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Title: The Relationship Between Pain Level and Quality of Life and Sleep Disorder in Patients with Central Post-stroke Pain

Running Head: Effect of Post-stroke Pain Level

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Abstract/Öz

Introduction: Stroke is the third most common cause of death and the first cause of disability in the world. Central post-stroke pain (CPSP) resulting from the dysfunction or primary lesion of the central nervous system after stroke is a common syndrome.

Methods: 75 ischemic stroke patients in total (31 females, 44 males) were included in our study. 28 of the patients (12 females, 16 males) experienced central pain within one year after ischemic stroke.

Results: The pain assessment of the patients was performed with the Leeds Assessment of Neuropathic Symptoms and Signs (LANSS) pain scale and the Visual Analogue Scale (VAS). The European Quality 5 Dimension (EQ5D) and EQ5D VAS life quality assessment carried out in the group with central pain indicated a stastistically significant correlation in the quality of life in both measurements as the VAS levelincreased ($p \leq 0.001$, 0.001). Similarly, it was identified that the quality of life (EQ5D and EQ5D VAS) was lower in the group with LANSS≥12 when compared to the group with LANSS<12 ($p \leq 0.006$, 0.016). Statistically significant data were obtained in the group with CPSP as the VAS score increased and in the cases with LANSS≥12 according to the Epworth Sleepiness Scale ($p \leq 0.001$, 0.002). When the groups with the Epworth score between <11 and ≥11 were compared, the daytime sleepiness ratio was found to be significantly higher in the group with LANSS≥12 ($p \leq 0.018$). A positive significant correlation was detected between the VAS score and daytime sleepiness ratio ($p \leq 0.001$).

Conclusion: It was demonstrated in this study that CPSP had a clearly negative effect on the quality of life of stroke patients. It is important for the literature to emphasize that it is possible to improve the comfort of patients with a correct diagnosis and treatment of sleep disorders, depression and anxiety accompanying CPSP.

Keywords: Central post-stroke pain, the leeds assessment of neuropathic symptoms and signs (lanss), visual analogue scale (vas), quality of life, sleep disorder

Amaç: İnme, dünyada en yaygın üçüncü ölüm nedeni ve birinci özürlülük nedenidir. İnme sonrası santral sinir sisteminin disfonksiyon ya da primer lezyonundan kaynaklanan, inme sonrası santral ağrı (İSSA), sık görülen bir sendromdur.

Yöntemler: Çalışmamıza 31 kadın, 44 erkek olmak üzere toplam 75 iskemik inme hastası dahil edildi. 28 tanesi (12 kadın, 16 erkek) iskemik inme sonrası 1 yıl içinde santral ağrı gelişen hastalardı. Hastaların ağrı değerlendirmesi, The Leeds Assessment of Neuropathic Symptoms and Signs (LANSS) ağrı skalası ve Visual Analogue Scale (VAS) ile yapıldı.

Bulgular: Santral ağrısı olan grupta yapılan European Quality 5 Dimension (EQ5D) ve EQ5D VAS yaşam kalitesi değerlendirmesi, VAS derecesi arttıkça yaşam kalitesinde, her iki ölçümde istatistiki olarak anlamlı korelasyon gösterdi (p=0.001, 0.001). Aynı şekilde LANSS≥12 olan grupta, LANSS<12 olan gruba göre yaşam kalitesinin (EQ5D ve EQ5D VAS) düşük olduğu saptandı (p=0.006, 0.016). İSSA olan grupta, VAS puanı arttıkça ve LANSS≥12 olanlarda Epworth Uykululuk Ölçeğine göre istatistiki olarak anlamlı verilere ulaşıldı (p=0.001, 0.002). Epworth skoru <11 ile ≥11 olan gruplar karşılaştırıldığında; LANSS≥12 olan grupta gündüz uykululuk oranı anlamlı düzeyde daha yüksek bulundu (p=0.018). VAS puanı ile gündüz uykululuk oranı arasında pozitif anlamlı korelasyon saptandı (p=0.001).

Sonuç: Bu çalışma ile İSSA'nın inme hastalarında yaşam kalitesi üzerinebelirgin negatif etkisi olduğu gösterilmiştir. İSSA'ya eşlik eden uyku bozuklukları, depresyon ve anksiyetenin doğru tanı ve tedavisi ile hastaların konforunun arttırılabilirliliğinin vurgulanması literatür açısından önem arz etmektedir.

Anahtar Kelimeler: İnme sonrası santral ağrı, the leeds assessment of neuropathic symptoms and signs (lanss), vizüel analog skala (vas), yaşam kalitesi, uyku bozukluğu

Introduction

Stroke is the third most common cause of death and the first cause of disability in the world. It has a significant share in both hospitalization and health expenditures in industrializedcountries (1).

The pain caused by the dysfunction or primary lesion of the central nervous system after stroke is called post-stroke pain and it is one of the reasons for central neuropathic pain (2, 3). Central post-stroke pain (CPSP) is a common syndrome after stroke and it is observed approximately in 1 of the 3 patients with post-stroke pain (4). It was first described by Dejerine and Roussy in 1906 as the pain occurring spontaneously after thalamic stroke (5). Thus, the expression of thalamic pain is sometimes used instead of CPSP. However, the researchers then comprehensively described the characteristics of the pain caused by extrathalamic lesions (6).

CPSP is characterizedby pain and sensory abnormalities in the body (when other reasons for significant nociceptive, psychogenic orperipheral pains are excluded) after cerebrovascular lesion of the somatosensorial system (7). Symptom onset is often gradual, coinciding with the improvement of perceived sensory loss and the appearance of dysesthesia. The pain is frequently severe and unrelenting, with pain-free episodes not exceeding a few hours (8). The prevalence of CPSP has been reported to be 7.3% (7).

By a year after stroke onset, quality of life (QoL) decreases 40% compared with before a stroke. As pain is known to affect recreational activities, vocational status, and quality of sleep, it can have a major role on QoL, mood, and rehabilitation outcome (9). In our study, the quality of life and sleep quality were evaluated comparatively according to the presence and level of pain in ischemic stroke patients with and without central pain.

Methods

The study is done through ethics committee approval and patient consent form on ischemic stroke patients which are followed by xxxxxxxx Medicine Faculty Neurology Clinic in 2017. The authors declare that there is no conflict of interest regarding the publication of this paper.

The patients with ischemic stroke diagnosis, at the age range between 30-85 years, with thyroid and parathyroid disease, use of corticosteroid and hormone replacement therapy, malnutrition, cancer diagnosis, psychiatric treatment use, chronic renal and liver disease, and without motor dysfunction due to a orthopedic discomfort and the ones who acknowledged their participation were included in the study.

75 ischemic stroke patients (31 females, 44 males) were included in the study. While 28 of the patients experienced central pain within one year after ischemic stroke, 47 of them (19 females, 28 males) did not experience central pain in one year following anischemic stroke. The patients were separated into two groups as thalamic and extrathalamic in terms of ischemic stroke localization.

The pain assessment of the patients was performed with the Leeds Assessment of Neuropathic Symptoms and Signs (LANSS) pain scale and the Visual Analogue Scale (VAS). The life quality assessment was performed with the European Quality 5 Dimension (EQ5D) and EQ5D VAS. Moreover, the Beck Anxiety Scale, the Beck Depression Scale and the Epworth Sleepiness Scale were applied to the patients.

In groups with and without central pain; gender, age, and infarct location were compared. In the group with central pain; with the values of LANSS <12 and ≥12 and according to VAS values; quality of life was assessed with EQ5D and EQ5D VAS. Among the same groups; comparisons were made with Beck Anxiety and Beck Depression Scale scores with the Epworth sleep score values of <11 and ≥11 (daytime sleepiness).

Statistical Analysis

The Fisher-Freeman-Halton test, Independent samples t-test, one-way analysis of variance, Kruskal-Wallis H test, one-way ANOVA, chi-square test and correlation analyses were used in the assessment of the data depending on the type and purpose of the characteristics. When the p value was found <0,05 in the statistical evaluations, the result was considered to have statistical significance. SPSS Version 18.0 (IBM Inc.; SPSS Statistics for Windows, Version 18.0. Armonk, NY, ABD) was used ststistical calculations.

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Results

While the lowest age was 32 and the highest age was 87 years, the average age in the group with central pain was 64.04±12.9 years, and the average age in the group without central pain was 62.8±13.9 years.

While there were 15 (53,6%) patients with thalamic infarct and 13 (46,4%) patients with extrathalamic infarct in the group with central pain, there were 7 (14,9%) patients with thalamic infarct and 40 (85,1%) patients with extrathalamic infarct in the group without central pain.

Gender and age distribution were found to be similar in the groups with and without central pain (p≤0.836 and 0.701). The rate of the cases with thalamic infarct was significantly high in the group with central pain (p≤0.001).

A significant difference was observed between the VAS average of 3.25±0.96 of the patients with LANSS<12 and the VAS average of 7.1±1.25 of the group with LANSS≥12 in the group with central pain (p≤0.001). According to this result, the VAS severity of those with LANSS of 12 and above was higher.

As a result of the EQ5D and EQ5D VAS life quality assessment carried out in the group with central pain, a significant positive correlation was found between both values (p≤0.001) and both measurements indicated a statistically significant correlation in the quality of life as the VAS level increased (p≤0.001, 0.001). Similarly, it was identified that the quality of life (EQ5D and EQ5D VAS) was low in the group with LANSS≥12 when compared to the group with LANSS<12 (p≤0.006, 0.016) (Table 1).

No statistically significant difference was observed between the groups with and without CPSP in terms of the Epworth Sleepiness point average (p≤0522). In the assessment performed in two separate groups as the Epworth score (daytime sleepiness condition) <11 and ≥11, no significant difference was determined between the cases with and without CPSP (p≤0.744).Statistically significant data were obtained in the group with CPSP as the VAS score increased and in the cases with LANSS≥12 according to the Epworth Sleepiness Scale (p≤0.001, 0.002).When the groups with the Epworth score <11and ≥11 were compared,the daytime sleepiness rate was found to be significantly higher in the group with LANSS≥12 and as the VAS score increased (p≤0.018, 0.001) (Table 2).
The Beck Anxiety and Beck Depression Scale values of the groups with and without CPSP did not indicate a significant change (p≤0.731, p≤0.249), and the anxiety and depression levels of both groups were found to be similar. In the group with CPSP, it was identified that the anxiety level determined with the Beck Anxiety scale was significantly higher in the cases with LANSS≥12 when compared to those with LANSS<12 (p≤0.007) and no significant difference was observed in terms of the depression level (p≤0.406). A significant positive correlation was found between the anxiety and depression levels in the group with central pain according to the VAS, and the Beck Anxiety and Beck Depression scales (p≤0.000, 0.001). In other words, as the VAS level increases, the anxiety and depression levels of patients increase significantly.

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Discussion

Neuropathic pain is the pain which cause sensory symptoms and findings caused by a lesion in the peripheral or central nervous system or in both of them. Neuropathic pain is divided into central and peripheral neuropathic pain. Post-stroke pain is one of the causes of central neuropathic pain (2, 3). Altough, there remain some mysteries as to the pathophysiology of CPSP, it is believed to be caused by stroke in the region of the thalamus and extrathalamic areas. The thalamus is a relay station for sensory information from all over the body (10). In our study, the patient group who had central pain after ischemic stroke was divided into 2 groups as thalamic and extrathalamic.

In most of stroke patients, central pain develops in the first month after stroke; however, it may also develop 6 months and more after stroke in some patients (11). The patients who experienced central pain within 1 year after stroke were included in our study.

Although central pain after stroke was originally described as 'thalamic pain', it is currently recognized that strokes involving the sensory tracts in the various brain regions can produce pain similar to central pain (12).

In some studies, higher pain intensities have been reported when the lesions were located in the brainstem or thalamus than in other areas; however, in another study, the symptoms and severity of CPSP in thalamic versus extrathalamic stroke did not differ (9).

28 of the 75 ischemic stroke patients had CPSP in our study. The rates of the 15 (53,6%) patients with thalamic infarct were similar with the rates of the 13 (46,4%) patients with extrathalamic infarct. There were only 7 (14,9%) patients with thalamic infarct in the group of 47 patients without CPSP. In other words, thalamic lesions are observed more frequently in the group with CPSP when compared to the group without CPSP ($p \leq 0.001$), moreover, the frequency of thalamic and extrathalamic lesions was found to be similar in the group. In the future studies to be conducted with more CPSP patients, this situation will become clearer.

It is hard to diagnose CPSP. In this process, it is beneficial to identify pain level with pain scales such as the Visual Analogue Scale and Numerical Rating Scale, however, no scale was developed especially for CPSP (7). In our study, the pain assessment was carried out with the LANSS and VAS in the group with CPSP and it was identified that the VAS severity was higher in the group with LANSS≥12 ($p \leq 0.001$), in other words, both tests were correlated in indicating the level of pain.

There are many studies on the fact that the presence of CPSP impairs the life quality of patients. For example, in a study conducted with 100 stroke patients by Kılıç et al., CPSP was determined in 20 patients. While CPSP was evaluated with the LANSS, the quality of life was evaluated with the Nottingham Health Profile (NHP). Central pain was related to a significant difference in the pain parameter of the Nottingham Health Profile (NHP) ($p \leq 0.001$). In conclusion, it was stated that CPSP is a complication that should not be ignored because it is not rare and has a negative impact on the quality of life of patients with stroke (13). In a

study conducted with 24 CPSP patients, while pain was evaluated with the LANSS and VAS, the quality of life was evaluated with the 36-item Short-Form Health Survey quality of life scale (SF-36 QoLS). The result was reported as the fact that CPSP has a negative impact on the physical subscale score of the SF-36 QoLS in patients with stroke (9).In our study, the quality of life of patients was assessed with EQ5D and EQ5D VAS. In the assessments performed with both the LANSS and VAS, the level of pain and the quality of life were statistically significant. It was observed that, as the severity of CPSP increased, the quality of life decreased in correlation with this. This condition did not indicate any difference between thalamic and extrathalamic groups. It is a fact that central pain has a negative effect on the quality of life; however, it is possible to increase the quality of life of patients with a correct diagnosis and treatment.

In many studies, it has beendemonstrated that as CPSP affects the quality of life, it also affects sleep quality. In a study conducted by Raffaeli et al. with 601 stroke patients with CPSP, half (50%) of the interviewed pain population could sleep in a restful way, 28.8% had some difficulty, and 21.8% could not sleep at all (14). 199 patients were examined to identify sleep disorders in a 3-month period after cerebral infarct and the nighttime sleep quality and excessive daytime sleepiness of the patients were evaluated with the VerranSnyder-Halpern sleep scale and Epworth Sleepiness Scale. Bad nighttime sleep was reported in 88 patients (44.2%) and excessive daytime sleepiness was reported in 28 patients (14.4%). No significant relationship was determined between post-stroke pain and post-stroke sleep disorders (15). In a study conducted with 3732 individuals aged 65 and older, as a result of the assessment with the Pitsburg Sleep Quality Index (PSQI) in the cases with subjective bodily pain; it was observed that those with serious and very serious bodily pain had the highest values and moreover, higher values were identified in the group with mild bodily pain when compared to the group without any bodily pain. It is known that painful syndromes cause sleep disorders. CPSP is one of the serious painful syndromes (16).

In our study, no statistically significant result was obtained between the groups with and without CPSP in terms of bad nighttime sleep and excessive daytime sleepiness. However, it was identified in the group with CPSP that the nighttime sleep quality decreased as the VAS score increased ($p \leq 0.001$). The nighttime sleep quality was worse in the group with LANSS 12 in the same group ($p \leq 0.002$). In the assessment conducted according to excessive daytime sleepiness, the rate was higher in the group with LANSS 12 and as the VAS score increased ($p \leq 0.018$, 0.001).

In general, it is known that painful syndromes cause sleep disorders. CPSP is one of the serious painful syndromes (16). These sleep disorders developing in CPSP patients further deteriorate the quality of life of patients.

Sleep disorders and functional disorders such as depression and anxiety are the important comorbid conditions accompanying CPSP (11). In our study, depression and anxiety were found at similar rates between the groups with and without CPSP, however, in the assessment with the LANSS and VAS in the group with CPSP, it was identified that the anxiety and depression levels increased as the level of pain increased. In other words, pain appears as a condition increasing depression and anxiety and deteriorating the quality of life

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in this regard. The importance of the diagnosis and treatment of these diseases accompanying CPSP has beenemphasized once again.

Conclusion

CPSP is frequently observed syndrome among the post-stroke pains. Besides our study; in many studies as well, it has been shown that it has a remarkable negative effect on the quality of life of stroke patients. It is important for the literature to emphasize that it is possible to improve the comfort of patients with a correct diagnosis and treatment of sleep disorders, depression and anxiety accompanying CPSP.

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TABLES

Table 1. The comparison of the quality of life and EQ5D in stroke patients with CPSP with LANSS and VAS.

	LANSS<12	LANSS≥12	p	VAS	p
	n	n		n	
EQ5D	4	24	0.006	28	0,001
EQ5D VAS	4	24	0,016	28	0,001

*The Leeds Assessment of Neuropathic Symptoms and Signs (LANSS)
**Visual Analogue Scale (VAS)
***The life quality assessment was performed with the European Quality 5 Dimension (EQ5D)

Table 2. The comparison of the Epworth Sleepiness Scale in stroke patients with CPSP with LANSS and VAS.

CPSP	LANSS<12	LANSS≥12	p	VAS	p
	n	n		n	
Epworth sleepiness score	4	24	0,002	28	0,001
Epworth score <11	4	11	0,018	15	0,001

Epworth score ≥11	0	13		13	

*Central post-stroke pain (CPSP)
**The Leeds Assessment of Neuropathic Symptoms and Signs (LANSS)
***Visual Analogue Scale (VAS)

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