

Autonomic Dysfunction in Interictal Period in Patients with Migraine

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Abstract

Background: migraine is a chronic neurovascular disorder characterized by intermittent attacks of severe headache with or without aura that can include various combinations of neurological, gastrointestinal tract (G.I.T), and autonomic changes, without evidence of primary structural abnormalities. The Autonomic nervous system involvement suggested by many symptoms and signs including nausea, diarrhea, constipation, coldness in the extremities, paroxysmal tachycardia and chest pain.

Objectives: To evaluate autonomic functions in patients with migraine and to clarify the autonomic dysfunction whether its sympathetic, parasympathetic, or combined. Also to assess the severity of this dysfunction and its relation to age, gender and type of migraine.

Methods: This study enrolled 60 patients with migraine, 42 females and 18 males with an age range between 14-45 y. with 30 healthy volunteer as control group, The using of a questionnaire paper, autonomic nervous system disability scale and set of autonomic cardiovascular reflexes test were also applied .

Results: The migraineurs with disabling attack may be prone to autonomic nervous system hypofunction which may be either a risk factor for migraine headache, or be a consequence of frequent disabling attacks, moreover

autonomic nervous system dysfunction and migraine may share a common neural substrate. The Parasympathetic part of autonomic nervous system is affected more than sympathetic according to Ewing classification of autonomic function tests which is significant statistically in comparison to control, and 16(26.7%) of patients showed definite dysautonomia(score >2) while 44(73.3%) of patients were normal. Palpitation and postural dizziness are the most frequent symptoms in patients with migraine . Autonomic dysfunction among migraineurs is not rare also prolong course of illness is strongly correlated with autonomic dysfunction which is affect parasympathetic part more than sympathetic, for this reason the clinician should look carefully for the autonomic symptoms when they assess patient with migraine because most of those symptoms were disabling

Conclusions: The assessment of autonomic function tests should be a routine work in patient with migraine. The heart rate response to deep breath and valsalva are simple informative and beside to evaluate the parasympathetic part of autonomic nervous system

Key words: migraine, autonomic dysfunction, sympathetic, parasympathetic.

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Introduction

Migraine is a chronic neurovascular disorder characterized by intermittent attacks of severe headache with or without aura, that can include various combinations of neurological, G.I.T and autonomic changes without evidence of primary structural abnormalities [1,2,3]

The pathogenesis of migraine is not completely understood, although it thought to be due to defective mitochondrial oxidative phosphorylation, low intracellular magnesium, increase level of neurotoxic amino acid, inherited dysfunction of calcium channels, or combination of these factors which can explain an interictal state of cortical hyperexcitability characterized by reduce threshold and increase that excitability [1,4]. Recent positron emission tomography investigation found spreading oligemia in the early phase of migraine attack. During the headache phase, increase cerebral blood flow was found in cortical sensory association area and unilaterally in the brainstem [5], which is considered the pathophysiologic core of migraine with its ascending and descending circuitry,

including the ascending pain modulating projection from the midbrain raphe nuclei [6,7].

The autonomic nervous system involvement may occur in patients with migraine either during the attack which suggested by many symptoms and signs or during normal daily activity between the attacks in which patient may have sympathetic instability and parasympathetic hypofunction [12,13]

In 1930 Harold Wolf reported on the autonomic nervous system involvement in migraine headache [8]. The autonomic nervous system involvement suggested by many symptoms and signs including, nausea, diarrhea, constipation, coldness in the extremities paroxysmal tachycardia and chest pain [9,10].

During normal daily activity in the headache free period, migraine patients have hypofunction in parasympathetic nervous system [11] also sympathetic instability, is clearly documented in migraineurs through spectral analysis of heart rate (H.R) fluctuation performed on 10 patients, they displayed markedly enhanced low frequency fluctuation during day hours and specially at night [12]. The migraineurs with disabling attacks may be

prone to autonomic nervous system hypofunction which may be either a risk factor for migraine headache or be a consequence of frequent disabling attacks. Moreover autonomic nervous system dysfunction and migraine may share a common neural substrate^[13].

Aims of the Study

- 1-To evaluate autonomic functions in patients with migraine.
- 2-To clarify the autonomic dysfunction whether its sympathetic, parasympathetic, or combined, also to assess the severity of this dysfunction and its relation to age, gender and type of migraine.

Method

Sixty patients with migraine were randomly collected between May 2009 and May 2010 in the headache clinic at neuroscience hospital /Baghdad. Their ages ranged between 14 – 45 y old .42 out of these 60 cases were females and the other 18 cases were males patients ,

Inclusion criteria includes :

1-Patient should fulfill typical criteria for migraine according to international headache society criteria for common and classical migraine

2-The patient should have normal neuroimaging scan (normal brain C.T scan)

Exclusion criteria include:

- 1- Abnormal neuroimaging[brain CT scan]
- 2- Patients with features of polyneuropathy
- 3- Patients with diabetes mellitus

With 30 healthy volunteer from medical staff 20 of them were female , their age were between 20 to 42 years as control group. Inclusion criteria includes:

- 1- The patients should have no history of headaches
- 2-Patients with no features of polyneuropathy
- 3-Patients with no diabetes mellitus

The using of a questionnaire paper, autonomic nervous system disability scale. and set of autonomic cardiovascular reflexes test were also applied.

Autonomic Function Tests:

Autonomic function test were done for all patients and control subjects using 5 standard cardio-vascular Ewing Tests {14}:

- 1, Heart rate response to the Valsalva Maneuver (VM) .
2. Heart rate (R-R interval) variation during deep breathing.
3. Immediate heart rate response to standing.
4. Blood pressure (B.P)response to standing.

5. Blood pressure response to isometric hand grip.

Each test of these was scored 0 for normal, 0.5 for border line and 1.0 for abnormal results . The total score were used for analysis , and patients with score 2 or more was labeled as having definite autonomic dysfunction^[15]

Also the severity of autonomic dysfunction symptoms was classified according to autonomic nervous system disability scale^[16].

Results

Table 1 : Type of migraine in relation to gender

gender	Type				Total	%
	Classical migraine	%	Common migraine	%		
Female	8	80 %	34	68%	42	70%
Male	2	20 %	16	32%	18	30%
Total	10	16.7%	50	83.3%	60	100%

- Common migraine is more than classical , females affected more than males

Table 2 : Distribution of autonomic symptoms among patients and control

Autonomic Symptoms	Patients		Control	
	No.	%	No.	%
Postural dizziness	31/60	51.7	5/30	16.7
Palpitation	34/60	56.6	6/30	20
Peripheral flushing	20/60	33.4	3/	10
Sweating	16/60	26.6	1/	3.3

Palpitation > postural Dizziness > peripheral flushing > sweating

Table 3 : The distribution of different autonomic symptoms assessed by autonomic nervous system disability scale for patients and control

Autonomic dysfunction symptoms	Patient no. 60						Patient no. 30						P value
	Normal score 0		Mild Score 1		Sever Score 2		Normal Score 0		Mild Score 1		Sever Score 2		
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	
Postural Dizziness	29	48.3	24	40	7	11.7	25	83.3	5	16.7	-	-	0,004
Palpitation	26	43.3	29	48.3	5	8.3	24	80	6	20	-	-	0,003
Peripheral flushing	40	66.7	19	31.1	1	1.7	27	90	3	10	-	-	0,05
Sweating	44	73.3	14	23.3	2	3.3	29	96.7	1	3.3	-	-	0,002

Table 4 : The Results of autonomic function tests in both patients and control

Autonomic Function Tests	Patient no. 60						Patient no. 30						P value
	Normal		Border Line		Abnormal		Normal		Border Line		Abnormal		
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	
B.P. response to standing	54	90	4	6.7	2	3.3	27	90	2	6.7	1	3.3	1,000
B.P. Response to handgrip	49	81.7	8	13.3	3	5	29	96.7	1	3.3	-	-	0,134
H.R. Response to Deep Breathing	39	65	12	20	9	15	27	90	1	3.3	2	6.7	0,035
H.R response to VM	36	60	13	21.7	11	18.3	26	86.6	2	3.3	2	6.7	0,036
H.R. Response to standing	49	81.7	7	11.7	4	6.7	29	96.7	1	3.3	-	-	0,130

Table 5 : The results of Ewing score among patients and control

Ewing Score	Patients		Control	
	no. 60	%	No. 30	%
Ewing < 2 group	44	73.3	29	96.7
Ewing ≥ 2 group *	16	26.7	1	3.3

* P = 0.008

Table 6 : Ewing score in relation to type of migraine

AFT Score	Type				Total	%
	classical	%	Common	%		
Score < 2	7	70	37	74	44	73.3
* Score ≥ 2	3	30	13	26	16	26.7
Total	10	100	50	100	60	100

* p = 0.75

Table 7 : Ewing score in relation to gender

gender	Ewing Score				Total	%
	<2	%	≥ 2	%		
Female	28	63.6	14	87.5	42	70
Male	16	36.4	2	12.5	18	30
Total	44	100	16	100	60	100

p = 0.75

Table 8 : Correlation between severity of autonomic dysfunction assessed by Ewing score with both age at investigation time and onset

	Ewing score <2	* Ewing score ≥2
Mean age at investigation	32.18	37.19
Mean age at onset of illness	30.02	24.38

* p = 0.01

Discussion

This is the first study investigating in details the autonomic function in Iraqi migraineurs during headache free period .

In this study 60 patients were classified according to the type of migraine.50 [83.3%] of them were common migraine including 34 [68%] females and 16 [32 %] males , while 10 [16.7 %] of them were classical migraine including 8 [80%] females and 2 [20 %] males as shown in table 1 . The study shows that common migraine are more common than classical migraine and females affected more than males which agree with all other studies, [1 , 17 , 18 , 19 , 20]

In table 2 the autonomic symptoms distributed among patients and control . We found that most common symptoms were palpitation [56.6 %] , postural dizziness [51.7 %] , peripheral flushing [

33.4 %] and sweating [26.6 %] . All these symptoms are common complain in our patients specially palpitation and postural dizziness which makes the patient apprehensive . This high prevalence of autonomic symptoms found in this study should encourage the clinician to look carefully for these abnormalities in the evaluation migraineurs and not emphasize on the usual features of migraine as this disturbance may be disabling and overcome of it will help the patient to improve there quality of life .

According to autonomic nervous system disability scale as shown in (table 3) , the patient divided into normal scale 0 (no autonomic symptoms) : postural dizziness 48.3 % , palpation 43.3 % , peripheral flushing 66.7 % , sweating 73.3 % , mild scale 1 [transient autonomic symptoms] : postural dizziness 40 % , palpitation 48.3 % ,

peripheral flushing 31.7 % , sweating 23.3% , and server scale 2 [Persistent autonomic symptoms] : postural dizziness 11.7 % , palpitation 8.3 % , peripheral flashing 1.7 % , sweating 3.3% .

The study shows most of our patients have mild or transient symptoms, while few have sever scale which is significant statistically in comparison to a matched control .

According to Ewing *et al* classification of autonomic function tests (table 4) , the study showed that HR response to VM [40 %] and HR response to deep breathing [35%] was the most frequent abnormality , these results are significant statistically in comparison to these of control while the other tests are not significant which give an idea that parasympathetic part of autonomic nervous system is affected more than sympathetic and this agree with other studies [11 , 13] . This may be due to that an autonomic nervous system imbalance play a phathophysiological role in migraine and this dysfunction may be a risk factor for migraine headache or be a consequence of frequent attacks , more over autonomic nervous system dysfunction and migraine may share a common neural substrate . [13]

According to the Ewing score (table 5) , 16 [26.7%] of our patients showed definite dysautonomia [score ≥ 2] , while 44 [73.3 %] of patients were normal , which is significant statistically in comparison to control . This means that the autonomic dysfunction is not a rare complication of migraine. There is no available to study to compare with it .

In spite of the fact that common migraine is more frequent than classical migraine and females are affected more than males , but this study showed no relationship between the severity of autonomic dysfunction with both type of migraine and gender as shown in (table 6 , 7) .

In table 8 , the study showed that patients with mean age at onset 24.38 and mean age at investigation 37.19 , have definite autonomic nervous system affection than patients with mean age at onset 30.02 and mean age at investigation time 32.18 which is statistically significant . This mean that in younger patients , the more is the need to use tests capable of detecting subtle changes in autonomic function , alternatively it could be argued that the longer duration of the illness , the more likely that autonomic function will be involved as in other disease such as diabetes .

Conclusion

Palpitation and postural dizziness are the most frequent symptoms in patients with migraine . Autonomic dysfunction among miqraineurs is not rare also prolong course of illness is strongly correlated with autonomic dysfunction which is affect parasympathetic part more than Sympathetic , for this reason the clinician should look carefully for the autonomic symptoms when they assess patient with migraine because most of those symptoms were disabling .The assessment of autonomic function tests should be a routine work in patient with migraine. The heart rate response to deep breath and valsalva are simple informative and beside to evaluate the parasympathetic part of autonomic nervous system.

Reference

- 1- Ferrari MD. *Migraine Lancet* 1998, Vol. 351: 1045 – 51.
- 2- Lance JW. *Approach to the patient with headache. In: William Kelly N.K [editor] textbook of internal medicine 2th ed. volume 2, J.B Lippincott Company. Philadelphia1993: 2277-83.*
- 3- Silberstein SD , Young WB , Lipton RB. *Migraine and cluster headache. In:Johnson RT , Griffin JW .[editor]. Current therapy in neurologic disease 5th ed , Mosby-year book.newyork , INC , 1997 : 85-92 . NM*
- 4- Moskowitz MA. *basic mechanism in vascular headache. neurol lin 1990 : 8:801-815.*
- 5- Diener HC. and A.May *New aspect of migraine pathophysiology : Lesson Learned from P.E.T., editorial JAMA, june 1996 , Vol 9. 199 – 201.*
- 6- Raskin NH .*on the origin of head pain. Headache 1998; 28:254-257.*
- 7- Silberstein SD. *Advances in understanding the pathophysiology and headache. Neurology 1992 ; 42 (suppl. 2 : 6 -10).*
- 8- Dalessio Dj. *Wolff s. headache and other head pain, 14th ed. New York, Oxford University press 1980 p 245.*
- 9- Cady R: *Treating the headache patients .in: Cady R [editor] ,headache ,4th edition .Marcel Dekker, INC, New york 1995: P 22*
- 10- Miller D. *Is variant angina the coronary manifestation for a generalized asospastic disorder? . New Engl. J.med, 1981: 304:763-766.*
- 11- Tabata M , Takeshima T, Burioka N , et al . *Analysis of Heart rate Variability in ambulatory migraineur . Headache 2002 Jun ; (6) : 457 – 63.*
- 12 – Appel S, Kuritzky A , Zahavi I , Zigelman M . *Evidence for instability of the autonomic nervous system in patients with migraine . Headache 1992 Jan : 32 (1) : 10 – 17.*

13- Schecter A, Stewart WF , Silberstein SD , Lipton RB . Migraine and autonomic nervous system function : Apopulation based case control study . Neurology 2002 : 58 : 422-427.

14- Ewing Dj , Clark BF . Diagnosis and management of diabetic autonomic neuropathy .BMJ .1982 : 258 : 915- 8.

15- Nelen PM.De-vosk , Horstink MW . Heofnagels WH , Autonomic dysfunction in Parkinson,s disease tested with computerized using afinapres device . Clin Auton Res 1995 ; 2 : 85-9.

16- Turkka JT. Correlation of the severity of autonomic dysfunction to cardiovascular reflexes and to plasma noradrenaline levels in Parkinson,s disease. Eur Neurol 1987;26:203.

17 Breslau N , Rasmussen BK. The impact of migraine Epidemiology , risk factors , and co-morbidities . Neurology 2001 : 65 (supply 6) : S4-S12 .

18- Beckett BE. Pharmacotherapy , pathophysiologic approach. . In : Dipiro JT, Talbert RL , YeeGC , et al . [editors] Headache disorder 3rd ed . Stamford , Appleton and Lange 1997 : 1291-91.

19- Roger P.Simon , Micheal J.Aminoff , David A.Greenberg , Headache and fascial pain : Migraine . In : Simon , Aminoff , Greenberg . Clinical Neurology , 4th ed ., Chap. 3 , Alange medical book . 1999 : 93 – 98 .

20- Neil H.Raskin , Stephen J.Peroutka , Headache , including migraine and cluster Headache, In : Braun wald E , Haser S, Fauci A, LongoD , KasperD , Jameson J , eds . Harrison's principles of internal medicine , 15th ed ., McGraw Hill , Med. Publishing division , 2001 ; (15) : 70 – 79

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