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Research Article

Effects of Obesity on Migraine in Women

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Abstract

Introduction: With a rapidly increasing prevalence worldwide in recent decades, obesity has started to be an important public health issue in all developed countries. There are few studies focusing on the relationship of obesity with migraine. We intended to study clinical features of migraine in obes women, frequency of attacks, severity and duration of pain, use of prophylactic drugs for migraine,, use of analgesics in attacks and the effects of migraine on daily lives.

Material and Methods: In this prospective study, 84 women patients with migraine were classified as group I for those with a body mass index of 30 and over, and group II for those with a body mass index of 25 and less. Groups were compared in socio demographical features, clinical properties, frequency and severity of migraine attacks, prophylactic drugs used for treatment, analgesics used in such attacks and the effects of pain on daily life.

Results: It has been found that migraine attacks were significantly earlier in women with obesity. In this group, frequency and severity of migraine attacks, prophylactic drugs used for treatment, analgesics used in such attacks, and restriction of daily activities due to pain differed significantly compared to the group with no obesity.

Conclusions: Obesity might be triggering migraine attacks in women thru endogenous mechanisms dependant upon hypothalamic dysfunction and thru exogenous mechanisms dependant upon excess food intake.

Keywords: Migraine, obesity, BMI body mass index, hypothalamus

Obesitenin Kadınlarda Migren Üzerine Etkisi

Özet

Giriş: Son dekadlarda tüm dünyada prevalansı hızla artan obesite tüm gelişmiş ülkelerde önemli bir halk sağlığı problemi olmaya başlamıştır.Obesitenin migrenle ilişkisine dikkat çeken çok az sayıda çalışma bulunmaktadır.Biz obesitenin kadınlarda migrenin klinik özellikleri, atakların sıklığı,ağrının şiddeti,süresi,proflaktik tedavi kullanımı,ataklarda analjezik kullanımı ve migrenin günlük yaşam üzerindeki etkisini araştırmayı amaçladık.

Metod: Bu prospektif çalışmada 84 migrenli kadın hasta body mass indexe göre 30 ve üzeri olanlar grup I,25 ve altı olanlar grup II olarak sınıflandı.Gruplar sosyodemografik özellikler, migren ataklarının klinik özellikleri, sıklığı, şiddeti, süresi ayrıca bu ataklarda kullanılan analjezikler, daha önce proflakside kullanılmış ilaçlar ve ağrının günlük yaşam üzerindeki etkisi yönünden karşılaştırıldı.

Sonuçlar: Obesitenin olduğu kadınlarda migren ataklarının anlamlı bir şeklide daha erken yaşta başladığı saptandı.Bu grupta migren ataklarının sıklığı,ağrının süresi ve şiddeti,proflaktik ilaç ve analjezik kullanım,ağrı nedeniyle günlük yaşam aktivitelerinin kısıtlanması obesitenin olmadığı gruba göre anlamlı farklılık gösteriyordu.

Tartışma: Obesite kadınlarda hipotalamik disfonksiyona bağlı endojen mekanizmalarla ve fazla gıda alımı ekzojen mekanizmalarla migren ataklarını etkiliyor olabilir.

Anahtar Kelimeler: Migren, obesite, BMI vucud ağırlık indeksi, hipotalamus

INTRODUCTION

With a rapidly increasing prevalence worldwide in recent decades, obesity has started to be an important public health issue in all developed countries [3,8].

Obesity is an important risk factor in human beings for early mortality and increasing morbidity rate, chronical diseases like diabetes mellitus type II hypertension, stroke, cardiovascular diseases, sleep apnea syndrome and pulmonary dysfunction, and malignity [7]. In addition to such diseases, obesity is also an additional risk factor for female diseases for breast and endometrial cancer, polycystic ovary and infertility [7].

Although migraine does not create any serious health problems in other systems like obesity, it is a chronic paroxysmal disease well known to be causing an important individual and social loss of work power.

There are very few studies focusing on the relationship between headache and obesity in literature. In a study, it has been detected that chronic daily headache is seen more frequently in women, and that obesity is an independent source of risk in the development of this type of pain in addition to other factor [10].

In studies examining the relationship of migraine and menstrual cycles in women, focus is given to the relationship of estrogen withdrawal without aura migraine attacks and in return high plasma estrogen concentration with aura migraine attacks [6].

In a recent study conducted on women with morbid obesity, a high incidence of migraine and particularly migraine with aura has been detected. In this study, it is emphasized that the reason for high rate of aura in women with high obesity may be connected with the excess production of estrogen and estrodiole in peripheral tissues like the fat tissue [5].

The aim of the present study was to assess and to compare clinical features of migraine, sociodemographic characteristics, frequency of attacks, severity and duration of pain, use of analgesics in attacks, use of prophylactic drugs for treatment and the effects of migraine on daily live in women with migraine who have obesity and who have no obesity.

METHODS

Study Design.- The study has been made prospectively between January 2005 and December 2005 and patients were randomly selected by sampling method.

Patients.- Eighty and four female patients diagnosed with migraine according to the recently described headache criteria of İnternational Headache Society (İHS) were included in the study. Female patients were among 356 patients admitted to the Department of Neurology.

The inclusion criteria were as follows:age 18 to 48 years; headache for at least two and more attacks per month and less than 15 headache days per month.

Pregnant patients, patients in natural or surgical menopause periods, undergoing hormone replacement treatment or using oral contraceptives, and patients undergoing migraine prophylaxis treatment were excluded.

Patients were divided into two groups based on body mass index (BMI). Group I contained 43 women with BMI 30 and over, and Group II contained 41 women with BMI 25 and less.

Patient evaluation.- Sociodemographical data survey form prepared for these patients were filled. Patients were queried for number of monthly attacks. The severity of the worst headache they have felt during the attack has been evaluated according to visual analog scale (VAS 0: no pain, VAS 10: most severe pain imaginable).

Moreover, in verbal evaluation, pain severity was classified as mild, medium, severe, and unbearable (mild=1, unbearable=4). Duration of attacks (in hours), types of prophylactic and analgesic drugs that patients consumed were recorded.

Patients were also queried with regards to activities restricted by pain in daily life. Patients in both groups were asked to reply in consideration of restriction in their daily lives, not only the restrictions during the attacks when evaluating activities restricted by pain.

Both groups were compared from the point of sociodemographical properties, clinical features of migraine attacks, frequency of attacks, severity of pain according to verbal evaluation and VAS, duration of pain, type of prophylactic drug used, type of analgesic used and the effects of pain on daily life.

Statistical Assessment: The variables of age, beginning age of pain, frequency, severity and duration of attacks, number of prophylactic drugs and BMI were summarized as medians and standard deviations (minimum-maximum). T-test was used for average values between groups. Categorical data were compared to Chi-Square test and Fisher Exact Chi-Square test. Mann Whitney U Test was employed when comparing pain frequency and BMI. The statistical significancy level was accepted as $p<0,05$. We used SPSS version 11,5 for statistical analyzes.

RESULTS

Sociodemographic characteristics.- The sociodemographic characteristics of the groups are listed in table 1. No significant difference in age, marital status, education, and occupation existed between the groups. However, beginning age of migraine attacks were found to be statistically significant earlier in group I when compared with group II (t: -2.674, p: 0.009) (table 2).

Table1.- Sociodemographic characteristics.

Parameters		Group I (n=43)		Group II (n=41)		x^2	p
		n	%	n	%		
Marital status	Maried	32	74.4	29	70.7		
	Single	6	14	8	19.5	0,497	0,780
	Other	5	11.6	4	9.8		
Occupation	worker	9	20.9	11	26.8	0.403	0.526
	nonworker	34	79.1	30	73.2		
Education	noneducation	3	7	4	9.8		
	Primary	18	41.9	20	48.8		
	Secondary	12	27.9	9	22	0.863	0.930
	High	6	14	5	12.2		
	University	4	9.3	3	7.3		

Table 2.-Age Differences in the Groups.

Parameters	Group I (n=43)	GroupII (n=41)	t	p
Age X±SD (min.-max.)	32.49±7.53 (18-48)	31.22±7.56 (18-48)	0.77	0.444
Beginning age of migraineX±SD (min.-max.)	22.07±4.43 (14-33)	24.46±3.72 (17-34)	-2.674	0.009*

Clinical features: Vomiting was found in 16 (37.2%) patients in group I, and 7 (17.1%) patients in group II. When groups were compared, vomiting ratio was statistically significant in group I (x^2:4.280,p: 0,039).

There were no significant differences between groups with regards to aura, existence of prodrome symptoms, characteristics and localization of pain, and symptoms accompanying pain. Findings are summarized in table 3.

Comparison of Attacks among Groups

Frequency of Attacks: When monthly frequency of attacks were compared for their average, there were 7.07±2.303 [range 2-13] attacks in group I, and 3.88±1.14 [range 2-8] attacks in group II and attacks were more frequent in group I, which was statistically significant (z:-6.174,p:0.0001) (table 4).

Duration: Duration of attacks was 15.7±10.46 [range 4-72] in group I and 10.12±7.788 [range 4-48] in group II. Duration of attacks was significant longer in group I compared to group II (t: 2.851,p: 0.006)(table 4).

Severity.-: Both in verbal evaluation and in evaluation under VAS, pain attacks were found to be statistically significant in group I. Pain severity in verbal evaluation was 3.12±0.879 [range 1-4] in group I, and 1.83±0.738 [range 1-4] in group II (t:7.251,p:0.0001). VAS was 6.84±2.023 [range 2-10] in group I, and 3.51±1.951 [range 1-9] in group II (t:7.662,p:0.0001) (table 4).

BMI was found 36±4.478 in group I, and 21±1.989 in Group II.

Table 3.- Clinical Features of Migraine in the Groups

Parameters		Group I (n=43)		Group II (n=41)		x^2	p
		n	%	n	%		
Pain quality	pulsating	38	88.4	36	87.8		1.000*
	other	5	11.6	5	12.2		
Location of pain	unilateral	37	86	33	80.5	0.467	0,494
	bilateral	6	14	8	19.5		
Nausea		31	72.1	30	73.2	0,012	0,912
Vomiting		16	37.2	7	17.1	4.280	0,039*
Photophobia		26	60.5	23	56.1	0.165	0,685
Phonophobia		24	55,8	22	53,7	0,039	0,843
Prodrome		34	%79.1	27	65.9	1.844	0.175
Aura		11	25,6	6	14,6	1,558	0,212
Aggravation by physical activity		28	65.1	24	58.5	0,385	0,535

Table 4.-Comparison of Attacks among Groups

Parameters	Group I (n=43)	Group II (n=41)	z	t	p
Frequency of attacks	7.07±2.303 (2-13)	3.88±1.144 (2-8)	-6.174	-	0.0001
Duration of headache	15.7±10.46 (4-48)	10.12±7.788 (4-36)	-	2.851	0.006
Severity of pain (verbal evulation)	3.12±0.879 (1-4)	1.83±0.738 (1-4)	-	7.251	0.0001
Severity of pain (VAS)	6.84±2.023 (2-10)	3.51±1.951 (1-9)	-	7.662	0.0001
Number of prophylactic treatment	1.56±0.652 (1-3)	1.051±0.229 (1-2)	-3.123		0.002
BMI	36±4.478 (30-50)	21±1.989 (18-25)	-7.908	-	0.0001

Prophylactic drug Usage: When the number of prophylactic treatments were compared for their average, it was 1.56 + 0.652 [range 1-3] for group I, and 1.05 + 0.229 [range 1-2] for group II. Prophylactic treatments were more frequent in group I, which was statistically significant (z:-3.123, p:0.002) (table 4).

Antidepressant and antiepileptic drug usage frequency in patients in group I was significantly higher compared to patients in group II (Table 5).

20 (46.5%) patients in group I used amitriptyline and 14 (32.6%) patients used valproate while 6(14.6%) patients in group II used amitriptyline and 5 (12.2%) used valproate. Amitriptyline and valproate usage frequency was significantly higher in group I ($p<0.05$)

Analgesic Usage: All patients in both groups reported that they used analgesics to cease migraine attack. Non-streoidal anti-inflamatory drugs (NSAID), selective 5-hydroxytryptamine -1 (5-HT1) receptor agonists and ergotamine usage frequency in patients in group I was statistically significant compared to patients in group II (Table 5).

Effects of pain on daily life activities: All patients in group I and 87.8% of group II patients reported that pain and prospect of pain restricted their lives. A statistically significant difference was found in all parameters with regards to activities restricted by pain between two groups of headaches (Table 6).

Table 5.- Comparison of Drug Usage among Groups

Parameters	Group I (n=43)		Group II (n=41)		x^2	p
	n	%	n	%		
NSAID	40	93	26	63.4	10.928	0.001
Selective 5-HT1 agonists	16	37.2	3	7.3	10.715	0.001
Ergotamine	13	30.2	3	7.3	7.148	0.008
Paracetamol	36	83.7	34	82.9	0.01	0.922
Other analgesics	23	53.5	17	41.5	1.217	0.270
Antidepressants	28	65.1	10	24.4	12,456	0.001
Antiepileptics	18	41,9	6	14,6	6,348	0,012
ß-blockeres	7	16,3	5	12,2	0,050	0,824
Calcium-channel blockers	2	4,7	2	2,4	-	1,000
Other	2	4,7	3	7,3	-	0,672

Tablo 6.- Comparison of effects of pain on daily life activities among groups

Parameters	Group I (n=43)		Group I (n=41)		x^2	p
	n	%	n	%		
Expectation	43	100	36	87.8	-	0,024
Daily life	43	100	35	85.4	-	0.011
housework/salaried work	40	93	27	65.9	9.598	0.002
Social activities	38	88.4	24	58.5	9.665	0.002
Personal care	41	95.3	30	73.2	7.892	0.005
Other	17	39.5	11	26.8	1.525	0.217

DISCUSSION

In this study, the effects of obesity in women diagnosed with migraine were investigated.It has been found that migraine attacks were earlier in women with obesity, with more frequent, longer and severe attacks.

There are very few studies paying attention to the relationship of obesity with migraine in women. As far as we are concerned, there are no studies in literature examining the relationship of obesity with the clinical features of obesity and its effect on pain attacks.

Among groups with similar socio demographical features, beginning age of migraine was earlier in group I compared to group II. It is well known that in women, migraine is seen in all decades as from the puberty period with higher prevalence compared to men. Although genetic properties are the major factor affecting the beginning date of puberty, it is reported that menarche is realized earliest in obese girls, then in slender and anorectic girls, respectively [(11)].

One may think that in such women obesity is an effective factor in the earlier start of puberty period and that as a result migraine may start in earlier ages in obese women. We, in this study, have no information on whether or not our patients have simultaneous obesity when their migraine attacks have begun. This hypothesis needs to be separately tested.

When the two groups are compared for the clinical features of pain, only vomiting was statistically higher in group I. Prodrome symptoms and aura prevalence was higher in group I, although not statistically meaningful. Covering many symptoms such as excessive sensitivity or reaction, state of cheerfulness, discomfort, depression, hungriness, increase or decrease of appetite, sense of thirstiness, urination frequency, the prodrome period indicates the primary hypothalamus, which is the anatomical region equivalent of symptoms [(9)].

Griffin et al. have shown that migraine prodrome symptoms might increase by 72% in migraine patients, if questioned well [(4)]. There are no studies reported in the literature regarding the incidence of prodrome symptoms in migraine patients with obesity. In our study, we have found that prodrome symptoms of the group with obesity are 79.1%, higher than that is reported in the literature.

It is well known that hypothalamus is the primary organ in controlling various biological rhythms and arrangement of many endocrine and autonomic functions [(9)]. It plays a role in many functions like the organization of body temperature and blood pressure thru interaction with other parts of the brain, and controlling body weight by providing appetite and energy homeostasis. Supraciasmatic nucleus of Hypothalamus is one of the two centers organizing circadian rhythms and it is reported that it can be responsible for periodicality, a very important feature of migraine. It has also been reported that some anatomical regions of hypothalamus and certain neuropeptides related with hypothalamus might have a role in pain perception and removal. Prodrome period is interpreted as a temporary disorder of hypothalamus and attention is given to the relationship of episodic brain diseases other than migraine with migraine [(9)].

Thru such information, we consider that prodrome period symptoms will be frequently seen in hypothalamus involvement having an important influence on appetite and weight control in women with migraine, and that it can make an additional contribution tot he pathophysiology of migraine depending on insufficient functioning of hypothalamic mechanisms in the process of pain initiation, organization of the rhythm of attacks and inhibition of pain attacks and it can worsen headaches.

In obese women with migraine, aura is related with excess production of estrogen in the increased fat tissue [(5)]. It has been

reported that migraine with aura accompanied increased risk of cerebrovascular disease in young women, and this risk has increased by many folds in case of existence of oral contraceptives, smoking, hypertension, hypercholesterolemia and obesity [(1)].

Whereas aura has been related to high levels of estrogen, migraine without aura has been shown to trigger migraine depending on estrogen withdrawal before mens during menstrual cycle [(5)]. It has been reported that hypothalamus might be effective in migraine-menstruation relationship in women, even without obesity.

Estrogen withdrawal may modulate hypothalamic ß-endorphin, dopamine, ß -adrenergic and serotonin receptors. This complex interaction causes significant downstream effects, such as a reduction in central opioid tone, dopamine receptor hypersensitivity, increased trigeminal mechanoreceptor receptor fields, and increased cerebrovascular reactivity to serotonin [(2)]. We think that hypothalamus involvement might also affect this endogenous mechanism in obese women and trigger the attacks.

Other than the endogen's above-mentioned triggering role of obesity on migraine attacks, consumption of many and various foods depending on increased appetite, exogen might be an additional triggering factor. We know that various foods forming a long list have triggering roles in migraine.

In group I, NSAI, selective 5HT receptor agonist and ergotamine using frequency was more compared to group II. One may think that obesity caused frequent analgesics usage in such patients as a result of increase of frequency and severity of attacks and that might cause pain becoming more complex depending on abuse analgesics usage as a result.

Patient in group I used numerous prophylactic drugs. The side effect of these drugs is generally weight-gain. We do not know the weight of the patients of the two groups before treatment. But the data suggests that obesity may be the result of side effects of numerous prophylactic drugs used by group I; and this may have caused frequent and strong pain attacks.

It is common knowledge that migraine alone caused a functional loss of work in patients, even with no obesity. All of the patients in Group I have reported that they expected the pain to come at any time and that pain restricted their daily life activities. In these patients with frequent and severe pain attacks, it is clear that one can observe more loses in daily life activities, business life, social activities and self care normal compared to a migraine population.

CONCLUSION

Numerous studies conducted on migraine so far have revealed the relationship of many endogenous and exogenous factors with pathogenesis. At the meeting with a patient with migraine, it is very important to explain the factors that are effective in the progress and morbidity of sickness at an earlier stage and develop appropriate treatment approaches. Naturally, such treatments may only target changeable factors. We, in this study, have examined the effects of obesity on attacks in women with migraine. In female patients where migraine prevalence is seen in almost all decades, it should be considered that obesity might be a triggering endogenous and/or exogenous factor.

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