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MIGRAINE SYMPTOMS IN PATIENTS WITH MRI WHITE MATTER HYPERINTENSITY AFTER AND BEFORE TREATMENT

[1]Mehrnoosh Ebadi, [2]Mohsen Ebrahimimonfared, [3]Reza Sadeghi, [4]Alireza Rezaei Ashtiani, [5]Amir Mohammad Eghbalnejad Mofrad, [*6]Fardin Faraji, [7]Maryam Mohammadi

[1]MD, postdoctoral research fellow, neurology department, Arak University of Medical Sciences, Arak, Iran
[2]Assistant Professor of Neurology, School of Medicine, Arak University of Medical Sciences, Arak, Iran
[3]General physician, Department of Public Health, Iranshahr University of Medical Sciences
[4]Assistant Professor of Neurology, School of Medicine, Arak University of Medical Sciences, Arak, Iran
[5]Student Research Committee, Ahvaz Jundishapur University of Medical Sciences, Iran
[6]Associate Professor of Neurology, School of Medicine, Arak University of Medical Sciences, Arak, Iran, dr.faraji@arakmu.ac.ir
[7]Neurology resident, Ahvaz Jundishapur University of medical sciences, Neurology department, Ahvaz, Iran.

Abstract

Objective and background: Migraine is one of the most common diseases and causes of parenchymal lesions in the brain, which is associated with symptoms of nausea and vomiting, visual impairment, and olfaction. One way to diagnose migraine headaches is to study magnetic resonance imaging (MRI). MRI T2 hyperintense lesions in migraines are usually found in the white matter and sometimes in the cerebral cortex.

Methods: 114 patients with informed consent were included in the study. They were then referred for MRI. Patients were then divided into two case and control groups according to the presence or absence of lesion in MRI. A complete neurological examination was performed, and clinical symptoms were recorded. The MIDAS headache questionnaire was. After three months of the treatment period, the patients again filled up the MIDAS questionnaire, and a complete neurological examination was performed.

Results: In this study, 101 patients with migraines were studied. Also, in a separate survey of patients' symptoms with headaches, the frequency of visual aura and night headache was statistically significant in both groups. The results show no significant difference between the mean scores of Midas after treatment in the two groups. The results show that the mean scores of Midas after the study decreased in all patients with abnormal MRI. But in patients who have lesions in BS, the mean scores of Midas have not been significant.

Conclusion: the mean score of Midas before starting treatment in the group whose brain MRI was normal was 33.06, and in the group whose brain MRI was abnormal was 55.15, which in statistical studies was significant. In this study, it was observed that the Midas score decreased significantly after starting treatment.

Keywords: Migraine, Brain MRI, Hyperintensity.

INTRODUCTION

Migraine is a common disease and one of the causes of parenchymal lesions of the brain (1). Migraine is most prevalent at a young age, and women are more affected than men (2). The etiology of this disease is unknown but attributed to factors such as vascular mechanism and dilation and constriction of vessels inside and outside the brain(3). One way to diagnose migraine headaches is an MRI evaluation(4). MRI in patients with migraine compared to normal individuals with hyper-signal lesions in T2 is mainly in the white matter and sometimes the cerebral cortex (13,14). Lesions can occur for various etiologies, including gliosis, myelin degradation, and edema (15). According to MRI studies, people with Aura migraine are the only headache associated with cerebral infarction12. According to an article published in the brain MRI study of 65 migraine patients, a significant number of these patients have hyperintense lesions in their brain MRI (5). In confirmation of this issue in 2012, it was announced that there is evidence of hyper signal foci in brain MRI. It helps diagnose the disease and the severity of brain damage(6,7, 8). Considering the above information, it was hypothesized that the condition might be different in people with abnormal MRI. We also decided to compare the severity of headache between the two groups with normal and abnormal lesions and the treatment outcome to investigate the effect of treatment on the case group. Suppose there is a relationship between the severity of headache in the case and control groups and the presence of brain lesions. In that case, alternative therapies can be used for patients in the case group.

METHODS:

In this study, 114 patients were admitted by considering the inclusion and exclusion criteria, providing the necessary information about the plan, and obtaining informed consent. The analysis was performed in two stages, first by cohort method and comparing the severity of headache in normal and abnormal MRI groups. In the next step, the case-control study was performed on the two groups, and the effect of the usual treatment was compared. Migraine diagnosis was based on the patient's history. Referrals were made to Valiasr Hospital and specialized neurology centers in Arak. Inclusion and exclusion criteria were considered. Then laboratory tests that may lead to headaches were performed, and abnormal cases were excluded from the study. All patients completed the MIDAS questionnaire for headache severity scoring at the beginning of the study. They were then referred for brain MRI. The brain MRI result was evaluated by a neurology specialist for the presence of the T2 lesion and its location. Then, according to the presence or absence of T2 lesion in MRI, patients were divided into two groups: case (presence of a lesion in MRI) and control group (lack of lesion in MRI). Then Patients in both groups were prescribed treatment (sodium valproate and daily nortriptyline) and followed by a physician. After three months of treatment, the patients filled out the Midas questionnaire again. A complete neurological examination was also performed. And changes were recorded. The data was then entered into Spss19 software. The two groups were compared in terms of headache severity at the beginning of treatment and response to treatment, and the resulting changes were subjected to statistical tests.

Sample size based on $\alpha = 0.05$, the prevalence generalizable to the migraine population was 0.12%.

$$N = \frac{(Z1 - a/2)^2 (p(1-p))^2}{(d)^2}$$

by Using the following formula, the sample size of 114 people was calculated. n= 114 p1=0.0054 d=0.05 p1=0.0054

Inclusion criteria was:1. Patients with migraine diagnosis 2. Those who have confusing cases such as hyperlipidemia, HTN, DM, and other causes of headache do not enter the study. 3- Aging range 20-50 years old. Exclusion criteria:1- Patients who do not want to continue

participating in the study. Existence of any space or pathological lesions on MRI 3- Systemic diseases such as heart and kidney failure, lupus and other vascular disorders, HTN, DM, etc.

RESULTS:

101 patients were studied to investigate the relationship between brain MRI changes and headaches' severity and clinical symptoms. According to the study, (80.2%) 81 people have normal brain MRI and (19.8%) 20 people have abnormal brain MRI. The distribution of sexuality is generally (21.8%) 22 males and (78.2%) 79 females. Of the patients with normal brain MRI, 23.5% were male, and 76% were female. The same study in abnormal patients was 15% male and 85% female. The Chi-square re-test results show no statistically significant difference between the frequency distribution of sex in the two groups. The average age of patients is 35.04 years. The youngest is 20 years old, and the oldest is 50 years old. According to the independent t-test, the mean age in the group with typical brain MRI and abnormal brain MRI was not significantly different. The results show that the mean age of patients in the two groups is not statistically significant. To evaluate the severity of headache based on Midas score, LITTLE Disability score (5-0), MILD disability score (6-10), Moderate disability score (11-20), and more than 21 severe disability scores were considered. To study the severity of headache before and after treatment, according to a study performed on migraine patients in the group with normal brain MRI, 11% were in the moderate group, and 88.89% were in the severe group. After treatment, 61.7% had a mild headache in the standard group, and 18.5% had s. In the group with abnormal brain MRI, 100% of patients had a severe headache. After treatment in the abnormal group, 20% of patients remained in the moderate group, and the rest (80%) remained in the influential group. Classification changes appear to be significant in patients after treatment. FIGURE (4-1),(4-2) the average score of Midas before treatment in the group with normal MRI is 33.06, and in the group with the abnormal brain, MRI is 55.15. the average Midas score after treatment in the abnormal brain MRI group was 36.3; in the normal brain MRI group was 16.64. the result lots of the Mann-Whitney test in the table show that the average Midas score before and after the study in the case and control groups is statistically significant. It means routine treatment in both groups is significantly effective. TABLE (1-1) The average of changes in Midas score in the group with normal MRI brain is -16.41, and in the group with the abnormal brain, MRI is -18.85, which according to the statistical study, is not significant by modifying the average and eliminating the distorting effect.. Table (1-2) The results show that the severity of headache after treatment does not depend on the site of involvement in MRI. The results show that the mean Midas score after treatment decreased in all patients regardless of the location of the lesion. For example, the average score of Midas in patients with frontal lesions fell from 53.9 to 34.05. The decrease in mean Midas score in patients with BS lesions was not significant. Table (1-3) The results show that the mean changes of Midas score in any brain MRI indices do not depend on the site of involvement (in terms of the right and left of the lesion). During the study of the location of the lesions and statistical agreement, the frequency distribution of the lesions was 82% in the right frontal area, which has the highest value compared to other sites. Also, during a separate study on the symptoms of headaches, it was shown that visual aura is more common in people with abnormal MRI. Symptoms of nocturnal headache were also more common in patients with weird brain MRIs. Table (1-4) In some cases, it was not possible for a patient to compare the location of the lesion with the severity of clinical symptoms due to data overlap and having multiple lesions. However, the formal examination of the lesion site in the form of non-overlap shows that in those who had a lesion in the frontal region, regardless of the lesion in other areas, visual acuity is higher than other symptoms.

DISCUSSION:

Primary headaches are among the most critical joint disorders in the general population. One of the most common types of these headaches is migraine(9). About 25% of people with migraines develop transient neurological symptoms before the onset of the headache and are called aura (10). The diagnosis of migraine is based on clinical manifestations. However, MRI findings have shown that migraine itself is an independent risk factor for deep white matter lesions in the supratentorial region, infarction in the posterior circulatory area, and hyperintense lesions in the MRI T2 of the infratentorial region (11). These lesions in migraine MRI are often similar to silent infarcts with hyperintense lesions in T2 in the white matter (12). However, accurate information on these white matter lesions is not available, and this study was performed to identify these lesions more accurately.

A study by Carla Uggetti et al. in 2017 Found that 26 out of 90 patients, or 29% of all patients, had an abnormal MRI brain (13). In the present study, 101 patients with migraine were examined; it was observed that 81 patients, or 80.2% of the total patients, had normal MRI brain and 20 patients equivalent to 19.8% of these patients had abnormal MRI brain. The results of these two studies examining the presence of lesions in the brain MRI of migraine patients are almost equal, confirming the results of the present study.

In a study conducted by Takashi YASUDA et al. In 2016, 74.8% of migraine patients were female. In the present study, it was also found that 79 patients, equivalent to 78.2% of the total 101 patients, were female. It was also observed that the mean age of the patients was 32.9 years with a standard deviation of 8.4 years (14). Also, in the present study, it was observed that the mean age of these patients was 35.04 years with a standard deviation of 8.75 years. In other studies, the ratio of women to men was more than doubled, and most of the patients were women.

The same study also showed that aging is an independent risk factor for increased lesions on brain MRI (14). Also, in the present study, the mean age of patients with normal brain MRI was 34.3, and in the group with the abnormal brain, MRI was 37.8. However, no statistically significant relationship was found between aging and lesions in the present study. But it seems that more accurate information can be obtained by increasing the number of samples.

In YASUDA'S study, there was no significant difference between WMLs and males or females (12). The present study showed that among patients with abnormal brain MRI, 15% were men, and 85% were women. This rate was 23.5% in men and 76.5% in women with patients with normal brain MRI. The results of these two studies seem to be the same. A 2017 study by Qiu F et al. found that visual aura was present in 55.3% of patients (15). The present study observed that a visual atmosphere existed for 32 patients in two groups, equal to 31.6%. A 2014 study by Igor Petrusic and colleagues on adolescents found that visual acuity was present in 37.5% of patients alone (16).

Another study by Christoph. J et al. In 2014, found that the overall prevalence of visual acuity was 30% (17).

The discrepancy between the Qiu F study and the present study is probably due to racial differences in the study populations or in-study errors. It is shown that the prevalence of visual aura is similar in the results of the present study of Igor Petrusic and the study of Christoph. J et al.

Also, in the present study, in the studies related to the frequency distribution of brain MRI lesions among patients, it was observed that 70% of brain MRI lesions were in the frontal, peritoneal and temporal lobes. Carla Uggetti and colleagues also stated that most brain MRI lesions are in these three lobes (13). It can be seen that this confirms the results of the present study.

A 2016 study by Korgun Okmen and colleagues found that Midas scores in migraine patients decreased significantly in the third and sixth months after treatment (18). In the present study, it was also observed that the mean score of Midas before starting therapy in the group

whose brain MRI was normal was 33.06, and in the group whose brain MRI was abnormal was 55.15, which in statistical studies was significant. In this study, it was observed that the Midas score decreased significantly after starting treatment. It can be seen that in both studies, the Midas score after treatment decreased especially compared to the initial score.

Also, after treatment, this scale was 16.64 in the group with typical brain MRI and 36.3 in the group with abnormal brain MRI. Also, statistical studies showed a significant difference between Midas scores before and after treatment in both groups.

Also, the mean change in Midas score in the group with normal brain MRI was -1.41, and in the group with the abnormal brain, MRI was -18.85.

No specific study is available to compare changes in Midas score and response to treatment in the two groups with normal and abnormal brain MRI. There seems to be little research on this.

The study results of Theodora Oikonomidi et al. Showed that 24.5% of patients with mild headache with moderate grade 3 were equivalent to intermediate, and 58.3% of patients with headache with grade 4 with moderate severity were severe (19). Also, based on the present study results, the severity of headaches is divided based on the Midas score. It was observed that.

11.11% of patients with normal brain MRI had a moderate headache, and 88.89% of those with normal brain MRI had severe headaches. Also, all patients whose brain MRI was abnormal had severe headaches. In comparison between these two groups, no significant difference was observed in headache severity. It is observed that the severity of headaches in patients differs in these two studies.

This discrepancy may be due to the lack of a classification of normal and abnormal brain MRI patients in the Theodora Oikonomidi study. It can also be due to differences in the studied populations.

The results show that the frequency distribution of headache severity classification in the two groups after the study has a statistically significant difference from each other.

And headache severity classification was significantly reduced in both groups.

Although previous studies have shown an association between the presence of lesions and the classification of Midas before treatment in patients, a few studies examine the effect of migraine treatment on the type of headache severity.

Also, the study of the frequency of lesions in different areas of the brain shows that the lesions were most frequent in the right frontal than on the left side. This difference is also observed in the right and left severe matter. There is no apparent difference between the temporal, parietal, occipital, and BS areas on the right and left.

Also, in the present study, the relationship between the severity of headache and lesions in the right and left areas was investigated, which was not significant.

In the present study, the relationship between clinical symptoms and areas of involvement of the brain MRI was studied. Aura was the most common symptom observed in people with lesions in all areas. In people with BS lesions, other symptoms are almost equally distributed.

Also, the most association between lesions of the occipital region and basal ganglia is the Aura symptom. People who had lesions in these two areas were also 100% associated with it, and the little correlation between lesions of the occipital region and menarche headache.

The overlap and sometimes several lesions in different areas is not possible statistically accurate analysis. It seems that the above parts of the study have not been studied before, or there are few studies in this regard.

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Conflicts of Interest:

The authors declare that they have no conflicts of interest

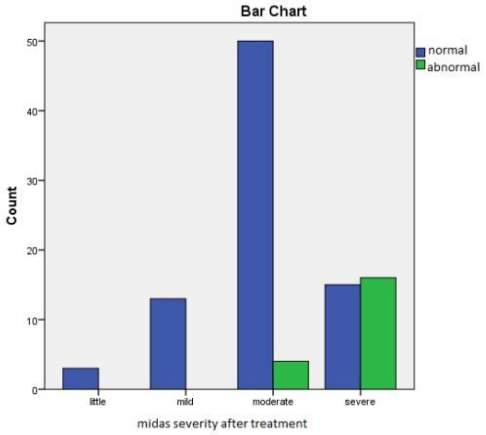

FIGURE (4-1)– MIDAS severity after treatment in case and control groups

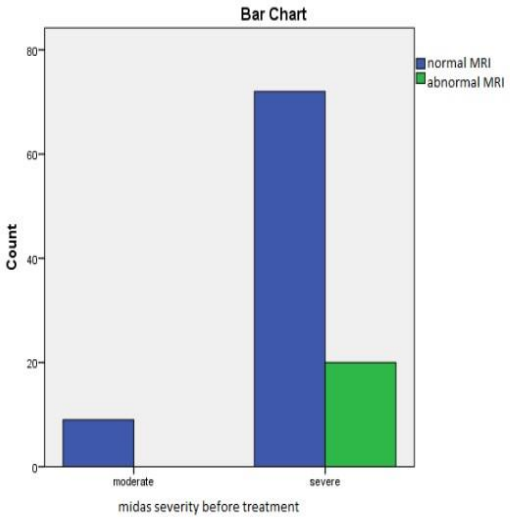

FIGURE (4-1)– MIDAS severity before treatment in case and control groups

Table (1-1) _ Comparison of level and standard deviation of raw Midas score before and after treatment in two groups

MIDAS	Significance	Abnormal MRI		Normal MRI	
		mean	SD	mean	SD
Before treatment	0,0001	55.15	20.01	33.06	14.16
After treatment	0,0001	36.3	19.94	16.64	11.4
Significance		0.0001		0.0001	

Table (2-1) - Comparison of average changes in Midas score in the two groups before and after treatment

Midas score	Mann-Whitney test		Abnormal MRI		Normal MRI	
	Significance	result	average	standard deviation	average	standard deviation
Midas before - Midas after	0.149	0.641	-18.85	7.40	-16.41	7.25

Table (3-1) _ Comparison of mean Midas score before and after treatment based on MRI index

	Wilcoxon test		Midas score- after		Midas score before	
	significance	result	mean	SD	mean	SD
frontal	0.0001	-3.623	34.05	19.16	53.94	20.7
temporal	0.005	-2.807	36.9	24.89	58.9	23.29
parietal	0.028	-2.201	37.83	22.71	55.5	19.59
occipital	0.043	-2.023	35.2	11.21	46.4	11.92
BS	0.068	-1.826	57	29.26	71.75	32.43
D.W.M	0.018	-2.366	26.28	11.61	45	15.07

Table (4-1) - Comparison of the frequency distribution of patients' symptoms in the two groups

Odds ratio	test		Abnormal MRI		normal MRI		Variable value	
	significant e	statistic s	frequent y	percentage e	frequent y	percentage e		
8.167 *	0.0001	16.916	14	70	18	22,2	yes	aura
			6	30	63	77,8	no	
0.930	0.887	0.02	12	60	50	61,7	yes	nausea
			8	40	31	38,3	no	
0.719	0.679	0.773	11	55	51	63	yes	photophobia
			9	45	30	37	no	
0.558	0.288	1.127	10	50	51	63	yes	phonophobia
			10	50	30	37	no	
3.728 *	0.008	6.926	11	55	20	24,7	yes	Nocturnal headache
			9	45	61	75,3	no	
1.615	0.342	0.901	12	70,4	39	62,9	yes	Menarche headache
			5	29;6	23	37,1	no	

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