



Effects of Caffeine Use in Hemifacial Spasm Patients

Hemifasiyal Spazm Hastalarında Kafein Kullanımının Etkileri

Mehmet Kara¹, Soner Kılıç²

¹Department of Medical Pharmacology, Kayseri City Research and Training Hospital, Turkey

²Department of Neurology, Kayseri City Research and Training Hospital, Turkey

Abstract

Aim: Hemifacial spasm is characterized by progressive, involuntary, irregular contraction of the muscles innervated by the facial nerve. Caffeine is a phytochemical that increases muscle contraction and neurotransmitter release. The aim of this study is to evaluate the effects of caffeine-containing food consumption on disease severity and disease-related quality of life in patients with hemifacial spasm.

Material and Method: In hemifacial spasm patients who applied to the neurology outpatient clinic; hemifacial spasm quality of life scale and hemifacial spasm severity scale were evaluated prospectively. The amount of caffeine taken by the patients with daily food and beverage was determined. The relationship between the results of the scales and the amount of caffeine consumed was analyzed.

Results: A total of 60 patients, 36 women (60%) and 24 men (40%), were included in the study. It was determined that 59 of the patients (98.3%) consumed an average of 303±144 mg/day of caffeine with food. The hemifacial spasm quality of life scale score was calculated as 8.5 (4-21) and the hemifacial spasm severity scale was calculated as 3 (1-4). No significant correlation was found between the amount of caffeine consumed by gender ($p=0.066$). A negative correlation was found between the amount of caffeine consumed by age ($r=-0.291$; $p=0.024$). There was no significant relationship between daily caffeine consumption and hemifacial spasm quality of life scale and hemifacial spasm severity (p values 0.297 and 0.839, respectively). There is a weak positive correlation between the hemifacial spasm quality of life scale and the severity of hemifacial spasm ($r=0.291$; $p=0.024$).

Conclusion: It has been determined that the consumption of foods containing caffeine in daily life does not affect the severity of spasm and quality of life in patients with hemifacial spasm.

Keywords: Hemifacial spasm, caffeine, theophylline

Öz

Amaç: Hemifasiyal spazm, fasiyal sinir tarafından innerve edilen kasların ilerleyici, istemsiz, düzensiz kasılması ile karakterizedir. Kafein, kas kasılmasını ve nörotransmitter salınımını artıran bir fitokimyasaldır. Bu çalışmanın amacı hemifasiyal spazmlı hastalarda kafein içeren gıda tüketiminin hastalık şiddeti ve hastalıkla ilişkili yaşam kalitesi üzerine etkilerini değerlendirmektir.

Gereç ve Yöntem: Nöroloji polikliniğine başvuran hemifasiyal spazm hastalarında; hemifasiyal spazm yaşam kalitesi ölçeği ve hemifasiyal spazm şiddet skalası prospektif olarak değerlendirildi. Hastaların günlük yiyecek ve içeceklerle aldıkları kafein miktarları belirlendi. Ölçek sonuçları ile tüketilen kafein miktarı arasındaki ilişki analiz edildi.

Bulgular: Çalışmaya 36 kadın (%60) ve 24 erkek (%40) olmak üzere toplam 60 hasta dahil edildi. Hastaların 59'unun (%98,3) yemekle birlikte ortalama 303±144 mg/gün kafein tükettiği belirlendi. Hemifasiyal spazm yaşam kalitesi ölçeği puanı 8,5 (4-21), hemifasiyal spazm şiddeti ölçeği 3 (1-4) olarak hesaplandı. Cinsiyete göre tüketilen kafein miktarı arasında anlamlı bir ilişki bulunmadı ($p=0,066$). Yaşa göre tüketilen kafein miktarı arasında negatif korelasyon bulundu ($r=-0,291$; $p=0,024$). Günlük kafein tüketimi ile hemifasiyal spazm yaşam kalitesi ölçeği ve hemifasiyal spazm şiddeti arasında anlamlı bir ilişki yoktu (p değerleri sırasıyla 0,297 ve 0,839). Hemifasiyal spazm yaşam kalitesi ölçeği ile hemifasiyal spazm şiddeti arasında pozitif yönde zayıf bir korelasyon vardır ($r=0,291$; $p=0,024$).

Sonuç: Hemifasiyal spazmlı hastalarda günlük yaşamda kafein içeren besinlerin tüketiminin spazm şiddetini ve yaşam kalitesini etkilemediği saptanmıştır.

Anahtar Kelimeler: Hemifasiyal spazm, kafein, teofilin



INTRODUCTION

Hemifacial spasm (HFS) is characterized by progressive, involuntary, irregular, clonic or tonic movements of the muscles innervated by the facial nerve (VII. cranial nerve). The distinguishing characteristic of the disease is involuntary clonic and/or tonic contraction of the facial muscles, usually unilateral.

^[1] Exposure of facial nerve roots to vascular compression (primary HFS) is the most common type. Excessive stimulation from the facial nerve afferent to the facial nerve nucleus and ephaptic transmissions occurring around the affected nerve region are responsible for the pathophysiology of the disease.

^[2] Secondary HFS causes; cerebellopontine corner tumor, aneurysms, infections (otitis media, tuberculous meningitis), epidermoid and arachnoid cysts.^[3]

Although it is perceived as a benign disease, it can cause increased shame and social withdrawal for the individual. In severe cases, symptoms can affect a person's quality of life by affecting vision, speech, and mental concentration.

One of the phytochemicals found in relatively high amounts in coffee, tea and cocoa is methylxanthines. Among these methylxanthines, caffeine is the most studied substance, which has clear effects on neuronal network activity, enhances cognitive performance, and is reported to be protective against stroke, Alzheimer's disease and Parkinson's disease.^[4,5] Caffeine causes muscle contraction and vasoconstriction by stimulating catecholaminergic and adenosine receptors. The net effect of caffeine in HFS patients is unknown.

The effect of caffeine, which is catabolized to dimethylxanthines by the cytochrome P450 system, disappears within a few hours.

^[6] The pharmacokinetics and bioavailability of caffeine are quite similar in subjects aged 20 and 71 years.^[7] This age group also includes our patient group included in our study. Therefore, in our study, we can accept that the pharmacokinetics and bioavailability of caffeine do not change with age.

The aim of this study is to evaluate the effect of caffeine consumed with hot or cold beverages on the quality of life and disease severity in primary HFS patients.

During the follow-up of our HFS patients in our neurology clinic, we have patients who consume caffeine-containing foods such as tea and coffee, etc. daily. Our motivation in our study was to think that the increase in the complaints of these patients due to HFS is related to caffeine consumption.

MATERIAL AND METHOD

In primary HFS patients who applied to Kayseri City Training and Research Hospital Neurology outpatient clinic; The HFS quality of life scale and the HFS severity scale were calculated prospectively.^[8,9]

Patients with intermittent, clonic and/or tonic spasm, mostly in the upper half of the face, were included in the study. Brain magnetic resonance imaging (MRI) was performed on the patients, and secondary pathologies that could cause facial nerve compression were excluded. Cases with a history of

peripheral facial paralysis, trauma and infection were not included in the study. Patients using hypnotic and sedative drugs were not included in this study.

The treatments of the patients were not designed specifically for the study. They continued to receive their treatment in accordance with their routine treatment algorithms.

The amount of caffeine taken by the patients with daily food and beverage foods was determined.^[10-12] The most consumed caffeine-containing food was determined as the food that contributed the most to total daily caffeine intake. In the calculation of food consumption, the statements of the patients were taken as basis. Informed consent was obtained from the patients at the time of participation in the study. No additional examination or analysis specific to the study was performed.

Patients' age, gender, daily caffeine consumption (mg/day), the most consumed caffeine-containing food (granulated coffee, black tea, green tea, Turkish coffee), HFS quality of life scale score (HFS-7) (between 0 and 28). : best, 28: worst quality of life) and HFS severity (0-4: no abnormality, 4: severe spasm).

Statistical Method

Data were analyzed with IBM SPSS V23. Kolmogorov Smirnov and Shapiro Wilk tests were used to fit the normal distribution. Descriptive statistics; number and percentage for categorical variables; For numerical variables, data that provided the normal distribution parameters were given as mean±standard deviation, and those that did not fit the normal distribution were given as median (minimum-maximum). One-way analysis of variance and independent samples t-test were used for normally distributed ones. Mann Whitney U test and Kruskal Wallis test were used for data not normally distributed. Pearson and Spearman correlation coefficients were used to analyze the relationships. Pearson chi-square test was used for categorical data. Significance level was taken as p<0.05.

RESULTS

Of the 60 patients, 36 (60%) were female and 24 (40%) were male. The mean age of the patients was 58.17±11.8 years. It was determined that 59 of the patients (98.3%) consumed an average of 303±144 mg/day of caffeine with food. The HFS quality of life scale score was calculated as 8.5 (4-21) and the HFS severity scale was calculated as 3 (1-4) (**Table 1**).

Table 1. General characteristics of the patients

	Average	Standard Deviation	Median	Minimum	Maximum
Age	58.17	11.814	57	39	82
Caffeine consumption, mg/day	303	144.216	301.5	0	682
Hemifacial spasm quality of life scale	9.6	4.001	8.5	4	21
Hemifacial spasm severity	2.63	0.736	3	1	4

The mean age values did not differ according to gender ($p=0.843$). While the mean value for women was 57.92 ± 12.63 years, it was 58.54 ± 10.72 years for men. Daily caffeine consumption, mg/day mean values do not differ according to gender ($p=0.066$). While the mean value in women was 275.06 mg, it was obtained as 344.92 mg in men. The median values of the HFS quality of life scale did not differ according to gender ($p=0.778$). While the median value was 8.5 (4-21) for women, it was 8.5 (5-21) for men. Median values of HFS severity do not differ according to gender ($p=0.300$). While the median value was 3 (2-4) in women, it was 2.5 (1-4) in men (**Table 2**).

Table 2: Comparison of quantitative data by gender

	Female		Male		p
	Mean± Standard Deviation	Median (minimum-maximum)	Mean± Standard Deviation	Median (minimum-maximum)	
Age	57.92±12.63	57 (39-82)	58.54±10.72	56.5 (42-79)	0.843 ^a
Caffeine consumption, mg/day	275.06±139.52	285 (0-555)	344.92±143.79	332.5 (130-682)	0.066 ^a
Hemifacial spasm quality of life scale	9.58±4.24	8.5 (4-21)	9.63±3.7	8.5 (5-21)	0.778 ^b
Hemifacial spasm severity	2.72±0.51	3 (2-4)	2.5±0.98	2.5 (1-4)	0.300 ^b

a Independent samples t-test; bMann Whitney U test

The distribution of the most consumed caffeine-containing foods does not depend on gender ($p=0.661$). While 74.3% of women consume black tea, the rate of black tea consumption in men is 79.2% (**Table 3**).

Table 3. Comparison of the most consumed caffeine-containing foods by gender

	Female	Male	P*
The most consumed caffeine-containing food			
Granular coffee	2 (5,7)	2 (8,3)	0,661
Black tea	26 (74,3)	19 (79,2)	
Green tea	2 (5,7)	0 (0)	
Turkish coffee	5 (14,3)	3 (12,5)	

*Pearson chi square

There is a negative relationship between age and only daily caffeine consumption ($r=-0.291$; $p=0.024$). As age increases, the amount of caffeine consumed decreases. There was no significant relationship between age, HFS quality of life scale and HFS severity (p values 0.892 and 0.653, respectively) (**Table 4**).

Table 4: Correlation analysis results of age and quantitative data

	Age	
	r	p
Caffeine consumption, mg/day	-0.291	0.024
Hemifacial spasm quality of life scale	-0.018	0.892
Hemifacial spasm severity	-0.059	0.653

r: Pearson correlation coefficient

While the average age of those consuming granulated coffee was 55.25 years, those consuming black tea were

58.82 years, those consuming green tea were 79 years, and those consuming Turkish coffee were 52.75 years. There is a difference between the mean ages according to the foods consumed ($p=0.034$). The mean age of those who consumed green tea was higher than the others (**Table 5**).

Table 5. Comparison of average age values according to consumed foods

	n	Mean± Standard Deviation	Median (minimum-maximum)	P*
Granular coffee	4	55.25±11.81 ^a	51.5 (46-72)	0.034
Black tea	45	58.82±11.31 ^a	58 (39-79)	
Green tea	2	79.00±4.24 ^b	79 (76-82)	
Turkish coffee	8	52.75±10.38 ^a	50.5 (42-72)	

*One-way analysis of variance; a-b No difference between foods with the same letter (Duncan test)

There was no significant relationship between daily caffeine consumption and HFS quality of life scale and HFS severity (p values 0.297 and 0.839, respectively) (**Table 7**).

Table 7. Correlation analysis results of caffeine consumption and quantitative data

	Caffeine consumption, mg/day	
	r	p
HFS quality of life scale	-0.137	0.297
HFS severity	0.027	0.839

r: Spearman correlation coefficient

The most consumed food was black tea (76.3%) (**Table 8**).

Table 8: Distribution of consumed foods

	n	%
Food		
Granular coffee	4	6.8
Black tea	45	76.3
Green tea	2	3.4
Turkish coffee	8	13.6

There was no difference between the median values of the HFS quality of life scale according to the foods consumed ($p=0.827$). The median value was determined as 8.5 (5-12) in granulated coffee, 8 (4-21) in black tea, 12.5 (6-19) in green tea and 8 (6-15) in Turkish coffee (**Table 9**).

Table 9. Comparison of HFS quality of life scale values according to consumed foods

	n	Mean± Standard Deviation	Median (minimum-maximum)	P*
Granular coffee	4	8.5±3.51	8.5 (5-12)	0.827
Black tea	45	9.56±3.82	8 (4-21)	
Green tea	2	12.5±9.19	12.5 (6-19)	
Turkish coffee	8	8.5±2.93	8 (6-15)	

*Kruskal Wallis

There was no difference between the median values of HFS severity according to the foods consumed ($p=0.287$). The median value was determined as 2.5 (2-4) in granulated coffee, 3 (1-4) in black tea, 3 (2-4) in green tea and 2 (2-3) in Turkish coffee (**Table 10**).

Table 10. Comparison of Hemifacial spasm severity values according to consumed foods

	n	Mean± Standard Deviation	Median (minimum-maximum)	p*
Granular coffee	4	2.75±0.96	2.5 (2-4)	0.287
Black tea	45	2.67±0.74	3 (1-4)	
Green tea	2	3±1.41	3 (2-4)	
Turkish coffee	8	2.25±0.46	2 (2-3)	

*Kruskal Wallis

There is a weak positive correlation between the HFS quality of life scale and the severity of HFS ($r=0.291$; $p=0.024$) (Table 11).

Table 11. Hemifacial spasm severity and Hemifacial spasm quality of life scale correlation analysis results

	Hemifacial spasm severity	
	r	p
Hemifacial spasm quality of life scale	0.291	0.024

r: Spearman correlation coefficient

DISCUSSION

Primary HFS is mostly 5th-6th grade. It occurs in the decade and is more common in females (2:1).^[3] Similarly, in our study, the mean age was 58 years and the female/male ratio was 1.5. The HFS severity scale developed by Chen et al., one of the clinical evaluation scales applied by different research groups, was applied to HFS cases. The overall mean score according to the HFS severity scale was 2.5 ± 0.6 , similar to that in our patient group.^[8] In addition, the short and simple HFS quality of life scale developed by Tan et al. was applied to evaluate the health-related quality of life.^[13] On this scale, 28 points are the highest and associated with being the worst in terms of quality of life.

Scores in the HFS quality of life scale may vary according to the severity of the disease, additional symptoms such as headache, and the presence of underlying comorbidities.^[14] Although HFS is more common in females, gender differences in the severity of the disease and the effect of age have not been determined. Although it is thought that the symptoms may disturb female patients and younger patients more cosmetically, the effect of gender and age on quality of life and disease severity was not found in the study.

Traditionally, black tea consumption of the Turkish population is common and accordingly, black tea consumption was high in our patient group. Green tea consumption was found to be higher in older age and female gender. It has been determined that the consumption of foods containing caffeine decreases with age.

Adenosine A1 receptors are found throughout the nervous system, with the highest levels in the hippocampus, cerebellum, cerebral cortex, and thalamus. Stimulation of adenosine A1 receptors inhibits transmitter release from neurons. Adenosine A2A receptors are located in dopamine-rich areas of the brain; They are found in the striatum, nucleus accumbens, and tuberculum regions.

As a result of caffeine's inhibition of adenosine receptors, effects such as insomnia, increased locomotor activity, neurotransmitter release, and contraction of skeletal muscles occur.^[15,16] In primary HFS, chronic irritation and facial demyelination develop as a result of vascular compression on the facial nerve. Abnormal overstimulation of the facial nerve leads to the development of symptoms. For this reason, it was predicted that the symptoms may increase with caffeine intake, depending on the increase in neurotransmitter release in HFS patients. However, in our study, no difference was found between caffeine intake and disease severity. The effect of caffeine on spasm severity and quality of life has not been reported in the literature.

The presence of symptoms affects the daily work of patients, causing them to feel depressed and depressed. As the severity of the disease increases, the quality of life deteriorates. In our study, a statistically significant relationship was found between the severity of the disease and the deterioration of the quality of life.

Caffeine taken into the body does not accumulate in organs or tissues. It is extensively metabolized by the liver. Patients followed by our clinic from different times were included in our study. We think that the effect of caffeine is not chronic. In this context, we aimed to determine the effect of caffeine prospectively with hemifacial spasm quality of life scale and hemifacial spasm severity scales. In our study, we showed that this effect did not exist.

It is predicted that drug groups such as Gabapentin, Baclofen, Carbamazepine, Selective serotonin reuptake inhibitors that our patients can use frequently and the caffeine dose taken with food in daily doses will not interact. Especially in our patient group with cardiovascular disease, the antihypertensive drugs they use may have a protective effect against the hypertensive effect of caffeine.

The limitation of the study was that the patients were evaluated independently of the treatment, and the treatments given could differ between the patients.

CONCLUSION

One of the results of this study is that caffeine taken with food has no effect on the severity of the disease and quality of life in HFS patients. Another result, as expected, is that the quality of life deteriorates as the severity of the disease increases. However, randomized controlled studies are needed to determine the effect of caffeine and its place in treatment modalities in HFS patients.

ETHICAL DECLARATIONS

Ethics Committee Approval: The study protocol was approved by the Gülhane Scientific Research Ethics Committee (Date: 08.11.2022, Decision No: 735)

Informed Consent: All patients signed the free and informed consent form.

Referee Evaluation Process: Externally peer-reviewed.

Conflict of Interest Statement: The authors have no conflicts of interest to declare.

Financial Disclosure: The authors declared that this study has received no financial support.

Author Contributions: All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

REFERENCES

1. Wang A, Jankovic J. Hemifacial spasm: clinical findings and treatment. *Muscle Nerve*. 1998;21(12):1740-1747.
2. Nielsen VK. Electrophysiology of the facial nerve in hemifacial spasm: ectopic/ephaptic excitation. *Muscle Nerve*. 1985;8(7):545-555.
3. Chaudhry N, Srivastava A, Joshi L. Hemifacial spasm: The past, present and future. *J Neurol Sci*. 2015;356(1-2):27-31.
4. Camandola S, Plick N, Mattson MP. Impact of Coffee and Cacao Purine Metabolites on Neuroplasticity and Neurodegenerative Disease. *Neurochem Res*. 2019;44(1):214-227.
5. Qi H, Li S. Dose-response meta-analysis on coffee, tea and caffeine consumption with risk of Parkinson's disease. *Geriatr Gerontol Int*. 2014;14(2):430-9.
6. Graham TE. Caffeine and exercise: metabolism, endurance and performance. *Sports Med*. 2001;31(11):785-807.
7. Nehlig A. Interindividual Differences in Caffeine Metabolism and Factors Driving Caffeine Consumption. *Pharmacol Rev*. 2018;70(2):384-411.
8. Chen RS, Lu CS, Tsai CH. Botulinum toxin A injection in the treatment of hemifacial spasm. *Acta Neurol Scand*. 1996;94(3):207-211.
9. Tanuma A, Saito S, Ide I, et al. Caffeine enhances the expression of the angiotensin II Type 2 receptor mRNA in BeWo cell culture and in the rat placenta. *Placenta*. 2003;24(6):638-647.
10. Tanda G, Goldberg SR. Alteration of the behavioral effects of nicotine by chronic caffeine exposure. *Pharmacol Biochem Behav*. 2000;66(1):47-64.
11. Nehlig A, Boyet S. Dose-response study of caffeine effects on cerebral functional activity with a specific focus on dependence. *Brain Res*. 2000;858(1):71-77.
12. Fredholm BB, Bättig K, Holmén J, Nehlig A, Zvartau EE. Actions of caffeine in the brain with special reference to factors that contribute to its widespread use. *Pharmacol Rev*. 1999;51(1):83-133.
13. Tan EK, Fook-Chong S, Lum SY, Thumboo J. Validation of a short disease specific quality of life scale for hemifacial spasm: correlation with SF-36. *J Neurol Neurosurg Psychiatry*. 2005;76(12):1707-1710.
14. Peeraully T, Tan SF, Fook-Chong SM, Prakash KM, Tan EK. Headache in hemifacial spasm patients. *Acta Neurol Scand*. 2013;127(5):e24-e27.
15. Lorst MM, Tops M. Caffeine, fatigue, and cognition. *Brain Cogn*. 2003;53(1):82-94.
16. George KC, Hebbar SA, Kale SP, Kesavan PC. Caffeine protects mice against whole-body lethal dose of gamma-irradiation. *J Radiol Prot*. 1999;19(2):171-176.