ORIGINAL REPORT

Pituitary Function Impairment after Moderate Traumatic Brain Injury

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Abstract- To determine the prevalence of pituitary hormone deficiencies after moderate traumatic brain injury (TBI). We conducted a prospective cohort and included 75 patients with moderate TBI with GCS between 9 and 13 who referred to emergency department of Shariati Hospital, Tehran/Iran, during 2004-2007. Pituitary hormones were assessed 3 and 6 months after injury. In 3rd month post-injury, 39 cases had not any pituitary dysfunction; however, deficiencies in one, two and three of the pituitary hormones were found in 26, 8 and 2 patients, respectively. Twenty one patients showed a deficiency in one of the pituitary hormones and only one case with deficiency of two after 6 months. The most prevalent changes occur in IGF-1 and LH/FSH after moderate TBI. However, the whole deficiencies decrease over the time.

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Introduction

Traumatic Brain Injury (TBI) is a worldwide health problem, a major cause of disability and death among young adults, and a cause of neuroendocrine dysfunction (1). TBI is a non-degenerative, non-congenital insult to the brain from an external mechanical force causing temporary or permanent neurological dysfunction, which may result in impairment of cognitive, physical and psychosocial functions.

The overall incidence of TBI in developed countries is about 200/100 000 population per year (2). Population-based studies show that the incidence of TBI is between 180 and 250/100 000 populations per year in the United States (2-5). Incidence is higher in Europe (ranging from 91/100 000 in Spain to 546/100 000 in Sweden) (6-10), in Southern Australia (322/100 000) (11) and in South Africa (316/100 000) (12), and lower in China (13). These numbers probably underestimate the true incidence of TBI, because they typically refer to the TBI patients admitted to hospital. Many patients with mild TBI (not presenting to the hospital) or with severe TBI (associated with death at the scene of the accident or during transport to a hospital) may not, in fact, be accounted for in the epidemiological reports (2). The highest incidence of TBI is among subjects aged 15–24 years or 75 years and older, with an additional incidence peak in children aged 5 years and younger (2, 14).

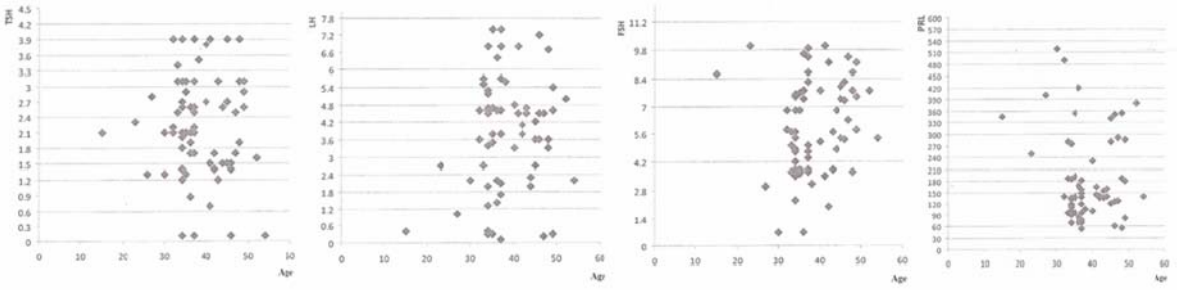

Figure 1. Scatter plot of pituitary hormones level among patients with TBI with respect to age. From left to right, TSH, LH, FSH, and Prolactin level.

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Incidence rate for males is almost twice that for females, with the highest male:female (M:F) ratio occurring in adolescence and young adulthood, and ranging from 1.2:1 to 4.4:1 in different populations (4–6, 9–12). M:F ratio approaches parity with ageing owing to the increased likelihood of TBI caused by falls, for which members of both sexes have similar risks in later life. TBI may impair cognition (concentration, memory, judgment and mood), movement abilities (strength, coordination and balance), sensation (tactile sensation and special senses, such as vision) and sexual function, leading to important behavioral changes and consequences on daily living activities. Pituitary dysfunction following traumatic events can be divided into: (a) functional alterations during the acute phase post-TBI, which result in a temporary increase or decrease in blood pituitary hormone concentrations; (b) alterations in pituitary hormone secretion that may occur at any time after TBI, resulting in permanent hypopituitarism caused by damage at pituitary and/or hypothalamic level. Despite the plenty of data in the literature, we face the lack of native survey; thus, we decided to perform a prospective study to prepare basic data which may be useful for healthcare providers in the cases of moderate head trauma.

Patients and Methods

We conducted a prospective cohort and included 75 patients with moderate TBI with GCS between 9 and 13 who referred to emergency department of Shariati Hospital, Tehran/Iran, during 2004-2007. Patients with the history of alcohol abuse, one or more pituitary insufficiency, recent corticosteroids application and pregnant were excluded. All of the patients gave informed consent. Pituitary hormones were assessed 3 and 6 months after injury. Data analysis performed using SPSS 13.

Results

The patients' mean age was 38.14 (ranged 15-54). In 3rd month post-injury, pituitary insufficiency was detected in 36 patients (48%). Isolated hormone deficiency in 26 patients was as follows: LH insufficiency in 7 cases, IGF-1 insufficiency in 13 cases, cortisol insufficiency in 4 cases, and TSH insufficiency in 2 cases. Combined hormone deficiency was abstracted in table 1.

IGF-1 insufficiency

There were 18 patients (24%) consisted of 15 males and 3 females who showed IGF-1 insufficiency 3 months after injury; Two cases out of 18 (11%) combined with FSH/LH deficiency, another two with cortisol and other two with hyperprolactinemia. There was no association of IGF-1 and TSH deficiencies. After 6 month of injury, only 7 cases of IGF-1 insufficiency remained including 5 males and 2 females.

LH/FSH insufficiency

In the third months post-injury, 3 patients (2 males and one female) and 9 patients (7 males and 2 females) indicated deficiencies in FSH and LH, respectively. Other pituitary hormone deficiencies associated with LH/FSH insufficiency were: IGF-1 in 2 cases, cortisol in one, and hyperprolactinemia in 2 patients. After another 3 months, there were 6 patients remained with LH and 2 with FSH insufficiency; the former consisted of a pair of 3 males and females and the latter was detected in two men.

Cortisol insufficiency

Ten patients, 9 males and one female, indicated cortisol insufficiency after 3 months of injury. Associated deficiency in LH/FSH, IGF-1, TSH, and hyperprolactinemia was seen in 1, 2, 1, and another one patients, respectively. The rate of cortisol insufficiency was decreased to 3 patients (2 men and one woman) after 6 months post-injury.

TSH insufficiency

TSH, T4 and T3 were evaluated. There were 2 males with isolated TSH insufficiency and another 2 with TSH insufficiency in association with cortisol deficiency after 3 months, decreased to 2 cases after 6 months.

Hyperprolactinemia

Hyperprolactinemia was detected in 4 patients consisted of 3 men and one woman, three months after injury.

Table 1. Varying degrees of hypopituitarism in patients 3 months after TBI.

Combined Pituitary Hormones Insufficiencies 3 months after TBI	No. of Patients
TSH + Cortisol	2
IGF-1 + Cortisol	2
LH + Cortisol	1
FSH + IGF-1	1
Cortisol + Hyperprolactinemia	1
FSH+ Hyperprolactinemia	1
LH + IGF-1+ Hyperprolactinemia	1
FSH + IGF-1+ Hyperprolactinemia	1

Association with LH/FSH insufficiency was seen in 2 cases whereas another 2 patients showed a combination with IGF-1 deficiency. There was only one patient with associated cortisol deficiency. After 6 months, three men remained with hyperprolactinemia.

Discussion

Injuries from trauma to hypothalamus, anterior pituitary stem, neurohypophysis and hypothalamus-pituitary portal system lead to pituitary hormones disorders. These injuries may be caused by different types of trauma to the head such as falling from the height, vehicle accident or blunt trauma associated with skull fracture.

We studied the function of pituitary gland in 75 patients with moderate traumatic brain injury (GCS 9-13), three and six months after injury.

Pituitary hormone deficiencies were detected in 38 patients out of 75 with the most common deficiencies in IGF-1 and sex hormones. We used IGF-1as an indicator of growth hormone axis with respect to the IGF-1 deficiency among the majority of patients with growth hormone (GH) defect; however, the most accurate evaluation of the axis needs to be performed by interventional tests including arginine in addition to GHRH, ITT and glucagon test.

IGF-1 deficiency found in 18 patients three months after injury decreased to 7 in the 6th month. This was the most common pituitary hormone insufficiency. Similarly, Kelly *et al.* in 2000 found 18% GH defect among patients with TBI, Liebermann *et al.* in 2001 reported 15%, whereas Agha *et al.* and Aimaretti *et al.* in 2004 indicated 18% and 37%, respectively (1-5).

Deficiencies in pituitary sex hormones were detected in 12 and 8 patients, three and six months after injury equal to 16% and 10.6%, respectively. Kelly *et al.* reported 22%, three months after injury whereas Libermann found only 2% after 13 months (2).

Hyperprolactinemia occurred in 4 patients after 3 months of injury decreased to 3 cases after 6 months, may be due to psychological stress, traumatic effects on hypophysis stem or application of some drugs with Dopamine antagonistic efficacy. Several authors reported different rate of hyperprolactinemia among patients with TBI including 3% by Benvenga *et al.* in 2000, 10% by Aimaretti *et al.* in 2005, 11.8% by Agha *et al.* in 2004, and 3% by Herrmann *et al.* in 2006 (1-5).

Due to the partial adrenal insufficiency and probable corticosteroids use in patients with brain edema, diagnosis of glucocorticoids deficiency is problematic in the acute phase of TBI. Although, we found 10 patients with cortisol deficiency 3 months after injury diminished to 3 patients after 6 months. Other authors reported a wide range of deficiency from 4.5% to 45.7% (1-5).

Central hyperthyroidism was detected in 4 patients after 3 months and limited to only 2 cases after 6 months. TSH deficiency may be due to the increase in Somatostatin level which leads to decrease in TRH. The rate of TSH deficiency ranged from 5% to 21.7% in the litratures (1-5).

With respect to the known effects of pituitary hormones on the functions of different body organs, it is clear that the screening, treatment and control of their deficiencies have a prominent significance among patients with TBI. It seems that GH and LH/FSH are the most sensitive to traumatic injury; however, a high percentage of pituitary hormones deficiencies are expected to resolve spontaneously over the time.

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