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ORIGINAL ARTICLE

Carpal Tunnel Syndrome and Migraine Lateralization

Karpal Tünel Sendromu ve Migren Lateralizasyonu

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ABSTRACT

Background/Aims: Within the scope of this research, we aimed to elucidate the relationship between carpal tunnel syndrome and migraine to explore both the pain intensity and the localization of carpal tunnel syndrome (CTS) in concomitant migraine. The primary outcome variable was elaborated as the pain lateralization, and the secondary outcome variable was the pain intensity.
Method: This is a cross-sectional, observational prospective study of 500 patients with preliminary carpal tunnel syndrome diagnosis at our institution. After patients with missing data were excluded from the study, 413 remained, 365 (88.4%) women and 48 (11.6%) men. After recording the demographic characteristics, the patient's migraine pain year of onset, pain characteristics, localization, frequency, duration, severity, triggering factors, symptoms, and findings accompanying the pain were recorded.
Results: The lateralization of migraine was on the right side (only on the right or mostly on the right) in 25.9% and on the left side (only on the left or mostly on the left) in 26.4% of the patients. Almost half of the patients (47.7%) experienced bilateral migraine headaches. Carpal tunnel syndrome was in the right hand in 13.3%, in the left hand in 11.6%, and bilateral in 75.1%. Of 197 patients with bilateral pain, 68 (34.5%) had mild, 116 (58.9%) had moderate, and 13 (6.6%) had severe CTS. The VAS level of migraine pain was higher only in patients with CTS in the left hand and in those with moderate CTS.
Conclusion: It has been determined that those with carpal tunnel syndrome on the right side have migraines mostly on the right, those with carpal tunnel syndrome on the left have migraines on the left, and those with carpal tunnel syndrome in both directions have migraines predominantly in both directions.

Keywords: Migraine; Carpal tunnel syndrome; Lateralization; Visual Analog Scale (VAS); Pain

ÖZ

Amaç: Bu araştırma kapsamında, eşlik eden migrende karpal tünel sendromunun (KTS) hem ağrı yoğunluğunu hem de lokalizasyonunu araştırmak için karpal tünel sendromu ile migren arasındaki ilişkiyi aydınlatmayı amaçladık. Birincil sonuç değişkeni, ağrının lateralizasyonu olarak detaylandırıldı ve ikincil sonuç değişkeni, ağrının yoğunluğuydu.
Yöntemler: Bu araştırma, kurumumuzda karpal tünel sendromu ön tanısı alan 500 hastanın katıldığı kesitsel, gözlemsel, prospektif bir çalışma olarak planlanmıştır. Verileri eksik olan hastalar çalışma dışı bırakıldıktan sonra 365'i (%88,4) kadın, 48'i (%11,6) erkek olmak üzere 413 kişi kaldı. Hastanın demografik özellikleri kaydedildikten sonra migren ağrısının başlangıç yılı, ağrının özellikleri, lokalizasyonu, sıklığı, süresi, şiddeti, tetikleyici faktörler, ağrıya eşlik eden semptomlar ve bulgular kaydedildi.
Bulgular: Migrenin lateralizasyonu hastaların %25,9'unda sağ tarafta (sadece sağda veya çoğunlukla sağda), %26,4'ünde ise sol tarafta (sadece solda veya çoğunlukla solda) idi. Hastaların neredeyse yarısında (%47,7) iki taraflı migren baş ağrısı görüldü. Karpal tünel sendromunun %13,3'ü sağ elde, %11,6'sı sol elde, %75,1'i ise iki taraflıydı. Bilateral ağrısı olan 197 hastanın 68'inde (%34,5) hafif, 116'sında (%58,9) orta ve 13'ünde (%6,6) şiddetli KTS vardı. Migren ağrısının VAS düzeyi sadece sol elde KTS'si olanlarda ve orta derecede KTS'si olanlarda daha yüksekti.
Sonuç: Sağ tarafta karpal tünel sendromu olanların migren hastalarının çoğunlukla sağda, solda karpal tünel sendromu olan hastaların migren ağrılarının solda, her iki yönde de karpal tünel sendromu olanların her iki yönde migren ağırlıklı olduğu belirlendi.

Anahtar Kelimeler: Migren, Karpal tünel Sendromu, Lateralizasyon, Vizüel Analog Skala (VAS), Ağrı

Introduction

Carpal tunnel syndrome (CTS) is the most common upper extremity peripheral neuropathy, which develops due to pressure on the median nerve at the wrist level within the wrist canal for different reasons. It accounts for approximately 90% of all entrapment neuropathies. It is seen in all age groups, especially between the ages of 40 and 60, and is nearly two times more common in women than men [1]. Although definite risk factors (most importantly environmental factors) are associated with CTS, they are mostly idiopathic. Long-term wrist flexion and extension repetitive movement of the flexor muscles and exposure to vibration are among the factors that facilitate the development of CTS [2]. While the prevalence of CTS has been reported as 10% and its incidence as 1–5% in previous studies, the incidence of CTS in the general

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population is 3 – 4 % [3]. The prevalence of carpal tunnel syndrome is 6% in men and 9% in women. It has been shown that CTS develops at a higher rate (14.5%) in specific occupational groups (especially in the dominant hand, due to straining and repetitive movements) in Western societies [3, 4].

Migraine is a common primary headache disorder that causes disability. Many epidemiological studies have documented the high prevalence of migraine and its socioeconomic and personal effects. In the Global Burden of Disease Study, migraine was ranked as the third most prevalent disorder in the world. Additionally, it ranked third in terms of causes of disability among men and women under the age of 50 worldwide [5]. According to the World Health Organization (WHO), migraine headaches are among the top 10 most common diseases in men and among the top five most common diseases in women. The estimated prevalence of migraine is between 12% and 16% of the population, and it is higher in women than men [6].

It has come to our attention that these two conditions, in addition to being common in society, have common characteristics such as being unilateral or bilateral, being more common in women, being affected by genetic and environmental factors, and having unclear physiopathogenesis. It brings to mind whether it is a coincidence that these two conditions have so much in common or whether there is a common mechanism for their co-occurrence. In recent years, a few studies have investigated whether these two conditions are related and reported positive results on their coexistence, but this relationship has not been clarified. For this reason, it was planned to evaluate the relationship between these two tables from a different perspective. Migraine occurring on the same side may be a trigger for carpal tunnel syndrome on the same side. Within the scope of this research, we aimed to elucidate the relationship between carpal tunnel syndrome and migraine to explore both the pain intensity and the localization of CTS in concomitant migraine. The primary outcome variable was elaborated as the pain lateralization, and the secondary outcome variable was the pain intensity.

Method

This is a cross-sectional, observational prospective study of 500 patients with preliminary carpal tunnel syndrome diagnosis at our institution. After patients with missing data were excluded from the study, 413 remained, 365 (88.4%) women and 48 (11.6%) men.

All procedures followed are in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2008. Ethics committee approval has been granted from our institution with protocol number 12129, and informed consent has been obtained from all participants.

Patient Selection

The patient selection was conducted in two stages. In the first stage, it was planned to include patients who came to our institution's electrophysiology laboratory with a preliminary diagnosis of carpal tunnel syndrome and were diagnosed with carpal tunnel syndrome due to nerve conduction measurements. Individuals who agreed to participate in the study were required to complete a questionnaire prepared according to the criteria determined by the International Headache Committee (IHC). Patients with migraine headaches were enrolled after completing the survey. After recording the demographic characteristics of all patients included in the study (age, gender, weight, comorbidities), the characteristics of the patient's migraine pain (year of onset of pain, pain characteristics, localisation, frequency, duration, severity, triggering factors, symptoms and findings accompanying the pain) were recorded. It was planned to examine separately the characteristics of CTS symptoms (initiation time, severity, localisation, time day/night, triggering factors, symptoms accompanying pain).

Statistical Analysis

The Kolmogorov-Smirnov test was used for normality distribution checking of continuous variable. Independent Sample t–test was used for the comparison between two independent normally distributed groups, and t statistics values were given. For non-normal independent two groups comparison, Mann-Whitney U test was used and Z values were presented. Kruskal-Wallis test was used more than non-normal two independent groups comparison, and Chi-square value was given. Mean and standard deviation for continuous variables were given as descriptive values. In addition, minimum and maximum values were given because of presence of non-normal continuous variables in tables.

Pearson Chi-Square test was used to compare categorical variables in crosstable and chi-square statistics value was given. Frequency and percentage for categorical variables were also presented.

The results were considered statistically significant when the p-value was less than 0.05. Patient data collected within the scope of the study were analyzed with the IBM Statistical Package for the Social Sciences (SPSS) for Windows 26.0 (IBM Corp., Armonk, NY) package program.

Results

A total of 500 patients were included in the study. After the patients with missing data were excluded, 413 patients remained: 365 (88.4%) women and 48 (11.6%) men. Among the patients' data examined in the study, Table 1 denotes the lowest, highest, and average values according to patient age, duration of headache, duration, frequency, and severity. Although it was observed that the severity of CTS increased with age, no statistical significance was achieved (p=0.111).

The lateralization of migraine was on the right side (only on the right or mostly on the right) in 25.9%

Tablo 1. Baseline demographics of the study population

	Gender	N	Mean	Standard Deviation	Minimum	Maximum	Test	P-value
AGE	Female	365	47.8	10.80	18.0	82.0	t=-1.309	0.191
	Male	48	50.0	12.25	25.0	78.0		
BMI	Female	364	30.5	5.62	16.0	66.0	Z=-1.268	0.205
	Male	48	29.5	5.22	17.5	44.0		
VAS MIGRAINE	Female	364	6.9	1.54	3.0	10.0	Z=-0.333	0.740
	Male	48	6.8	1.67	3.0	9.0		
Duration of Migraine	Female	365	14.2	8.38	1.0	40.0	Z=-0.511	0.610
	Male	48	15.1	9.39	2.0	35.0		
Migraine Attacks (hours)	Female	365	13.3	15.22	2.0	72.0	Z=-1.303	0.192
	Male	48	13.2	16.6	3.0	72.0		
Migraine Attach Frequency	Female	365	8.4	6.22	1.0	35.0	Z=-0.243	0.808
	Male	48	8.1	4.94	1.0	20.0		

Tablo 2. The lateralization/localization of migraine and carpal tunnel syndrome

Migraine Lateralization	Carpal Tunnel Syndrome			Total
	Right N (%)	Left N (%)	Both N (%)	
Right	22(20.6)	11(10.3)	74(69.2)	107(25.9)
Left	13(11.9)	17(15.6)	79(72.5)	109(26.4)
Both	20(10.2)	20(10.2)	157(79.7)	197(47.7)
Total	55(13.3)	48(11.6)	310(75.1)	413(100)

*Chi-square=9.026, p=0.060

Tablo 3. The association between carpal tunnel syndrome (CTS) and VAS in migraine patients

	Severity of CTS	N	Mean	Standard Deviation	Minimum	Maximum	Kruskal Wallis Test	P-value
General	Low	136	6.8	1.84	3.0	10.0	Chi-square=1.411	0.494
	Medium	247	7.0	1.35	3.0	9.0		
	Severe	29	6.6	1.68	3.0	9.0		
Right hand	Low	34	7.1	1.72	4.0	9.0	Chi-square=1.206	0.272
	Medium	16	6.6	1.66	4.0	9.0		
Left hand	Low	22	5.9	1.92	3.0	9.0	Chi-square=5.119	0.024*
	Medium	19	7.2	1.31	4.0	9.0		
Both hands	Low	80	6.9	1.81	3.0	10.0	Chi-square=1.140	0.565
	Medium	212	7.1	1.33	3.0	9.0		
	Severe	29	6.7	1.68	3.0	9.0		

Table 4. CTS severity and number of years of headache experience

	Severity of CTS	N	Mean	Standard Deviation	Minimum	Maximum	Kruskal Wallis Test	P-value
General	Low	136	12.4	8.32	2.0	35.0	Chi-square=12.903	0.002*
	Medium	248	15.2	8.49	1.0	40.0		
	Severe	29	15.5	8.04	1.0	30.0		
Right hand	Low	34	11.9	8.48	2.0	35.0	Chi-square=2.486	0.115
	Medium	16	15.5	8.79	5.0	30.0		
Left hand	Low	22	13.1	8.32	3.0	28.0	Chi-square=2.400	0.121
	Medium	19	17.0	8.18	1.0	30.0		
Both hands	Low	80	12.4	8.3	2.0	35.0	Chi-square=7.802	0.020*
	Medium	213	15.0	8.5	1.0	40.0		
	Severe	29	15.5	8.0	1.0	30.0		

and on the left (only on the left or mostly on the left) in 26.4% of the patients. Almost half of the patients (47.7%) experienced bilateral migraine headaches. Carpal tunnel syndrome was in the right hand in 13.3%, in the left hand in 11.6%, and bilateral in 75.1%. It was observed that 20.6% of the patients with migraine pain on the right side had CTS on the right while 15.6% of those with migraine on the left had CTS on the left, and 79.7% of those with bilateral headaches had bilateral CTS (Table 2).

Of the 107 patients with migraine pain on the right side, 27 (25.2%) had mild, 71 (66.4%) had moderate, and 9 (8.4%) had severe CTS. Of the 109 patients with migraine pain on the left, 41 (37.6%) had mild CTS, 61 (56.0%) had moderate CTS, and 7 (6.9%) had severe CTS. Of 197 patients with bilateral pain, 68 (34.5%) had mild, 116 (58.9%) had moderate, and 13 (6.6%) had severe CTS.

When the VAS values showing the severity of CTS and the severity of migraine headaches were compared, the VAS level of migraine pain was higher only in patients with CTS in the left hand and in those with moderate CTS. Migraine pain levels were partially lower in those with low and severe CTS. As a result, no statistical significance was found between CTS severity and migraine pain level VAS (p=0.494) (Table 3).

When all groups were included, it was determined that those with mild CTS had headaches for an average of 12.4 years while those with moderate CTS had headaches for 15.2 years, and those with severe CTS had headaches for 15.5 years. This showed that as the number of years of headache experience increased, the severity of CTS also increased statistically significantly (p□0.002) (Table 4). However, the severity of CTS and the duration of headache exposure in hours was not statistically significant.

When the relationship between CTS severity and headache frequency (month/day) was examined, it was observed that those with mild CTS experienced pain for an average of 8.4 days per month while those with severe CTS experienced pain for an average of 9.8 days per

month. Similar results were found in those with bilateral headaches and those with bilateral CTS.

Discussion

Migraine and carpal tunnel syndrome are two separate diseases that affect the peripheral nervous system, and migraine affects the central nervous system. They are completely different from each other but are common in society. Some recent studies have investigated whether these two tables coexist and published positive results. Although these studies have published results indicating that this relationship may exist, it is unclear whether it exists. In our recently published article, Koyuncu reported that 80.3% of the patients with carpal tunnel syndrome had migraines, and 12.6% of individuals with migraines had carpal tunnel syndrome [7]. In a large cohort of 401.656 individuals from the United Kingdom Biobank, migraine and carpal tunnel syndrome denoted a significant epidemiological association. A genetic correlation with shared genetic susceptibility at the TRIM32 locus underpinned this association [8]. Nerve compression also triggered an inflammatory response in the affected area. Inflammation is also known to play a role in migraine pathophysiology that might contribute to an overall increase in inflammation, potentially exacerbating migraines [2, 4].

In previous literature, it was reported that head and neck compressive neuropathies triggered headaches. However, the entrapment neuropathies of the extremities have traditionally been perceived as separate clinical entities. Gferer et al. claimed a significant clinical presentation, treatment, and anatomical abnormality overlap. The relationship between nerve compression headaches, carpal tunnel syndrome, and other upper extremity compression neuropathies have common pathologies and comorbidities [9]. Upper extremity nerve compression syndromes and migraines caused by nerve entrapment have many similarities, including patient presentation, anatomical findings, and treatment by surgical decompression of affected nerves, thus indicating a possibility of shared predisposition. Gferer et al. have stated that patients who undergo median and multiple nerve decompression are more likely to experience migraine headaches [10].

Recent evidence has suggested that some types of migraine headaches may be associated with nerve compression [11–14]. Members of the American Headache Society (AHS) commonly use nerve blocks and trigger point injections to treat migraine headaches, and several other studies support targeted injections of botulinum toxin or local anesthetic for the treatment of migraine headaches [15, 16]. The first community-based study that demonstrated an association between carpal tunnel syndrome and migraine headaches was published by Law et al. (2010) [17]. It utilized the data from 25.880 respondents of the cross-sectional 2010 National Health Interview Survey. They stated that 34% of people with carpal tunnel syndrome had migraine, compared to 16% of people without the syndrome. Additionally, 71% of the participants underwent median nerve decompression surgery performed on the wrist to relieve nerve pressure, and thus reduce carpal tunnel syndrome symptoms, 14% of participants underwent ulnar nerve decompression, and 6.5% had decompression surgery at multiple sites in the body. Those who had median nerve decompression and multiple nerve decompression were 30% and 70% more likely to have migraine than those who had ulnar nerve decompression [17].

Migraine is a typically unilateral disorder, and its lateralization is thought to be related to manual dominance. La Pegna et al. [18] conducted retrospective research and reported that the right-handers had 3412 unilateral episodes; 62.8% of the pain attacks were on the right side and 37.2% by pain on the left. On the other hand, the left-handed subjects had 803 unilateral pains, with 63.5% of unilateral pain episodes on the left side and 36.5% of attacks with

lateralized pain on the right (p<0.001). Their data suggested that manual dominance might influence the side of pain lateralization in migraine [18]. Similar to these outcomes, an association between carpal tunnel syndrome and hand dominance has been identified [19].

Blum et al. [20] published an interesting review stating that left- and right-sided migraine differed across a wide range of domains, raising the possibility that the left- and right-side pathophysiology may not be identical. They indicated that left- and right-sided migraine was found to differ across multiple domains as left- and right-sided migraine was associated with ipsilateral handedness, tinnitus, onset of first Parkinson's symptoms, white matter hyperintensities on MRI, activation of the dorsal pons, hippocampal sclerosis, and thalamic NAA/Cho and NAA/Cr concentrations [20]. In our study, the intensity of migraine headaches and carpal tunnel syndrome was found as follows: in right-sided migraine, 25.2% had mild, 66.4% had moderate, and 8.4% had severe carpal tunnel syndrome. In left-sided migraine, 37.6% had mild, 56.0% had moderate, and 6.9% had severe carpal tunnel syndrome. In patients with bilateral pain, 34.5% had mild, 58.9% had moderate, and 6.6% had severe carpal tunnel syndrome.

Last but not least, left-sided migraine was associated with worse quality of life, anxiety, bipolar disorder, PTSD, lower sympathetic activity and higher parasympathetic activity. In contrast, right-sided migraine was associated with poorer performance on multiple cognitive tests, a greater degree of anisocoria, changes in skin temperature, higher diastolic blood pressure, changes in blood flow through the middle cerebral and basilar arteries, and changes in EEG [20]. In our study, the lateralization of migraine was on the right side in 25.9% of the patients and on the left side in 26.4%. Almost half of the patients (47.7%) experienced bilateral migraine headaches. Carpal tunnel syndrome was in the right hand in 13.3%, in the left hand in 11.6%, and bilateral in 75.1%. It was observed that 20.6% of the patients with migraine pain on the right side had carpal tunnel syndrome on the right. In comparison,15.6% of those with migraine on the left had carpal tunnel syndrome on the left, and 79.7% of those with bilateral headaches had bilateral carpal tunnel syndrome.

One expected result was the increase in the intensity of headaches and duration of migraine, as denoted by VAS scores. As the severity of carpal tunnel syndrome deteriorated, migraine attack periods increased.

Conclusion

Regarding the outcomes of this research, it has been determined that those with carpal tunnel syndrome on the right side have migraines mostly on the right, those with carpal tunnel syndrome on the left have migraines on the left, and those with carpal tunnel syndrome in both directions have migraines predominantly in both directions.

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Competing interests

The authors declare that they have no competing interests.

AI Statement

The authors used AI and AI-assisted Technologies (Grammarly and MS Word Editor) in the writing process. These technologies improved the readability and language of the work. Still, they did not replace key authoring tasks such as producing scientific or medical insights, drawing scientific conclusions, or providing clinical recommendations. The authors are ultimately responsible and accountable for the contents of the whole work.

Consent for Publication

The original article is not under consideration by another publication, and its substance, tables, or figures have not been published previously and will only be published elsewhere.

Data Availability

The data supporting this study's findings are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

Ethical Declaration

All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2008. Ethics committee approval has been granted from our institution. Informed consent has been obtained from participants.

Author Contributions:

Research idea, design of the study, acquisition of data for the study, analysis of data for the study, interpretation of data for the study, drafting the manuscript, revising it critically for important intellectual content: GK

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