than 0.05 were considered significant. Age- and sex-specific parameters were also calculated. Body mass index was calculated as weight (kg) divided by the square of height (m^2).

Results

Demographic data of the patients with TN and chronic facial pain (group A) and with atypical facial pain (group B) are shown in Table 1. Both the groups were similar by age and gender or educational level, and no significant differences in these baseline characteristics were observed ($P>0.05$). According to the data obtained from the self-administered questionnaire, the prevalence of reported facial pain in both groups was almost the same among men and women; therefore, in the further research, these data were not separated. However, obvious differences were seen when the VAS was applied for the identification of pain intensity. As Table 1 shows, the intensity of facial pain was about twice higher in the patients of group A (89.7±2.5) vs. group B (44.0±2.9) ($P<0.0001$). In the group A, patients identified their facial pain intensity as the severest pain imaginable (n=21, 70%), severe pain (n=8, 26.6%), and moderate pain (n=1, 3.3%) according to the VAS. All the patients in the group A had symptoms of unilateral pain, mainly located on the right side, and pain was experienced from 1 to 30 years (mean duration, 7.4±1.47 years). General characteristics of pain in the patients of group A are outlined in Table 2. The majority of them reported pain in the trigeminal nerve mandibular branch region (n=19, 63.3%), while fewer patients reported pain in other regions innervated by the trigeminal nerve, i.e., in the maxillary branch region (n=7, 23.33%), ophthalmic-maxillary branch region (n=2, 6.66%), and maxillary-mandibular branches region (n=2, 6.66%). Up to 50% of these patients suffered from prickly, shooting, and burning pain attacks, but only a few of them had breaking pain attacks, which lasted about 5 minutes. However, long-lasting pain attacks (30–60 min) were indicated by fewer patients. Pain in all patients of group A was accompanied with other troublesome complaints; the main of them were awakening (n=25, 83.3%), sleep disturbance (n=22, 73.3%), fear (n=20, 66.7%), and worry (n=23, 76.7%). More than half of them complained of tiredness and weight loss as well, but only 8 (26.7%) consulted with a psychiatrist because of excruciating pain, disability, and depression, and they already used psychotropic drugs. Other patients in the group A (n=22, 73.3%) had not visited a psychiatrist before, and they had used nonsteroidal anti-inflammatory drugs (ibuprofen or

Table 2. Pain Characteristics of Patients With Trigeminal Neuralgia and Chronic Facial Pain (Group A)

Characteristic	Value
Duration, mean±SEM (range), years	7.4±1.47 (1–30)
Intensity of pain, mean±SEM (range), score	89.7±2.47 (0–100)
Quality, %	
Prickly	46.7
Shooting	43.3
Burning	43.3
Edgy	26.7
Gnawing	26.7
Breaking	10
Side, %	
Right	70
Left	30
Location (trigeminal nerve branches), %	
V1	0
V2	23.33
V3	63.33
V1–V2	6.66
V2–V3	6.66
Duration of the paroxysm, %	
5 minutes	36.7
10 minutes	23.3
30 minutes	13.3
60 minutes	10.0
Pain between attacks, %	
Pain-free	66.7
Dull ache	46.7
Pain provocative agent, %	
Frost	40
Eating	26.7
Touching	20
Pain-relieving agent, %	
Rest	20
Drugs	10
Pain-reducing drugs, %	
Antiseizure drugs	63.3
Nonsteroidal anti-inflammatory drugs	26.7
Accompanying symptoms, %	
Awakening	83.3
Sleep disturbance	73.3
Fear	66.7
Worry	76.7
Tiredness	56.7
Anorexia	56.7

V1, ophthalmic branch; V2, maxillary branch; V3, mandibular branch.

nimesulid) and anticonvulsant drugs (carbamazepine) for pain relief. On the other hand, none of the patients (0%) in the group B complained of facial pain as excruciating or severest, while some of them indicated their pain as severe (n=11, 36.67%), moderate (n=10, 33.3%), and mild (n=9, 30%). Some patients in the group B did not use medications at all, and only part of them used nonsteroidal anti-inflammatory drugs.

During the second part of examination, the data on emotional status and patient's quality of life of both groups were collected. The least square mean changes ± SEM from the baseline for the SDS total score in both groups are presented in Table 3. There

Table 3. Clinical Data of Patients With Trigeminal Neuralgia and Chronic Facial Pain (Group A) and With Atypical Facial Pain (Group B)

Measure	Group A n=30	Group B n=30	*P**
SDS (Sheehan disability scale)	17.43±1.257	6.40±0.680	<0.0001
CAS (Covi's anxiety scale)	9.67±0.326	3.63±0.141	<0.0001
BDI (cognitive-affective subscale)	27.17±1.797	3.73±0.380	<0.0001

Values are mean ± standard error of the mean.
*Mann-Whitney *U* test.

were significant differences in the total SDS score and its individual items comparing patients of both groups ($P<0.0001$). The same tendency was noted for the mean CAS scores, which were significantly different between both the groups: 9.67±0.33 in the group A and 3.63±0.14 in the group B ($P<0.0001$). At the same time, the depression level using the BDI was assessed as well. The mean BDI score in the group A was 27.17±1.79, whereas in the group B, it was 3.73±0.38 (Table 3). This study showed that the depression levels in both groups were significantly different ($P<0.0001$). In the group A, only one patient (n=1, 3.33%) was without depression symptoms, while the majority of all these patients rated depression as severe (n=14, 46.7%) or moderate (n=9, 30%). Meanwhile, in the group B, all the patients (n=30, 100%) had normal levels of depression, i.e., there were no depressive symptoms observed. According to our data, the SDS, CAS, and BDI scores (Table 3) as well as the VAS values (Table 2) were much higher ($P<0.0001$ for each scale) in the group A than the group B.

The logistic regression analysis clearly showed that severe depression and disability symptoms were significant risk factors for pain intensity. In patients with depression symptoms, the risk of severest possible pain was increased 1.1-fold ($P=0.028$), whereas in case of severe depression, up to 51.2-fold ($P=0.046$). There was a significant positive correlation between depression level and VAS scores ($r=0.47$, $P=0.008$).

Discussion

The present study describes the characteristics of facial pain in 60 persons referred to the Department of Maxillofacial Surgery, Hospital of the Lithuanian University of Health Sciences (former Kaunas University of Medicine), in 2008 because of sudden and severe lancinating facial pain. After thorough clinical examinations, 30 (50%) of them fulfilled the typical pain characteristics, defined for TN by the IASP, i.e., sudden, unilateral, severe, brief, stabbing, or burning in quality, and recurrent pain in

the distribution of one or more branches of the fifth cranial nerve. Paroxysmal attacks of facial or frontal pain lasted from a few seconds to several minutes, whereas the patients were entirely asymptomatic between the paroxysms (4, 5). In this study, the diagnoses were based on a careful pain history and the results of clinical examination. All the targeted patients were face-to-face interviewed and evaluated. In order to determine the painful disorder and the pain suffering, different questionnaires were given for patients to be answered.

The perception of pain involves intensity, quality, duration, and location of the pain. Therefore, self-reported data play a critical role in pain assessment (22). A patient's description of the pain and a therapeutic trial of medications are generally the most reliable methods to confirm TN.

The results of this study have clearly shown a significant difference in facial pain intensity between patients with and without TN chronic pain, when the same questionnaires were used. Self-evaluation of the intensity of facial pain by using the VAS revealed that patients in the group A indicated about twice higher pain level than in the group B, i.e., 89.7±2.47 and 44.0±2.98, respectively. The severest pain imaginable or severe pain was experienced in the group A by 21 (70%) and 8 (26.6%) patients, respectively. Occasionally, the pain was so severe that it interfered with drinking or eating. Meanwhile in the group B, no patient indicated facial pain as very severe.

In our study, the patients in the group A most often complained of the appearance of pain in the area of the upper cheek extending down to the level of the jaws, the mandibular (V3=63.3%) and maxillary (V2=23.33%) branches of the trigeminal nerve. Meanwhile, the ophthalmic division (V1), transmitting sensation from the skin of the forehead and the eye, was less commonly involved, i.e., only two patients experienced facial pain in the ophthalmic-maxillary branches (V1–V2=6.66%). This is in line with general observation that the pain of TN occurs in the region innervated almost exclusively by the mandibular nerve (V3, the largest branch of the trigeminal nerve) and/or maxillary nerve (V2, the intermediate branch in size) divisions, since in the area innervated by the ophthalmic nerve (V1, the smallest branch, containing only sensory fibers), the pain is usually experienced not frequently (5, 23).

There is evidence that patients affected by a chronic illness, including orofacial pain, are at higher risk of anxiety and depression than the general population (16, 24, 25). In our study, significantly higher scores of physical disability, anxiety, and depression were reported in patients with TN and chronic facial pain (group A) than patients with atypical facial pain (group B). It seems reasonable that chronic facial pain is a risk factor for the development of depression. If so, an effective early treatment of facial pain, attenuating the severity of pain, should reduce the risk of TN. At this point, we would like to mention that the majority of our patients with TN, despite that pain had a significant impact on their health status, including well-being, total disability, anxiety, or depression, did not consult a psychiatrist. In order to reduce the severity of pain, they used alternate therapies having no evidence of efficacy in neuropathic pain, including over-the-counter medications such as paracetamol (acetaminophen), aspirin, analgesics, topicals, and supplements. However, the pain experienced by some TN patients could be somatic expressions of mental and psychosocial disturbances (26). Only 8 patients in our study had consulted a psychiatrist and were prescribed medications for depression, anxiety, and sleep disturbance related to TN. Unfortunately, after some improvement, they discontinued the treatment. These patients returned to the Clinic of Maxillofacial Surgery just when severe facial pain attacks were renewed. Therefore, anxiety and depression in these 8 patients was not so very different as in other patients of group A. It was documented that in some cases, the therapeutic effects of antipsychotics could be a potential means in the treatment of chronic facial pain (27). However, to date, the role of classic antipsychotics is not clear. The way in which antipsychotic drugs act to relieve pain is still under debate and may differ between different agents.

It is important to mention that the debate whether pain causes depression or depression causes pain continues. The current opinion considers that both actions can be possible, and that the order in which they develop depends on the individual patient. It is often difficult to determine, which action takes place first. The pain-depression relationship in TN patients has been examined in only few studies (28). In our study, a relationship between the levels of depression as measured by the BDI and the intensity of pain was revealed. That was confirmed when the logistic regression analysis was used to test the hypothesis that patients with severe depression and disability symptoms complained of more severe pain than those without such symptoms. The logistic regression analysis clearly showed that severe depression and disability symptoms were significant risk factors for the perception of pain intensity. In patients with depression symptoms, the risk of severest possible pain was increased 1.1-fold (P=0.028), whereas in case with severe depression, up to 51.2-fold (P=0.046). A correlation was used to assess the relationship between depression symptoms and VAS scores, and a significant positive correlation was found between both parameters (r=0.47, P=0.008). This is consistent with the data of other

studies (29, 30), showing a positive correlation between the level of depression and pain intensity in patients with chronic pain. The incidence of depression in chronic pain patients ranges from 30% to 54% (26). Our findings on the incidence of depression in patients with TN are similar with these results, and they are statistically more prevalent in patients with chronic than those with atypical facial pain.

In general, the data suggest that TN patients with concomitant chronic facial pain have a higher risk of anxiety and depression, and there is direct relationship between these parameters and pain intensity level. This may be a possible adaptive mechanism for the development of chronic pain. Furthermore, the possibility of psychological problems should be taken into account, especially in complex and chronic cases. When no response to conservative treatment is achieved, a multidisciplinary team, including mental health professionals, will be needed in both the diagnosis and the treatment. This study provides support for a suggestion that in the future, an individualized treatment of the patients with TN should be based on the particular features of the patient, which could improve the efficacy of treatment.

Conclusions

Patients with trigeminal neuralgia and chronic facial pain have a significantly higher level of pain perception than those with atypical facial pain, and they reported the higher level of anxiety, depression, and total disability than those with atypical facial pain. A multidisciplinary approach is needed to better assess the emotional status of patients in order to improve the efficacy of treatment and patient's quality of life.

Statement of Conflict of Interest
The authors state no conflict of interest.

Lėtinio skausmo ir depresijos simptomų ryšys sergantiesiems trišakio nervo neuralgija

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Raktažodžiai: trišakio nervo neuralgija, lėtinis skausmas, depresija.

Santrauka. Trišakio nervo neuralgija – reta neuropatijos forma, siejama su nepakeliamu veido skausmu. Nenuspėjami skausmo priepuoliai gali sukelti nerimo bei depresijos simptomus.

Tyrimo tikslas. Įvertinti lėtinių veido skausmų parametrų dydį ir jų santykį su nerimo ir depresijos pasireiškimu.

Tirtųjų kontingentas ir tyrimo metodai. Ištirta 30 pacientų, sergančių trišakio nervo neuralgija, kuriuos vargina lėtinis veido skausmas (A grupė – 25 moterys ir 5 vyrai; amžiaus vidurkis – 64,2±3,2 metų) bei 30 – netipinis veido skausmas (B grupė – 26 moterys ir 4 vyrai; amžiaus vidurkis – 64,8±1,9 metų). Visiems pacientams buvo pateiktas standartizuotas klausimynas, apimantis: 1) demografinius rodiklius ir skausmo intensyvumo nustatymą pagal vizualinę skausmo skalę; 2) emocinės būsenos įvertinimą pagal *Sheehan* negalios, *Covi's* nerimo ir *Beck* depresijos skales.

Rezultatai. A grupės pacientų skausmo intensyvumas (89,7±2,5) buvo žymiai ($p<0,0001$) stipresnis nei B grupės (44,0±2,9). Taip pat jiems nustatyti didesni balų vidurkiai pagal negalios bei nerimo simptomų stiprumo skales (atitinkamai – 17,4±1,3 ir 9,7±0,3 palyginus su 6,4±0,7 ir 3,6±0,1, $p<0,0001$). Daugumai A grupės pacientų nustatyta sunki (46,7 proc.) arba vidutinė (30 proc.) depresija ($p<0,0001$), B grupėje – depresijos simptomų nenustatyta.

Išvados. Lėtinį veido skausmą patiriančių pacientų skausmo suvokimas buvo reikšmingai stipresnis ir žymiai stipriau išreikšti nerimo simptomai bei depresiškumas nei pacientų, kuriuos vargino netipinis veido skausmas. Optimizuojant pacientų gyvenimo kokybę bei gerinant gydymo rezultatus, reikalingi papildomi pacientų emocijų tyrimai bei tikslingas įvairių sričių medicinos specialistų bendradarbiavimas.

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