Serum prolactin and migraine

S. Ali Masoud,* E. Fakharian,†

*From the *Department of Neurology and †Department of Neurosurgery, Kashan University of Medical Sciences, Kashan, Iran*

Correspondence:
S. Ali Masoud, MD
Neurology Department
Kashan University of Medical Sciences
Kashan, Iran

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Prolactin is a polypeptide, consisting of 198 amino acids, secreted from the anterior pituitary gland. Prolactin secretion is influenced by physiologic factors (sleep, pregnancy, stress, exercise, intercourse, nipple stimulation), pathologic factors (pituitary adenoma, primary hypothyroidism, renal failure, hypothalamic diseases), and drugs (phenothiazines, butyrophenones, morphine, estrogens, reserpine, methyldopa). Prolactin is unique because its secretion is controlled by a central inhibitory mechanism, mediated by dopamine.[1,2]

Migraine is a chronic, common disease that presents with mild to severe recurrent headaches, accompanied by autonomic and neurologic symptoms.[1,4] There are several explanations for the pathophysiology of migraine headache attacks. Scutari explained the pathogenesis of migraine headache with the dopamine hypothesis in 1977.[1] In this hypothesis, prodromal, clinical and postdromal signs and symptoms of migraine headache are attributed to increased activity of the dopaminergic system.[3-11,12] Administration of dopaminergic drugs can intensify the symptoms during an acute attack.

Decreased levels of prolactin after increased secretion of dopamine would confirm the accuracy of the above hypothesis. Considering this, we decided to measure the serum prolactin level during acute migraine attack in patients referred to Shahid Beheshti hospital and private neurologic clinic in 2002. On the base of the results, we demonstrate the role of increased dopaminergic activity as a major clue in migraine pathophysiology and we also can use the results for finding effective drugs for ameliorating the intensity of frequency of migraine attacks.

Patients and Methods

In a case-control study, we selected 74 patients, 37 with migraine headache as a case group and 37 with non-migraine headaches as a control group. Migraine headache was based on the criteria of the International Headache Society. Non-migraine patients had tension headache. Patients were referred to the Shahid Beheshi Hospital and private neurology clinic in Kashan in the first 6 months of 2002. Exclusion criteria included pregnancy, use of phenothiazines, butyrophenones, methyldopa or reserpine, intercourse or vigorous exercise in the last 12 hours, and a history of prolactinoma, pituitary adenoma, hypothyroidism, chronic renal failure or cirrhosis. A questionnaire was completed for each patient, including age, sex, confounding factors and family history of migraine headache. From all patients in each group, we took two samples of blood, one sample during an acute attack and another between attacks and at least 2 weeks after the last attack. We checked the serum prolactin level in each blood sample using the ELIZA method with 1 IU/mL sensitivity. We analyzed the data with the Student *t* test and chi-square test.

Table 1. Age and sex distribution of cases and controls.

Age range (years)	Female	Male	All
Migraine (cases)			
15-30	13 (32.4)	1 (2.7)	14 (37.8)
31-45	10 (27)	2 (5.4)	12 (32.4)
46-50	4 (10.8)	1 (2.7)	5 (13.5)
>50	5 (13.5)	1 (2.7)	6 (16.2)
Non-migraine (controls)			
15-30	9 (24.3)	2 (5.4)	11 (29.7)
31-45	5 (11.6)	1 (2.7)	6 (16.2)
46-50	4 (10.8)	1 (2.7)	5 (13.5)
>50	12 (32.4)	3 (8.1)	15 (40.5)
Total	30 (81.1)	7 (18.9)	37 (100)

Data are number of patients with percentages in parentheses.

Table 2. Family history of migrane in 37 patients with migraine.

Family history	Female	Male	All
Positive	20 (54)	2 (5.4)	22 (59.4)
Negative	12 (32.4)	3 (8.1)	15 (40.5)
Total	32 (86.5)	5 (13.5)	37 (100)

Data are number of patients with percentages in parentheses.

Table 3. Distribution of sex and family history in patients with migraine headache referred to Shahid Beheshti hospital and private neurology clinic in Kashan (In the First 6 months of 2002)

Sex / Family History	Female	Male	T
Positive	20 (54)	2 (5.4)	22 (59.4)
Negative	12 (32.4)	3 (8.1)	15 (40.5)
T	32 (86.5)	5 (13.5)	37 (100)

Table 4. Statistical indices of decreased serum prolactin during attacks of headaches in patients with migraine and nonmigraine headaches referred to Shahid Beheshti hospital and private neurology clinic in Kashan (In the First 6 months of 2002).

Statistical Indices / groups	NO	Mean	Standard deviation	P value
Migraine headache	37	-68.64	218.5	0.03
Non-migraine headache	37	-38.3	217.0	
T	74	-53.42	217.75	

Results

The 37 patients with migraine headache included 5 men (13.5%) and 32 women (86.5%). Most patients were 15 to 30 years old (Table 1). The control group of 37 patients with nonmigraine headache included 7 men (18.9%) and 30 women (81.1%) and most were more than 50 years old. Twenty-two (59.4%) patients with migraine headache had a positive family history of migraine (Table 2). The mean decrease in prolactin level during acute attack in the case group was -68.6 IU/mL (SD=218.5 IU/mL); in the control group the decrease was -38.3 IU/mL (SD=217.0 IU/mL), a statistically significant difference (P=0.03).

Discussion

In a study of 107 patients with migraine and nonmigraine headache, the mean decrease in prolactin level was -86.3 in the case group and -33.6 in the control group, a clinically important difference.[16] In another study, Mapou and colleagues showed that many dopamine antagonist drugs could stop migraine attacks and they showed the effectiveness of these drugs in migraine prophylaxis.[13] Peres in 2001 and Delzompo in 1995 showed that dopaminergic hypersensitivity could induce migraine attacks.[12,15] In 2000, Fanciulocci showed a reverse effect of dopamine on prolactin secretion in an exaggerated state, so they concluded that hypersensitivity of dopaminergic receptors is the main pathophysiologic mechanism in migraine attack.[11] In 2001, Seddighi detected that prolactin level decreased during migraine attacks in 20 men with migraine headache and 20 men with non-migraine headache, but he found no clinically important difference between the two groups. This result may have been due to the scanty number of patients.

In conclusion, decreased prolactin levels during acute migraine headache are due to increased dopaminergic system activity. This is a major point in the explanation of pathophysiology of migraine attacks. Therefore, a decreased serum prolactin level during headache attacks can be used as a predictor for detecting migraine headache. In addition, we may use antidopmaine drugs for relieving or preventing migraine headache.

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