

The Demographic and Clinical Characteristics of the Patients with Complex Regional Pain Syndrome: A Tertiary Clinic Experience

Kompleks Bölgesel Ağrı Sendromlu Hastaların Demografik ve Klinik Özellikleri: Üçüncü Basamak Tecrübesi

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ABSTRACT Objective: The aim of our study was to determine the demographic and clinical characteristics of the patients with complex regional pain syndrome (CRPS) and to reveal the epidemiological features of CRPS. **Material and Methods:** Eighty-eight patients with CRPS, admitting to our clinic between January 2010 and December 2018 were included in the study. Patients were evaluated retrospectively in terms of demographics, symptom characteristics (sensory, vasomotor, sudomotor/edema and motor/trophic), involved extremity and side; etiological factors (orthopedic surgery history, soft tissue trauma, stroke, immobilization, cast using), possible risk factors (smoking, menopause, migraine, osteoporosis, asthma and anxiety disorders) and used therapeutic modalities. **Results:** Mean age of the patients was 51.14±15.25 years (min:18, max: 82). In 60.2% (n: 53) of the patients, upper extremity was involved but there was no statistically significant difference in terms of the involved side (p: 0.754). Soft tissue traumas were the most common factor in etiology in both genders. Most of the patients presented with sensory symptoms. The most common risk factor was menopause in females and smoking in males. Fifty patients (56.8%) had a history of cast using and the mean duration of cast using was 41.60±11.33 days (min: 20 days; max: 70 days). While 63.6% (n: 56) of the patients were included in a physical therapy program; the mean number of the physical therapy sessions was 33.42±10.70 (min: 20 sessions; max: 60 sessions). There was a statistically significant positive correlation between the duration of cast using and the number of physical therapy sessions (r: 0.571, p<0.001). **Conclusion:** The results of our study suggest that CRPS can affect both genders and different age groups, and that the upper extremity is involved more than the lower extremity. The most common etiological factor is soft tissue traumas. Menopause in females and smoking in males were the two most common risk factors. The determination of the epidemiological characteristics of the patients with CRPS will enable to predict the risky patients and early diagnosis and treatment of the disease.

ÖZET Amaç: Bu çalışmanın amacı, kompleks bölgesel ağrı sendromlu (KBAS) hastaların demografik ve klinik özelliklerini belirleyerek KBAS'ın epidemiyolojik özelliklerini açığa çıkarmaktır. **Gereç ve Yöntemler:** Çalışmaya, Ocak 2010 ve Aralık 2018 tarihleri arasında kliniğimize takip edilen KBAS tanılı 88 hasta dahil edildi. Hastalar retrospektif olarak demografik özellikler, semptom karakteristikleri (duyusal, vazomotor, sudomotor/ödem ve motor/trofik), tutulan ekstremité ve etkilenen taraf, etyolojik faktörler (ortopedik cerrahi öyküsü, yumuşak doku travması, inme, immobilizasyon, alçı kullanımı), olası risk faktörleri (sigara kullanımı, menopo, migren, osteoporoz, astım ve anksiyete bozukluğu) ve kullanılan tedavi yöntemleri açısından değerlendirildi. **Bulgular:** Yaş ortalaması 51,14±15,25 yıl (min: 18, maks: 82) idi. Hastaların %60,2 (n: 53)'sinde üst ekstremité tutulumu vardı ancak etkilenen taraf açısından istatistiksel olarak anlamlı bir fark yoktu (p: 0,754). Yumuşak doku travmaları her iki cinsiyette de etyolojideki en sık faktördü. Hastalar en fazla duyuşsal semptomlar ile başvurmuşlardı. Kadınlarda belirlenen en sık risk faktörü menopo, iken erkeklerde ise sigara kullanımı idi. Hastaların %56,8 (n: 50)'inde alçıda kalma öyküsü varken ortalama alçıda kalma süresi 41,60±11,33 gün (min: 20 gün; maks: 70 gün) idi. Hastaların %63,6 (n: 56)'sı fizik tedavi programına alınırken; ortalama seans sayısı 33,42±10,70 (min: 20 seans; maks: 60 seans) idi. Alçıda kalma süresi ile fizik tedavi seans sayısı arasında istatistiksel olarak anlamlı pozitif bir korelasyon var idi (r: 0,571, p<0,001). **Sonuç:** Çalışmamızın sonuçları KBAS'ın, her iki cinsiyeti ve farklı yaş gruplarını etkileyebilen bir hastalık olduğunu, üst ekstremitenin alt ekstremitéye göre daha fazla etkilendiğini; etyolojide belirlenen en sık etkenin yumuşak doku travmaları olduğunu göstermektedir. Kadınlarda menopo, erkeklerde ise sigara kullanımı belirlenen en sık iki risk faktörü idi. Hastalığın epidemiyolojik özelliklerinin belirlenerek riskli hastaların öngörülebilmesi, erken tanı ve tedaviyi mümkün kılacaktır.

Keywords: Complex regional pain syndrome; physical therapy; rehabilitation, disability

Anahtar Kelimeler: Kompleks bölgesel ağrı sendromu, fizik tedavi, rehabilitasyon, sakatlık

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Complex regional pain syndrome (CRPS) is characterized by sensory, vasomotor, sudomotor and trophic changes.¹ Etiology is usually related with trauma, fracture, stroke and coronary artery disease.²⁻⁶ Regional inflammation, peripheral and central sensitization are thought to play a role in the pathogenesis of CRPS.¹ This syndrome is characterized by heterogeneous symptoms such as persistent pain, allodynia or hyperalgesia, edema in the painful area, abnormal sudomotor activity disproportionate to the triggering event and changes in skin blood flow are usually seen distally to the involved extremity.⁷⁻⁹ The diagnosis is based on clinical signs and symptoms. However, various imaging modalities such as direct radiography, computed tomography, magnetic resonance imaging and bone scintigraphy may be needed to support the diagnosis in CRPS cases with atypical localization. The most common treatments for CRPS include physical therapy applications, non-steroidal anti-inflammatory drugs (NSAIDs), corticosteroids, antidepressants, calcitonin, anticonvulsants, opiates, Bier block, sympathetic ganglion blocks and especially in the treatment of resistant cases, some alternative methods like hyperbaric oxygen therapy and manual lymph drainage.¹⁰⁻¹³

Early and multidisciplinary approach forms the basis of an optimal and successful treatment.⁹⁻¹⁴ Response to the treatment varies individually and there is no definitive treatment method.⁸ In addition to the need for long-term physical therapy and rehabilitation programs; many patients cannot return to work despite the multiple medical treatments and even some patients have advanced therapies such as surgical sympathectomy. Also, treatment processes including long rehabilitation programs may be associated with severe work productivity loss.

Successful treatment depends on early diagnosis and prevention of the complications.⁹ In this respect, CRPS is a medical problem involving long and costly treatments and also it is a serious socioeconomic problem considering both compensation costs and resulting disability.¹⁵ The aim of this study was to determine the epidemiological characteristics of the patients with CRPS including the patients' demographics, etiological factors, treatment modalities applied and clinical outcomes of the treatments. In this

way, early diagnosis and treatment of the patients considered to be at risk for CRPS will be possible.

MATERIAL AND METHODS

The approval of Gaziosmanpaşa University Faculty of Medicine Ethics Committee was obtained for our study (approval number: 19.02.2019/19-KAEK-033). Eighty-eight patients (39 females, 49 males; mean age 51.14±15.25 years) that were evaluated and diagnosed with CRPS according to the validated "International Association for the Study of Pain Budapest criteria" between January 2010 and December 2018 were included in the study.¹⁶ For the diagnosis of CRPS, at least one symptom of all 4 categories (sensory, vasomotor, sudomotor/edema and motor/trophic dysfunction) and at least 2 signs of the same 4 categories should be provided.¹⁶

Data were collected from electronic medical records of the patients retrospectively. The study included the patients over the age of 18 who were diagnosed with CRPS by completing the Budapest criteria and whose data on the hospital registry were complete. Patients under the age of 18, not meeting the diagnostic criteria and whose data were missing were excluded from the study. The patients' demographics and symptom characteristics were recorded. Symptom characteristics were evaluated under four categories according to Budapest criteria for CRPS. These are:

1. Sensorial dysfunction: hyperalgesia (by needle penetration) or allodynia (light touch or sensitivity to temperatures or deep somatic pressure or movement of the joints).
2. Vasomotor dysfunction: color changes on the skin or asymmetry of skin color or asymmetry of temperature (more than one degree Celsius).
3. Sudomotor dysfunction/edema: asymmetry in perspiration, changes in sweating, edema.
4. Motor/trophic dysfunction: limited range of motion (ROM) or motor dysfunction (weakness, dystonia, tremor) or trophic changes (skin, nails, hair)^{17,18}

Also involved extremity and side; etiological factors (orthopedic surgery history, soft tissue trauma, stroke, immobilization, cast using), possible

risk factors (smoking, menopause, migraine, osteoporosis, asthma, anxiety) and used therapeutic modalities were recorded.

The study was conducted in accordance with the principles of the Declaration of Helsinki.

STATISTICAL ANALYSIS

Descriptive analyzes were conducted to give information about the general characteristics of the study group. Data of the continuous variables were expressed as mean \pm standard deviation; categorical variables were given as number and percent. For comparing the mean of the quantitative variables between the groups, the Significance of Difference Between Two Means test was used. Cross-tables and chi-square tests were used to evaluate the relationship between qualitative variables. Pearson correlation coefficient was used for correlation analysis between quantitative variables. *p* values less than 0.05 were considered statistically significant. IBM Statistical Package for Social Sciences (SPSS) version 19.0 software was used for data analysis (IBM SPSS Statistics 19, Somers, New York).

RESULTS

The study involved 88 patients (39 females, 49 males). The mean age of the patients was 51.14 ± 15.25 years (min: 18, max: 82). The mean age of the females was 54.79 ± 12.38 (min: 18, max: 77); while the mean age of the males was 48.22 ± 16.76 (min: 19, max: 82). The mean age of the males was significantly lower than the females (*p*: 0.044). In 60.2% (n: 53) of the patients, upper extremity and in 39.8% (n: 35) of the patients lower extremity were involved. Soft tissue trauma was the most common etiological factor in both genders. The most common risk factor was menopause in females and smoking in males. Table 1 presents the clinical characteristics of the patients by gender. Of the patients, 63.6% (n: 56) were admitted to a physical therapy program (transcutaneous electrical stimulation, therapeutic ultrasound, whirlpool or contrast bathing, elevation of the affected extremities, postural correction, active assisted ROM exercises and NSAIDs if needed); the remaining 32 patients received a 3-months home-based exercise program (contrast bathing, active ROM exercises, elevation and NSAIDs if needed).

TABLE 1: Clinical characteristics of the patients by gender.

Variables	Gender		p
	Female(n=39)	Male (n=49)	
Involved extremity			
<i>Upper limb</i>	26 (66.7)	27 (55.1)	0.098
<i>Lower limb</i>	13 (33.3)	22 (44.9)	
Involved side			
<i>Right</i>	17 (43.6)	23 (46.9)	0.754
<i>Left</i>	22 (56.4)	26 (53.1)	
Etiology			
<i>Fractures</i>	12 (30.8)	16 (32.7)	0.367
<i>Soft tissue injury</i>	26 (66.7)	27 (55.1)	
<i>Hemiplegia</i>	1 (2.6)	5 (10.2)	
<i>Myocardial infarction</i>	0 (0)	1 (2)	
Risk factors			
<i>Smoking</i>	2 (5.1)	26 (53.1)	<0.001
<i>Menopause</i>	30 (76.9)	-	<0.001
<i>Migraine</i>	1 (2.6)	1 (2)	0.870
<i>Osteoporosis</i>	4 (10.3)	0(0)	0.022
<i>Asthma</i>	3 (7.7)	2 (4.1)	<0.001
<i>Anxiety</i>	4 (10.3)	5 (10.2)	0.994

Data are shown as n(%).

TABLE 2: The number of physical therapy sessions and the duration of cast using by gender.

Variables	Gender		p
	Female	Male	
Cast using duration	40.83±11.76	42.31±11.10	0.650
The number of PTS	30.45±5.54	35.39±12.76	0.094

The Significance of Difference Between Two Means test was used.

PTS: Physical therapy sessions.

TABLE 3: The correlations between age, duration of cast using and the mean number of physical therapy sessions of all patients.

Variables		Age	Cast using	The number
			duration	of PTS
Age	r	1	-0.337	-0.241
	p		0.017	0.076
Cast using duration	r	-0.337	1	0.571
	p	0.017		<0.001
The number of PTS	r	-0.241	0.571	1
	p	0.076	<0.001	

Pearson correlation coefficient was used. PTS: Physical therapy sessions.

In addition, 31.8% (n: 28) of the patients received medical treatments including pregabalin/gabapentin (n:16) and/or corticosteroids (n:14) in addition to the NSAIDs given if needed. Twenty of these 28 patients were from the physical therapy receiving group, while the remaining 8 patients were from the home-

based exercise program group. Fifty (56.8%) patients had a history of cast using, while the mean duration of cast using was 41.60±11.33 (min: 20 days; max: 70 days). The patients included in the physical therapy program received 33.42±10.70 sessions (min: 20 sessions; max: 60 sessions) of physical therapy. Table 2 shows the number of physical therapy sessions and the duration of cast using by gender. There was a statistically significant positive correlation between the duration of cast using and the number of physical therapy sessions (r: 0.571, p <0.001). The correlations between age, duration of cast using and the mean number of the physical therapy sessions of all patients are shown in Table 3. Table 4 shows the correlations between age, duration of cast using and the number of the physical therapy sessions by gender. Sensorial dysfunction was the most commonly observed symptom in patients with CRPS. The second common symptom that the patients complained of was motor dysfunction. Hyperesthesia was the most common sensorial sign and decreased ROM was the most common motor sign.

DISCUSSION

In this study, we investigated the demographic and clinical characteristics of the patients with CRPS to reveal the epidemiological features of the disease. Thus, we aimed to increase the awareness of this disease, where the diagnostic delay can reach 3.9 years

TABLE 4: The correlations between age, duration of cast using and number of physical therapy sessions by gender.

Gender			Age	Cast using duration	The number of PTS
Female	Age	r	1	-0.193	-0.413
		p		0.365	0.056
	Cast using duration	r	-0.193	1	0.630
		p	0.365		0.007
	The number of PTS	r	-0.413	0.630	1
		p	0.056	0.007	
Male	Age	r	1	-0.442	-0.169
		p		0.024	0.348
	Cast using duration	r	-0.442	1	0.501
		p	0.024		0.041
	The number of PTS	r	-0.169	0.501	1
		p	0.348	0.041	

Pearson correlation coefficient was used. PTS: physical therapy sessions.

and to protect patients from conditions such as unnecessary surgical practices or worsening of pain.¹⁹

De Mos et al. reported that CRPS was observed more frequently in women aged 60-70 years and that the upper extremity was more frequently involved than the lower extremity.²⁰⁻²² In a study of 172,194 cases in which the incidence and risk factors of CRPS after distal radius fracture (DRF) were evaluated, Jo et al. found out that the incidence of CRPS was higher in women aged between 50-60 years. This result was associated with the more frequent prevalence of DRF in postmenopausal women.²³ The mean age of the patients in our study was consistent with the literature; but 55.7% (n: 49) of our patients were male. This result may be due to the fact that our study included different patient groups from different etiologies for CRPS, unlike Jo et al. Upper extremity was affected in 60.2% (n: 53) of the patients; however, there was no statistically significant difference in terms of involved side (p: 0.754) and these results were consistent with the results of Harden et al. This may be due to the fact that the upper extremity is more vulnerable.^{20,24}

In etiology of CRPS, there are different factors such as surgery, cast using and visceral problems.²⁵ In our study, soft tissue trauma was the most common factor of the etiology in two thirds of the patients.

In their study using the criteria of Budapest, Lee et al. detected skin color change in 70.4% of the patients, edema in 61.4% and asymmetry in sweating in 43.8%.²⁶ In our study, sensorial dysfunction was the most common symptom, while hyperesthesia was the most common sensorial sign.

Some of the risk factors for CRPS are a history of smoking, migraine, menopause, osteoporosis, asthma and anxiety.¹²⁻¹⁴ In our study, half of the males were smoking; while 76.9% (n: 30) of the females were in the postmenopausal period.

CRPS is a clinical diagnosis of exclusion and treatment should be instituted immediately upon diagnosis to alleviate the debilitating pain patients suf-

fer with this disorder.²⁷ The aim of the CRPS treatment is to restorate the function of the involved limbs by reducing pain and increasing the ROM. In the treatment of CRPS; steroids and nonsteroidal anti-inflammatory drugs, a variety of medical therapies ranging from antiepileptics to opiates, many different methods such as sympathetic ganglion blocks and hyperbaric oxygen treatments are used.^{11,13,26,28} Unfortunately, there is no head to head comparative study evaluating the effectiveness of these methods in CRPS.²⁹ In our study, 63.6% (n: 56) of the patients needed a physical therapy program and 31.8% (n: 28) of the patients received medical treatments including pregabalin/gabapentin (n:16) and/or corticosteroids (n:14) in addition to the NSAIDs given if needed.

LIMITATION

Due to the retrospective design of our study, our data on the educational and occupational status of our patients were missing. Also our results were obtained from a single tertiary university hospital, and therefore, it is difficult to fully generalize the findings. Larger epidemiological studies are also needed to evaluate parameters such as occupational status and work-day loss of patients with CRPS.

CONCLUSION

The results of our study suggest that CRPS is a disease that can affect both genders and different age groups, and that the upper extremity is involved more than the lower extremity; and also the most common factor determined in etiology is soft tissue traumas. Being in menopause in females and smoking in males were the two most common risk factors for CRPS. The knowledge of the epidemiological characteristics of the patients with CRPS will enable to predict the risky patients and early diagnosis and treatment of the disease.

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