Plasma cortisol levels in migraineurs between attacks

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ÖZET
Migrenlilerde ataklar arasında plazma kortizol düzeyleri
Migrande hipotalamo-pituitary-adrenal aksın rolünü araştırmak için baş ağırsı atakları arasında migrenlilerde plazma kortizol düzeyini araştırdık. 25 migrenli ve 24 sağlıklı kontrol grubundan saat 8.30-9.30 arasında alınan kan örneklerinde bakılan kortizol düzeylerinde gruplar arasında istatistiksel anlamlılık bulunmadı.

Anahtar kelimeler: Kortizol, migren

SUMMARY
We have studied the plasma cortisol levels between attacks in order to investigate the role of hypothalamic-pituitary-adrenal axis in migraine patients. We have not found any statistically significance between plasma cortisol levels of patients and control group, after taking the blood of 25 patients and 24 healthy controls between 8.30-9.30 am.

Key words: Cortisol, migraine

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**Introduction**

Migraine headache may be stimulated by psychological stress (Olesen et al. 2000). Hypothalamic-pituitary-adrenal axis may be activated by m-CPP (serotonin receptor agonist). This causes cortisol release and a few hours later headache initiates. The intensity of pain is related with the amount of the cortisol release (Rainero et al. 2006, Nappi et al. 2003). During migraine headache or intervals, the cortisol level may increase. During attacks migraine patients feel chilly, may complain of cold extremities, and drowsiness (Silberstein and Saper 2001). These symptoms suggest hypothalamic involvement in migraine. Sympathetic nervous system is activated and plasma epinephrine, norepinephrine and cortisol concentrations increase during the attack. The increased cortisol concentration in intervals may be related to the sympathetic imbalance (Peroutka 2004, Shechter et al. 2002, Silberstein and Saper 2001, Grazzi and Bussone 1993).

The purpose of this study is to investigate, how hypothalamic-pituitary-adrenal axis affects during intervals of attack free period. Accordingly we measured the plasma cortisol levels in patients and in control group.

**Material and Method**

The patients, who were evaluated at our headache outpatient clinic of our hospital with the following criteria are included in this study:
- Subjects, who complained migraine with and without aura according to the criteria of the International Headache Society;
- Patients without any additional type of headache;
- Patients with normal neurologic examination;
- Patients without any metabolic-endocrine disorders and hypertension;
- Patients, who have not taken medication for migraine prophylaxis at least for the last twenty days;
- Patient must experience the last headache attack at least longer than two days before.

Blood samples were taken from 24 control subjects and 25 patients in an attack free period between at 8.30-9.30 a.m. The blood samples were taken once from each patient while arterial pressure was stable at the resting position. Cortisol level was measured by chemiluminescence method, BID-DPC kit and Immulite 2000 device as ng/ml in our hospital biochemistry laboratory. Statistical analysis was performed by student's t test for the comparison of the cortisol concentrations of the two groups. The $\chi^2$ test was used for categorized variables (sex, age). Significance levels were set at $p<0.05$ in all cases and 95% confidence intervals were estimated. Study protocol was approved by Institutional Ethics Committee.

**Results**

The patients composed 21 women and 4 men. The mean age of the patients was 33.4±7.8 (ranged 20-49) years. The control group comprised 22 women and 2 men. The mean age of the control group was 27.7±6 (ranged 19-40) years. 11 patients had migraine with aura and 14 patients had migraine without aura. The duration of attacks were 1-4 days (mean 1.5 days), the number of attacks in a month were 2-10 (mean 5 times per month).

There was no statistically significance in age and sex between the patients and the control group ($t=0.82$, $p>0.05$; $\chi^2=0.87$, $p>0.05$ respectively). Plasma cortisol levels were 6.51-29.6 ng/ml (15.13±5.76) among patients and 8.69-34.2 ng/ml (16.70±6.75) among control group. There was no statistically difference in the serum cortisol levels between the patients and the control group ($t=0.91$, $p>0.05$), and also between the patients with aura and without aura ($t=0.58$, $p>0.05$). Table 1 showed demographic data of subjects and cortisol concentrations.

<table>
<thead>
<tr>
<th>Variables</th>
<th>Patients, n=25</th>
<th>Controls, n=24</th>
<th>$p$ Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, Years</td>
<td>33.4±7.8</td>
<td>27.7±6</td>
<td>$p=0.82$</td>
</tr>
<tr>
<td>Sex, Male/Female</td>
<td>4/21</td>
<td>2/22</td>
<td>$p=0.87$</td>
</tr>
<tr>
<td>Cortisol concentration, ng/ml</td>
<td>15.13±5.76</td>
<td>16.7±6.75</td>
<td>$p=0.91$</td>
</tr>
</tbody>
</table>
As a result, we didn't find an increase value in the serum cortisol levels between attacks in migraineurs.

Discussion
The circadian production of cortisol is altered during cluster periods and in chronic cluster headache. Hyperactivity of the hypothalamic-pituitary-adrenal axis in cluster period is indicated by the finding that 24-hour cortisol production and morning levels are increased (Olesen et al. 2000). Functional imaging studies with positron emission tomography (PET) points out that in acute cluster headache attack, ipsilateral inferior hypothalamic grey area is activated (Olesen et al. 2000). The hypothalamus, or closely related structures, are candidate sites for triggering the acute attack of cluster headaches (May et al. 2000, May et al. 1998). Brain stem was shown to be activated in functional neuroimaging studies of migraine patients (Bahra et al. 2001, May et al. 1998).

Various results are obtained in studies concerning cortisol level. In the study of Patacchioli and co-workers, the concentration of salivary cortisol of migraine patients was found significantly high (Patacchioli et al. 2006). Van Hilten and co-workers measured body temperature and interleukin-1, tumour necrosis factor, ACTH, cortisol levels and determined that serum cortisol level was high and ACTH was normal during the attack (Hilten et al. 1991). Grazzi and co-workers found that, serum cortisol and norepinephrine levels were significantly high during and between the attacks and they concluded that there was persistant sympathetic imbalance in migraineurs (Grazzi and Bussone 1993). M. Leone and co-workers couldn’t find statistically difference in serum cortisol levels between migraine group and control group (Leone and Biffi 1994). Hypothalamic functions and migraine was studied by Peres and co-workers and found that serum cortisol concentrations increased concomitantly with the decreased serum prolactin, melatonin levels (Peres et al. 2001). However, this study is different than ours, because they were evaluated chronic migraine patients.

In conclusion, migraine headache is not triggered primarily hypothalamic-pituitary-adrenal axis as cluster headache, but trigeminovascular system is strongly responsible by triggering the migraine. Hypothalamic-pituitary-adrenal axis is activated during attack due to psychological and stressing factors. However, these studies in this context is not sufficient, and it will be more enlightening to determine the serum catecholamine levels and measure the serum cortisol level during and before or after the attack in patients, who experience migraine. We also believe that it will be more enlightening to do new studies by using other methods such as PET.

References


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