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RELATIONSHIP BETWEEN MIGRAINE AND PROLACTIN HORMONE.

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ABSTRACT

This study was carried out to investigate the causative relation between migraine and prolactin hormone (PRL) level. Ninety four patients of both sexes were selected (45 males and 49 females). Prolactin level was estimated in both middle aged patients (15 -45 years old) and aged one (above 45 years) in both sexes during acute attacks of migraine headache and compared to its levels during attacks of acute of non-migraine headache.

Results showed that, there was significant decrease in PRL level ($p<0.01$) during acute attacks of migraine headache if compared to their decrease levels during acute attacks of non-migraine headache. The same results were obtained in both male and female groups in either middle aged or aged groups. More specifically, the decrease in PRL level was highly significant in female groups ($p< 0.001$) than male groups. It is clear also from the results that PRL level was significantly decreased in middle aged group more than in aged groups.

Conclusion: from the present study it could be concluded that there is a certain relationship between PRL hormone and migraine that might be a causative one.

INTRODUCTION

PRL is a polypeptide hormone consisting of 198 amino acids and secreted from anterior pituitary gland. PRL secretion is influenced by physiological factors such as sleep, pregnancy, stress, exercise, intercourse, and nipple stimulation and also by pathologic factors such as pituitary odema, pituitary hypothyroidism, renal failure and hypothalamic diseases (**Abrams and Zimmeran, 2000**).

PRL is unique as its normal secretion is controlled by a central inhibitory mechanism which is mediated by dopamine (**Kudrew et al., 1987 and Abrams and Zimmermon.,2000**). On the other hand, migraine is a chronic common disease that presents with mild to severe recurrent headaches which are accompanied by autonomic and neurologic symptoms (**Hartman , 1995 and Kudrow et al., 1997**).

There are several explanations for the pathogenesis of migraine headache attacks. Serotonin (5HT) appears to play a role in pathogenesis of migraine. Reserpine acts on a central nervous 5HT depleting agent can precipitate in migraine headaches (**Cassidy et al., 2003**). Similarly, sleep reduces CNS 5HT. Therefore, it is a well established method of aborting migraine. Biochemical studies demonstrate that plasma drugs used to prevent headaches are 5HTs antagonists (**Weiller et al., 2005**).

Other neurotransmitters and mediators such as catecholamines, histamine, vasoactive peptides, endogenous opiates, prostaglandins, free fatty acids, steroids and PRL hormone are also implicates in the pathogenesis of migraine, but other specific effects are less clearly established (**Siberstien, 2003 and Crnzia et al., 2006**).

It seems that there is a big relation between dopamine and migraine,

according to dopamine hypothesis of **Marie et al. (2007)**.

This hypothesis, prodromal signs and symptoms of migraine headaches are attributed to increase activity of the dopaminergic system (**Franciullacci et al. ,2000 and Peres and Sanchez,2001**). Administration of dopaminergic drugs can intensify the symptoms during an acute attack. Decreased levels of PRL after increased secretion of dopamine would confirm the accuracy of the above hypothesis

Considering this, it was decided to measure serum PRL levels during acute migraine attack in patients referred to hospital and also to private neurological clinics in 2008 and 2009.

MATERIALS AND METHODS

Patients

In this study 94 patients were selected: 45 males and 49 females. The male patients were divided into 2 groups: one group in which patients were complaining of non-migraine headache (n=25; 13 patients aged from15 to 45years old and 12 aged from 45 up to 60 years old).

The other group included patients suffering from migraine headache (n= 20; 10 patients aged from 15 to 45 years old and 10 aged from 45 up to 60 years old).

On the other hand, the female patients were also divided into 2 groups: one group of patients was complaining of non-migraine headache (n=22; 10 patients aged from15 to 45years old and 12 aged from 45 up to 60 years old).

The other group included 27 female patients complaining of migraine headache (15 aged from 15 to 45 years old and 12 aged from 45 up to 60 years old).

Non-migraine headache group was taken as a control group. All patients were apparently healthy and none of them was complaining of any other disease except headache

None of the patients was taking phenothiazines, bntyrophenones, methyl dopa, reserpine, or practicing vagarious muscular exercise 12 hours before taking blood samples. Also, all of them did not show a history of prolactinoma; pituitary adenoma, hypothyroidism, chronic renal failure or cirrhosis. None of the female patients was pregnant. Moreover, a questionnaire was completed for each patient including age, sex, and any other abnormal habits.

From each patient 2 ml of venous blood samples were taken; one sample was taken during the acute attack of headache and the other sample was taken in between the headache attack.

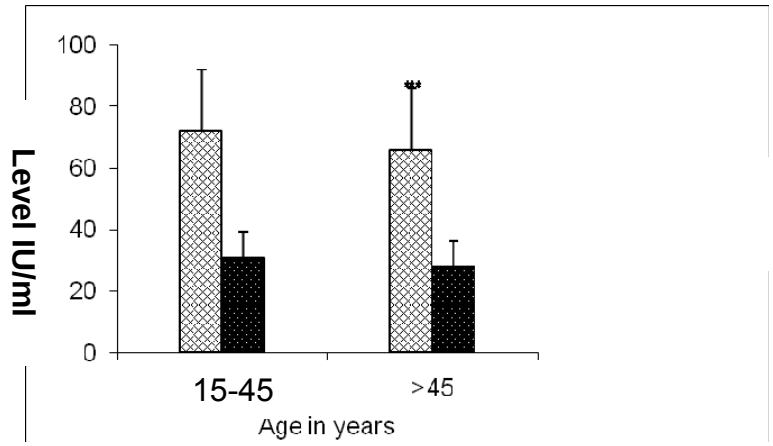
Serum PRL level was estimated using the ELIZA method with 11µ/ml sensitivity according to

Obtained data were analyzed by using Student t-test for comparison between 2 corresponding data **(Snedector and Coshran, 1974)**.

RESULTS

Relationship between PRL and migraine headache in males

It was found that middle aged male patients (n=13) complaining of migraine headache showed significant decrease ($p<0.001$) in prolactin level during acute attack of headache if compared to its level in between migraine headache attack (Fig 1).



■ = Migraine-headache(black spotted bar). ▩ = non-migraine headache(gray diamond bar)

Figure (1): Showing the level of PRL in two different male groups in different ages: migraine-headache(black spotted bar). and non-migraine headache(gray diamond bar). At each time bar together with standard error bars. We found statistical difference in PRL level between non-migraine headache patients and migraine-headache patients above 45. In this and subsequent figures the results of Student t-test, comparing means and standard error of migraine-headache patients to non-migraine patients, are presented as stars over each group of patients bar indicating the P-value. * = *(P < 0.05)*, ** = *(P < 0.02)*, *** = *(p < 0.01)*. Bars without stars are not significantly different from their non-migraine headache.

Moreover, male patients suffering from non-migraine headache (n=12), also showed less significant decrease in PRL level during acute non-migraine headache attack if compared to its corresponding value in between acute attacks (Fig 1). It was noticed that PRL level was more decreased during migraine attacks of headache than during non-migraine attack of headache (Tables.1&2).

Table 1: Denoting the relationship between serum PRL level and migraine headache in males

Male						
	Age in years					
	١٥ - ٤٥			>45		
	n	mean	S .E	n	mean	S .E
Migraine	١٠	٧٢	١٩.٩٤	10	٦٦	١١
non-migraine	13	٣١	٨.٤٢	12	٢٨	٦.٠٨

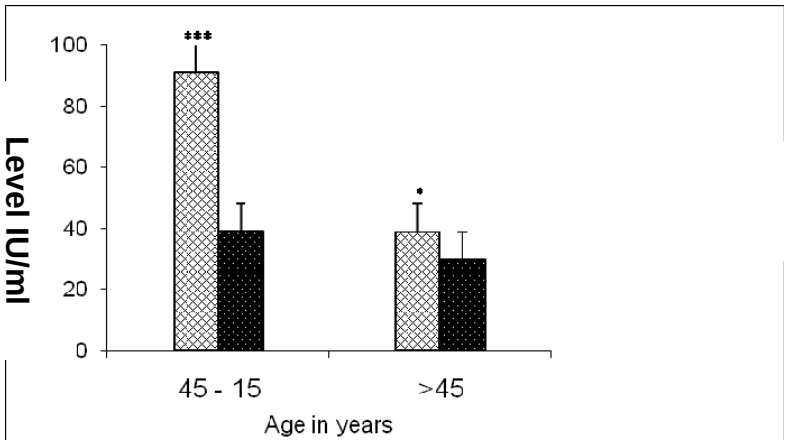
Table 2: Depicting the decrease in serum PRL level of all male groups during attacks of non-migraine and migraine headache.

Total No	45			
	non-migraine headache n = 25		migraine headache n = 20	
Age (years)& No.	Middle aged (15-45)	Aged above 45	Middle aged (15-45)	Aged above 45
	13	12	10	10
Decrease in PRL level IU/ml	31	28	72	66
SD	26.1	19.2	27.3	31.3
SE	8.42	6.08	19.94**	11.00**

Where $p<0.01$ = significant

Relationship between PRL and migraine headache in females

Nearly similar results were obtained in female patients of middle and old aged groups complaining of migraine headache



■ = Migraine-headache(black spotted bar). ▩ = non-migraine headache(gray diamond bar)

Figure (2): Showing the level of serum PRL in two different female groups in different ages: migraine-headache, (black spotted bar) and non-migraine headache(gray diamond bar) We found statistical difference in serum PRL level between non-migraine headache patients and migraine-headache patients below 45.

Table 3: Illustrating the relationship between PRL and migraine headache in females

Female						
	Age in years					
Age	١٥ - ٤٥			>45		
	n	mean	S .E	n	mean	S .E
Migraine	15	91	9.17	12	38.8	8.61
non-migraine	10	39.2	8.8	12	29.9	8.44

Table4: Showing the decrease in serum PRL level in all female groups during attacks of non-migraine and migraine headache.

Total No	49			
	Non-migraine headache n=22		migraine headache n=27	
Age (years)& No.	Middle aged (15-45)	Aged above 45	Middle aged (15-45)	Aged above 45
	10	12	15	12
Decrease in PRL level IU /ml	39.2	29.9	91	38.8
SD	27.8	28.7	35.5	29.8
SE	8.80	8.44	9.17***	8.61***

Where *P<0.001* = highly significant

Therefore, the Serum Prolactin level is decreased in both migraine and non-migraine headache attacks but the decreases during migraine headache attacks are more compared with the non-migraine.

DISCUSSION

In the present study, serum PRL level was found to be significantly decreased during acute attacks of headaches and it is more in attacks of migraine headache than during attacks of non-migraine headache. It could be suggested that decrease PRL levels during acute migraine attack are due to increased dopaminergic activity or sensitivity.Our results are in agreement with previous studies. It could be suggested that decreased serum PRL levels during acute migraine headache are due to increased dopaminergic sensitivity .The hypersensitivity of dopaminergic receptors is the main pathophysiological mechanism in migraine attack (**Franciullacci *et al.,* 2000**; **Peres. and Sanchez ,2001**;**Marie *et al* .,2007 and Hattero *et al.,* 2008).**

Moreover, **Seddighji (2002)** detected that serum PRL level decreased during migraine attack in 20 men with migraine headache and in 20 men with non-migraine headache, but he found no investigational difference between the two groups.

Mapou and his colleagues (**2001**) found that many dopamine antagonist drugs

could stop migraine attacks and they also studied the effectiveness of these

drugs in migraine prophylaxis. This will support the hypothesis that migraine attack is caused by decreased in PRL

level and this is due to hyper activity of dopamine action

Conclusion: It could be concluded that ,the decrease in serum PRL levels during acute migraine attack might be due to increased dopaminergic activity or sensitivity. This is a major point of view in the explanation of pathophysiology of migraine attack. Therefore, a decreased serum PRL level during headache attacks can be used as a predictor for detecting migraine headache. In addition, anti-dopaminergic drugs could be used for relieving or preventing migraine headache.

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