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Prediction of Post-Traumatic Headache in Iraqi Civilians by Measuring S- 100B and Neuron Specific Enolase concentrations and by regarding head-ache in the emergency room

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ABSTRACT

Post-traumatic headache (PTH) is defined by the International Headache Society as a headache developing within seven days of the injury or after regaining consciousness. PTH is commonly associated with memory and concentration problems, sensitivity to loud sounds or bright lights, fatigue and many symptoms including insomnia, dizziness, poor and personality changes like depression and nervousness. The total number of participants in this study is one hundred and three, fifty-three of them (36 males and 17 females) are in the case group while the other fifty (29 males and 21 females) are in the control group. All of them aged between 20-40 years. Only 25 patients had headache in ER, while 29 of them visited the out patient's clinic suffering from post traumatic headache in the next two months. The mean of S100B and that of NSE in case group are higher than that in control group. Regarding the gender, the mean of S100B is higher in males of case group than that in control group, while the mean of NSE in males and females in case group is higher than that in control group. The means of S100B and NSE in patients who had a headache in ER are higher than that in patients with no headache. The means of S-100 B and NSE in patients complaining of a post-traumatic headache who had a headache in ER are higher than that in patients also complaining from a posttraumatic headache but had no headache in ER. S-100 B and NSE are useful biochemical markers for brain injury in mild traumatic brain injury (MTBI) patients and seem to be associated with the presence of a headache in ER after trauma. These biochemical markers with a headache in ER can predict a post-traumatic headache in the near future.

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INTRODUCTION

A post-traumatic headache (PTH) is the most common complaint after mild head trauma (Headache_Subcommittee, 2004). This type of a headache is often very difficult to deal with because of the problems in assessment and treatment of a subjective symptom, the vague clinical picture, and little proof of organic abnormality (Carroll et al., 2004). In most patients, the frequency and severity of the headache decrease with the passage of time, and the headache usually cured within six to 12 months (Faux and Sheedy, 2008). There appears to be no association between the severity of the injury and the intensity of post-traumatic headache (Lieba-Samal et al., 2011). Many considered that

the symptoms after mild head injury were psychological because the neurological examination is normal, routine tests and imaging studies (MRI or CT of the head) fail to detect abnormalities (Levi et al., 1990; Lew et al., 2006; Lieba-Samal et al., 2011; Lucas et al., 2013; Mandel, 1989). But microscopic studies have shown slight damage to the nerve fibers in the brain due to the stretching forces of the trauma (Bernstein, 1999). Other subtle changes have been seen in the functions of the brain. The clinical pictures of post-traumatic headache vary from one person to another (Walker et al., 2005). Most headaches are classified as chronic tension-type headache. These headaches are usually a steady ache occurring daily or almost every day (Defrin et al., 2010; Lucas et al., 2013; Radanov et al., 2001; Sjaastad, 1988) they consist of a dull pain affecting both sides of the head, with different degrees of intensity (Sacks et al., 2009). The most common cause of a chronic headache after trauma is the contraction of muscles of the neck and scalp. Another type is a vascular headache which characterized by vascular changes. This headache often takes on the characteristics of a migraine (American Osteopathic Association. and Monti, 1901).

Many studies show that the PTH usually resolves within few months, however, in a good number of cases, it may last longer and is then referred to as persistent PTH. Many factors can increase the risk of persistent PTH such as a pre-existing headache, female gender and family history of a migraine. Severe head trauma does not necessarily lead to persistent headaches, while patients with mild head injury can suffer for a long time.(Bernstein, 1999; Sacks et al., 2009). Tension or stressful conditions can increase headaches. Mixed PTH is also common; which is a combination of two mentioned types of a headache (Defrin, 2014). Unfortunately, people complained of a post-traumatic headache also have other symptoms of the post-traumatic syndrome. There may be other neurological symptoms such as vague blurring of vision, ringing in the ears, dizziness, psychological symptoms may occur such as anxiety, depression, personality change, sleep disturbance, and decrease libido.(Margulies, 2000; Maskell et al., 2006).

People with the post-traumatic syndrome also have changes in their mental functioning, primarily difficulty in concentration, inability to work properly and difficulty in maintaining attention and retaining memory (Carroll et al., 2004; Cicerone and Kalmar, 1995).

Biochemical markers

S-100B protein is secreted by astrocytes or can spill from injured cells and enter the extracellular space or blood stream. Serum levels of S-100B increased in patients during the acute phase of brain damage. Elevated S-100B levels give an idea to the presence of neurons injury, such as traumatic head injury (Biberthaler et al., 2006; Blyth et al., 2009).

NSE is a glycolytic enzyme, it is regarded as the dominant enolase isoenzymes found in neuronal and neuroendocrine tissues. It directly reflects traumatic damage to neurons. In several studies of mild traumatic brain injury (MTBI), NSE has been investigated as an indicator of acute brain injury (Burghuber et al., 1990; Ergun et al., 1998; Fischer et al., 2015; Herrmann et al., 2001; Pleines et al., 2001; Skogseid et al., 1992; Yamazaki et al., 1995). Elevated levels of NSE in acute phase have been reported to be associated with neuropsychological dysfunction and the marker has been found valuable for prognostic purposes in patients with MTBI (De Kruijk et al., 2002; Herrmann et al., 2001).

PATIENTS AND METHODS

This study is conducted in Iraq/ Diyala Governorate/ Baquba Teaching Hospital from the first of July 2015 to the first of December 2017. Fifty-three patients involved in this study, 36 males and 17 females, all of them aged between (20-40) years. Fifty subjects have been chosen as a control, 29 males and 21 females, all of them aged between (20-40) years.

For males, the cause of minor head injury was road traffic accidents, while domestic violence was the major cause for the females.

Inclusion criteria for case group

- Males and females aged between 20-40 years.
- All of them have a mild head injury. After clinical examination in the emergency room (ER), only 25 of patients having a headache, no skull fracture, no seizures, no vomiting and no loss of consciousness.
- No findings on computed tomography scan (CT scan).
- Only 29 patients visited the out-patients clinic throughout the following two months suffering from a posttraumatic headache.

Analytical methods

For determination of the concentrations of S100B and NSE in serum, the sensitive electrochemiluminescence immunoassay (ECLIA, Roche Diagnostics) on Cobas Integra 400 plus, was used by drawing venous blood which then separated in the centrifuge to get serum. The reference value of S-100B =5-15 ng/dl, and for NSE is ≤ 16.3 ng/ml.

RESULTS

Gender

The distribution of study participants' groups by gender is shown in figure (1).

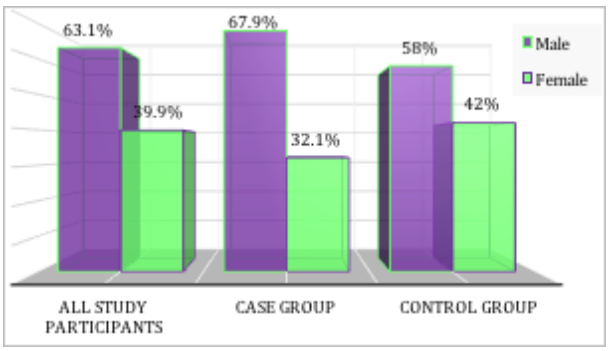

Figure 1: Distribution of study participants' groups by gender

In this study, we noticed that the proportion of male was higher than that of a female in all study groups (63.1% versus 39.9%, 67.9% versus 32.1%, and 58% versus 42% in all study participants, case group, and control group respectively).

S-100 B Concentration

Figure (2) and table (1) show a comparison in S-100 B concentration between case group and control group. The mean of S-100 B concentration was significantly higher among patients of case group than that in control group (20.26 versus 19.42, P=0.019).

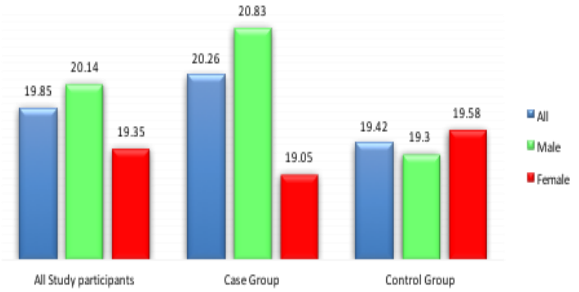

Figure 2: S-100 B concentration among participants in all study groups

Regarding male gender, also the mean of S-100 B concentration was significantly higher among males of case group than that in control group (20.83 versus 19.3, P=0.001), while it was not significantly higher in females of a control group than that of case group (19.58 versus 19.05, P=0.309).

NSE Concentration

Figure (3) and table (2) show a comparison in NSE concentration among participants in all study groups. The mean of NSE concentration was significantly higher among patients of case group than that in control group (20.97 versus 18.93, P=0.001).

Regarding gender, also the mean of NSE concentration was significantly higher among males and females of case group than that in control group (21.32 versus 18.85, P=0.001 for males and 20.25 versus 19.04, P=0.04).

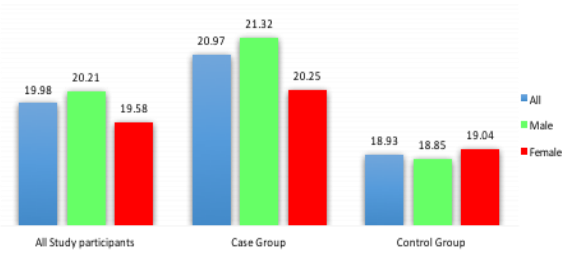

Figure 3: NSE concentration among participants in all study groups

Patients with trauma and headache in ER

The total number of patients presented to ER for trauma complaining from a headache was 25 (18 males and 7 females).

S-100 B Concentration

Table (3) shows the comparison in S-100 B concentration between patients complaining of a headache and patients without a headache in ER. The mean of S-100 B concentration was significantly higher among patients complaining from a headache than that in patients without a headache in ER (22.07 versus 19.56, P=0.001).

NSE Concentration

Table (4) shows the comparison of NSE concentration between patients complaining of a headache and patients without a headache in ER. The mean of NSE concentration was significantly higher among patients complaining from a headache than that in patients without a headache in ER (21.4 versus 20.02, P=0.005).

Patients with Posttraumatic Headache

The total number of patients who complained from a posttraumatic headache after two months was 29 (17 males and 12 females). 18 of them had a headache in ER, while 11 had no headache in ER.

S-100 B Concentration

Table (4) shows the comparison in S-100 B concentration between patients complaining of a posttraumatic headache who had a headache in ER and patients also complaining from a posttraumatic headache but had no headache in ER. The mean of S-100 B concentration was significantly higher among patients complaining from a posttraumatic headache and had a headache in ER than that in patients with a posttraumatic headache but without a headache in ER (21.25 versus 19.1, P=0.004).

NSE Concentration

Table (4) shows the comparison of NSE concentration between patients complaining of a posttraumatic headache who had a headache in ER and patients also complaining from a posttraumatic headache but had no headache in ER. The mean of NSE

Table 1: Comparison in S-100 B concentration among participants in all study groups

Variable	Case Group (S-100 B)	Control Group (S-100 B)	P-Value
	Mean ± SD	Mean ± SD	
All Participants	20.26 ± 2.1	19.42 ± 1.38	0.019
Male	20.83 ± 1.98	19.3 ± 1.47	0.001
Female	19.05 ± 1.88	19.58 ± 1.25	0.309

Table 2: Comparison in S-100 B concentration among participants in all study groups

Variable	Case Group (NSE)	Control Group (NSE)	P-Value
	Mean ± SD	Mean ± SD	
All Participants	20.97 ± 1.99	18.93 ± 1.35	0.001
Male	21.32 ± 1.96	18.85 ± 1.14	0.001
Female	20.25 ± 1.94	19.04 ± 1.62	0.04

Table 3: Comparison of concentrations between patients complaining of a headache and patients without a headache in ER

Concentration	Patients with a Headache in ER (Mean ± SD)	Patients without a Headache in ER (Mean ± SD)	P-Value
S-100 B Concentration	22.07 ± 1.8	19.56 ± 2.65	0.001
NSE Concentration	21.4 ± 1.76	20.02 ± 1.62	0.005

Table 4: Comparison of concentration between patients complaining of a posttraumatic headache who had a headache in ER and patients also complaining from a posttraumatic headache but had no headache in ER

Concentration	Posttraumatic Headache		P-Value
	A headache in ER Mean ± SD	No Headache in ER Mean ± SD	
S-100 B Concentration	21.25 ± 1.6	19.1 ± 2.02	0.004
NSE Concentration	22.13 ± 1.99	19.84 ± 1.44	0.003

concentration was significantly higher among patients complaining of a posttraumatic headache and had a headache in ER than that in patients with a posttraumatic headache but without a headache in ER (22.13 versus 19.84, P=0.003).

DISCUSSION

Although few studies have shown that S100B concentrations are elevated after extracranial injuries without brain involvement (De Kruijk et al., 2002), many other studies have approved that S100B is highly specific and sensitive biochemical marker for injury of the brain (de Kruijk et al., 2001; Heidari et al., 2015). Results from previous studies concluded that there is a relationship between serum levels of NSE and MTBI outcome and prognosis (Yardan et al., 2011).

The current study showed that S-100 B and NSE are useful biochemical markers for brain injury in MTBI patients and seem to be associated with the presence of a headache in ER after trauma and these findings agree with previous studies which proved that: S100B and NSE were valuable factors for identification of the MTBI patients and they are prognostic parameters for many neurological disorders (Yardan et al., 2011).

CONCLUSION

S100B and NSE can be used as a predictive biomarker in the assessment and follow up of MTBI patients.

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