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DISTRIBUTION OF HEADACHES AND ROLE OF ASSOCIATED BIOGENIC AMINES METABOLITES IN BLOOD AND URINE

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ABSTRACT

Significant number of patients with headache also suffers from psychiatric disorder like depression and psychosis. The pathogenesis of headache and the psychiatric disorders has been explained on the basis of biogenic amine neurotransmitters and peptide. Most of the data on central 5-HT metabolism in depression have been recorded by measuring CSF concentration of 5-HT metabolite, 5-hydroxytindoleacetic acid (5-HIAA) before and after probenecid loading. Blood and urine examination for level of 5-HIAA (major metabolite of serotonin) and HVA (major metabolite of dopamine) was estimated in 262 patients in present study. We observed significant results ($p<0.05$) in the level of 5-HIAA and HVA in blood of group II. Group I and Group II showed higher values of 5HIAA and HVA in urine than Group V. Present study showed insignificant higher levels of 5HIAA and HVA in Group I and significant lower levels in Grouup II.

Introduction

Headache is one of the most common neurological disorders and has a great variety of medical, social and psychiatric implication. It has been seen that 57% men and 76% women complain about at least one significant headache per month and more than 90% people encounter at least one significant headache in their life [1]. The symptom of headache is therefore a public health problem need to get serious attention. Traditional classification of the most common recurring headache in to tension and migraine type is open to challenge [2]. Migraines limit the sufferer's ability socially and professionally during onset as well as between attacks. Significant number of patients with headache also suffers from psychiatric disorder like depression and psychosis. The pathogenesis of headache and these psychiatric disorders like depression, anxiety has been explained on the basis of biogenic amine neurotransmitters and peptide [3,4]. Another study revealed a greater incidence of mood disorders in CDH (chronic daily headache) than in migraine and CLBP (chronic low back pain). A single past depressive episode is more frequent in migraine while recurrent major depressive disorder is present more often in CDH, considering the longer course of disease. On the contrary, CLBP patients were not found with frequent mood disorders [5]. Most of the data on central 5-HT metabolism in depression have been recorded by measuring CSF concentration of 5-HT metabolite, 5-hydroxytindoleacetic acid (5-HIAA) before and after probenecid loading. Probenicid inhibits the transport of 5-HIAA from CNS to blood and results in accumulation of 5-HIAA in brain. Accumulation of the main metabolite of dopamine in the CSF after probenecid loading is diminished indicating reduced dopamine metabolism, this is true for depression with mark motor retardation [6]. It would be interesting to know about the levels of these neurotransmitter metabolites in patients of headache and psychiatric disorder.

Material and methods

The total patients 262 included in the study were categorised in to five groups according to diagnosis.

Group I = headache with evidence of other psychiatric disorders. n= 124 (47.3%)

Group II = headache with evidence of depression. n= 49 (18.7%)
Group III = headache without any evidence of any psychiatric disorder.

n = 12(10.3%)
Group IV = miscellaneous. n = 12 (4.5 %)
Group V = control. n = 50 (19%)

Patients aged between 15 and 60 years with headache were selected. Patients with any other chronic serious physical illness or organic brain syndrome due to some cause other than epilepsy were excluded. Patients were interviewed and their mental state examination was carried out. Blood and urine examination for level of 5-HIAA (major metabolite of serotonin) and HVA i.e homovanillic acid (major metabolite of dopamine) was estimated for each patient.

Statistical analysis

Data obtained from the study were analysed to observe the relationship between level of 5-HIAA and HVA in blood and urine in patients with different groups. (Table 1-4).

Independent t-test was applied to compare the different groups and to determine correlation between headaches and associated biogenic amines in blood and urine.

Table 1: Average levels of 5-HIAA in blood (ng/ml) in different groups of total (male and female) patients

	G I	GII	GIII	GIV	Control
Total no.	124	49	27	12	50
Mean	4.44	3.70	3.99	4.51	4.36
SD	1.52	1.72	1.82	1.31	1.21
t	0.332	2.212	1.075	0.379	
p	>0.05	<0.05	>0.05	>0.05	
		Significant			

Table 2: Average levels of HVA in blood (ng/ml) in different groups of total (male and female) patients

	G I	GII	GIII	GIV	Control
Total no.	124	49	27	12	50
Mean	5.02	3.92	4,69	4.52	5.03
SD	1.68	2.02	2.20	156	1.61
t	0.036	3.027	0.777	0.991	
p	>0.05	<0.05	>0.05	>0.05	
		Significant			

Table 3: Average levels of 5- HIAA in urine (mg/24 hrs) in different groups of total (male and female) patients

	G I	GII	GIII	GIV	Control
Total no.	124	49	27	12	50
Mean	3.49	3.87	3.74	3.88	3.50
SD	1.66	1.79	1.95	1.88	1.72
t	0.035	1.049	0.558	0.676	
p	>0.05	>0.05	>0.05	>0.05	

Table 4: Average levels of HVA in urine (mg/24 hrs) in different groups of total (male and female) patients

	G I	GII	GIII	GIV	Control
Total no.	124	49	27	12	50
Mean	3.63	3.68	3.95	3.86	3.57
SD	1.28	1.48	1.66	1.20	1.32
t	0.277	0.390	1.101	0.694	
p	>0.05	>0.05	>0.05	>0.05	

Results

We observed significant results ($p<0.05$) in the level of 5-HIAA and HVA in blood of G-II but the values were statistically insignificant ($p>0.05$) in G-I (Table: 1). G- III showed lower values than G-I and the results were not significant (Table: 1, 2).

G-I and G-II showed higher values of 5HIAA and HVA in urine than G-V but these results were found statistically insignificant ($p> 0.05$). Present study showed insignificant higher levels of 5HIAA and HVA in G-I and significant lower levels in G-II (Table: 3, 4). Alteration of HVA levels can be explained by increase turnover of dopamine in CNS and in blood of G-I.

Discussion

Incidence and prevalence rate of headache shows that it is a major public health problem. Psychiatric disturbance is a possible complication in headache and previous studies have found that increased incidence of psychiatric morbidity in patient with headache [7, 8]. To obtain information about the role of serotonin and dopamine in pathophysiology of headache and headache associated with various psychiatric disorders, we measured 5-HIAA and HVA in plasma and urine in patients of various headaches with or without psychiatric involvement.

A study conducted by Srikialkhachorrn found 60 diagnosed cases with CDH (male to female ratio 1:5.7). Mental stress was the most commonly reported precipitating factor [9]. In present study, CDH was more common in 21- 30 year of age group. Prevalence of migraine was found highest in 31-40 year of age group in both genders. Another study estimated 22.3% prevalence of migraine (male 20.2%, female 24.35) and 16.2% prevalence of tension type headache (male 17.8%, female 14.7%). Maximal prevalence of migraine was noticed in 15-19 year age group in both genders whereas prevalence of tension type headache was highest in 50-59 year men and 20-29 year age of women [10]. A patient with five similar attacks of migraine over a period of time and left untreated or with overuse of analgesic migraine can evolve into a chronic daily occurrence from episodic attacks. It is known as chronic daily headache or transformed migraine or mixed tension vascular headache [11]. In present study, we considered headache with other psychiatric disorder (>4 hrs and >6 months persistence) as chronic daily headache, headache with depression (> 4 hrs and > 6 months persistence) as an migraine attack and headache (< 4 hrs and < 6 months persistence) as cluster headache.

We observed significant results ($p<0.05$) in the level of 5-HIAA and HVA in blood of G-II but the values were statistically insignificant ($p>0.05$) in G-1 (Table: 1). G-III showed lower values than G- I and the results were not significant (Table: 1, 2). G-I and G-II showed higher values of 5HIAA and HVA in urine than control group but these results were found statistically insignificant ($p> 0.05$). Present study showed insignificant higher levels of 5HIAA and HVA in G-I and significant lower levels in G-II (Table: 3, 4). Alteration of HVA levels can be explained by increase turnover of dopamine in CNS and in blood of G-I.

Serotonin is widely distributed in body tissues, 90% in enterochromoffin cells of GIT and remaining in platelets and brain. A trace amount is found unbound to platelets in plasma. A decreased level of platelet serotonin and an increased level of urinary serotonin were noticed in 85% patients during headache attack [12]. Hsu et al observed the patients waken up from sleep due to headache. A significantly higher level of plasma norepinephrine was recorded during 3 hrs before wakening up. Plasma levels of norepinephrine declined during headache attack and gradually returned to normal over a period of time as the intensity of headache diminished [13]. Blood levels of serotonin metabolites (5HIAA) was diminished while urinary concentration of serotonin metabolites was increased during an attack of migraine [14].

Conclusion

Following points were observed from the study:

- Increase incidence of psychiatric morbidity in patients with headache.
- Psychiatric morbidity was more common in patients with CDH followed by migraine and cluster headache.
- The patients of headache with depression had lower concentration of 5-HIAA and HVA in blood.

A positive circulation was found in the level of 5 HIAA and HVA in G I and in GII. This study demonstrated that abnormalities in blood monoamine metabolites occur in patients of headache with and without psychiatric disorders in both treated and untreated patients. These changes indicate a generalized metabolic disturbance that contributes to predisposition of headache.

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