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ARAŞTIRMA MAKALESİ **RESEARCH ARTICLE**

The Relationship of Vitamin B 12 with Two Difficult Complications of Shingles: Who has Pain and Who has Itch?

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Abstract

Aim: Both herpetic pain and itching in shingles are two symptoms whose pathogenesis has not been elucidated, although they are thought to be due to nerve damage. These two symptoms are difficult to treat and negative impact quality of life. In addition, It is unclear which patient will have the symptoms of itching or pain. Vitamin B 12 is a neurotropic agent which is contributes to the treatment of nerve damage, and effective in treating neuropathic pain and itch. In this study, we aimed to investigate the effect of vitamin B12 values on the itching and pain symptoms that patients with shingles may have in the acute period.

Materials and Methods: In this study, we investigated the effect of vitamin B12 values on itching and pain symptoms that patients with shingles have in the acute period. Vitamin B 12 values of 53 adults with patients with shingles with herpetic pain or herpetic itching were recorded and compared with the control group.

Results: We found that patients with herpetic pain had lower vitamin B12 values than the control group (p=0.046) and patients with herpetic itch (p=0.021). Vitamin B12 values of herpetic itch patients did not show significant difference from the control group (p=0.816).

Conclusion: Although vitamin B12 deficiency plays a role in the etiology of herpetic pain, it has no effect on herpetic itching. Our study supports that the etiopathogenesis of HI is different from herpetic pain and will help studies focusing on herpetic itching etiopathogenesis.

Keywords: *Herpes, itch, pain, shingles, vitamin B 12*

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B12 vitamini ile zona hastalığının iki semptomu arasındaki ilişki: Kimlerde ağrı, kimlerde kaşıntı görülür?

Özet

Amaç: Zona sonrası gelişen ağrı ve kaşıntı, patogenezi henüz açıklığa kavuşturulamamış,sinir hasarına bağlı olduğu düşünülen semptomlardır. Bu iki semptomun tedavisi zordur ve yaşam kalitesini olumsuz etkiler. Ayrıca, hangi hastanın kaşıntı veya ağrı semptomları göstereceği belirsizdir. Vitamin B12, sinir hasarının tedavisine katkıda bulunan ve nöropatik ağrı ve kaşıntının tedavisinde etkili olan bir nörotropik ajandır. Bu çalışmada, akut dönemde zona hastalarının yaşayabileceği kaşıntı ve ağrı semptomları üzerinde B12 vitamini değerlerinin etkisini araştırmayı amaçladık.

Gereç ve Yöntem: Bu çalışmada, akut dönemde zona hastalarının yaşadığı kaşıntı ve ağrı semptomları üzerinde B12 vitamini değerlerinin etkisini araştırdık. Herpetik ağrı veya herpetik kaşıntı yaşayan 53 zona hastasının B12 vitamini değerleri kaydedildi ve kontrol grubu ile karşılaştırıldı.

Bulgular: Herpetik ağrı olan hastaların kontrol grubuna göre (p=0,046) ve herpetik kaşıntı olan hastalara göre (p=0,021) daha düşük vitamin B12 değerlerine sahip olduğunu bulduk. Herpetik kaşıntı hastalarının vitamin B12 değerleri kontrol grubundan önemli bir fark göstermedi (p=0,816).

Sonuç: Vitamin B12 eksikliği herpetik ağrının etiyolojisinde rol oynasa da, herpetik kaşıntı üzerinde herhangi bir etkisi yoktur. Çalışmamız, HI'nın etiyopatogenezinin herpetik ağrıdan farklı olduğunu desteklemekte ve herpetik kaşıntının etiyopatogenezine odaklanan çalışmalara yardımcı olacaktır.

Anahtar Kelimeler: *Herpes, kaşıntı, ağrı, zona, vitamin B 12*

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INTRODUCTION

Shingles occurs due to the reactivation of a dormant varicella zoster virus infection in the dorsal root ganglia. Secondary bacterial infections, ophthalmic problems, cranial and peripheral nerve palsy and herpetic neuralgia are common complications. Additionally, it negatively impacts patients' quality of life by causing this herpetic pain (HP) and/or herpetic itching (HI) (1). The severity of HP accompanying in the acute period constitutes a risk factor for developing post-herpetic neuralgia (2). HP affects the daily lives of patients negatively both physically and emotionally by causing symptoms such as sleep disorders, depression, weight loss, and chronic fatigue (3). There is a complex relationship between HP and HI, and the answer to the question of which patients develop HP and in which HI is not clear. HI, which has been studied as frequently as HP, can occur alone or accompany HP. While HP does not involve an approach that traumatizes the skin, HI causes patients to scratch themselves and even harm themselves (4).

Although HP and HI accompanying shingles appear to be associated with neural tissue damage and functional abnormality such as subepidermal nerve plexus, afferent fibers, and epidermal nerve fiber endings, the etiopathogenesis has not been clarified yet (5,6).

Vitamin B 12 supports myelinization and axonal transport, helps the regeneration of peripheral nerve cells and is used in the treatment of neuropathic pain due to this feature6. Additionally, it has been reported that vitamin B 12 deficiency plays a role in the etiology of neuropathic itching by causing small-fiber neuropathy (7,8). Although HP and HI be associated with neural tissue damage and functional abnormalities such as subepidermal nerve plexus, afferent fibers, and epidermal nerve fiber endings, the etiopathogenesis has not been clarified yet (8,9). In this study, it was investigated the effect of vitamin B12 on itching and pain symptoms that patients with zona have been in the acute period.

MATERIALS AND METHODS

This study was conducted retrospectively. Data of patients diagnosed with shingles between June 2017 and July 2020 were analyzed. Patients who did not have shingles and who applied to family medicine because of general control were accepted as the control group. The localizations of the lesions (head and neck, thoracic, lumbosacral, extremities) of the patients with shingles, the presence of subjective symptoms (pain, itching), and vitamin B 12 values of both the control and study groups were recorded. Patients who took vitamin supplements, breastfeeding and pregnant women, children in growth and development age, those with central and peripheral neurological diseases, those with symptoms both pain and itching, and those using opioids and non-opioid analgesics were excluded from the study.

The SPSS 21.0 program was used for data analysis. Frequency (n), percentage (%), mean ± standard deviation values were used as descriptive statistics to evaluate the data obtained from the study. Relationships between numerical data were evaluated using Student's t test for independent samples when normality assumptions were provided, and nonparametric equivalents of the same tests in cases where normality were not be achieved. Relationships between categorical variables were determined using the Ch-square test. The P value <.05 was considered statistically significant.

RESULTS

The study included 27 females, 26 males, 53 patients diagnosed with shingles, and 17 females, 10 males, as a control group. The mean age of the patients was 45.90 ± 18.07, the mean age of the control group was 40.64 ± 16.49, and there was no difference between the control group and the patient groups in terms of gender and age. In order of frequency, shingles lesions were located on the extremity in 5 patients (9.5%), in the head and neck region in 9 patients (17%), in the thoracic region in 17 patients (32.1%), and in the lumbosacral region in 22 patients (41.5%). 66% of the patients (n: 35) had pain symptoms, and 34% (n: 18) had itching symptoms (Table 1).

Table 1. Demographic characteristic and lesion localization of patients

	n	%
Gender		
female	**27**	**50.9**
male	**26**	**49.1**
Localization		
Extremities	**5**	**9.5**
Head	**9**	**17**
Thorax	**17**	**32**
Lumbosacral	**22**	**41.5**
Pain	**35**	**66**
Pain and ıtching	**7**	**13.2**
ıtching	**18**	**34**

There was no difference in gender and age between patients with HP symptoms and patients with HI symptoms (respectively $p = 0.22$, $p = 0.55$). Vitamin B12 values in patients with HP (295.50 ± 86.37) were found to be lower than HI (364.72 ± 119.22) and control group (355.88 ± 113.91) (respectively $p = 0.021$, $p = 0.046$). No significant relationship was found between vitamin B12 values of patients with HI and the control group (p = 0.816), (table 2).

Table 2. The comparison with vitamin B12 levels between herpetic pain, herpetic pruritus, and control

	Herpetic Pain (n: 35)	**P≈**	**Control (n:28)**	**P≈**	**Herpetic ıtching (n:18)**	**P≈**
Age	46.91±18.68	0.165	40.64±16.49	0.544	43.82±17.09	0.557
Gender		0.112		0.535		0.220
Female	16		18		11	
Male	19		10		7	
Vitamin B12 level	295.50±86.37	**0.046**	355.88±133.91	0.816	364.72±119.22	**0.021**

≈Difference between controls and herpetic Pain patients
˚Difference between controls and herpetic ıtching
˜Difference between herpetic pain and herpetic ıtching

DISCUSSION

In our study, it was observed that patients with HP had lower vitamin B12 levels compared to those with HI and the control group. In addition, also the vitamin B12 values of the patients with HI did not differ from the control group.

The relationship between HP and HI, which are two symptoms whose etiopathogenesis is not fully understood, has inspired many studies before (8-11). Diagnostic biopsies show that epidermal innervation is almost completely lost in HI while excessive electrical activity of peripheral nociceptive neurons in sensory ganglia or distal axon ends is the main cause for HP (6). In a study conducted with 586 shingles patients, it was reported that HI accompanies both acute zoster and post herpetic neuralgia, and although increased age is a risk factor for HP, no relation was found between HI and age (10). In the study conducted by Ishikawa et al., although HI accompanies 44% of patients with post herpetic neuralgia and regresses with HP treatment, no relation was found between itching and pain intensity and emphasizing that there is no major neuropathic component for and HI, they reported that HP and HI may have

different mechanisms (11). There are limited studies examining the relationship between vitamin B 12 and HP and HI (12,13). The study of Chen et al. reported that vitamin B12 values of the shingles patients with HP were lower than the control group (12). In the study investigating the effect of local injections of B vitamins on HP and HI, Xu et al. reported that Vitamin B1 has a significant atipruritic effect, while vitamin B12 has an analgesic effect, and reported that combinations of these vitamins have both antipruritic and analgesic dual effects (13).

Both HP and HI are two important symptoms of shingles that negatively affect the quality of life (14). In the treatment of HP; gabapentin, pregabalin, tricyclic antidepressants, lidocalin, and capsaicin can be used, but satisfactory results cannot be obtained (15). Antihistamines and corticosteroids are ineffective for HI, and although pain and itching are thought to have similar pathways, many drugs effective in relieving neuropathic pain are ineffective in relieving neuropathic itching, nor even opioid analgesics used for treating HP can cause HI (10). HI is not uncommon among zona patients, althougt it is not elucidated in literature yet, and this reveals the fact that a separate treatment modality required for HI (11).

In our study, while the level of vitamin B 12 was found to be low in HP, we did not find a relationship with HI. Our findings contradict the previous literature examining the relationship between vitamin B12 and HI and HP, supporting the idea that HI has a different pathway than other HP.

According to our study, vitamin B12 deficiency is associated with HP formation but has no association with HI formation. In this context, as the pathophysiology of herpetic pain and itching is elucidated, detailed studies can be conducted for more effective approaches. Further studies focusing on the etiopathogenesis of HI will contribute to the treatment of this symptom, which negatively affects quality of life.

Author's contribution: Conceptualization; İÖ, GK, DİY., writing; İÖ, GK, DY, review; DY, RD, AA, editing; İÖ, RD, AA, proofreading; DİY, RD.

Conflict of interest: The authors declare that they have no conflicts of interest.

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