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Original Article

Traumatic Brain Injury and Metabolic Dysfunction Among Head Injured Patients in a Tertiary Hospital in North-Central Nigeria

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Abstract

Traumatic Brain Injury (TBI) is a common health problem which is one of the main causes of chronic disability and it is associated with hormonal and metabolic disorders. This work was carried out to investigate the relationship between some stress hormones (i.e. prolactin and cortisol) and plasma glucose level in TBI patients. Twenty-five TBI patients were included in the study consecutively. All patients underwent basal hormonal and plasma glucose evaluation within 24 hours of admission. One of the patients died during the acute phase. The results of the study show that prolactin and glucose levels were positively correlated with the Glasgow Coma Scale (GSC). Cortisol levels were observed to be highest in the moderate TBI group with GSC score of 9-13. The results also showed that 80% (20 patients) of the patients were age 40 years and below and 84% (21 patients) were males. In conclusion, present data show that prolactin, cortisol and plasma glucose are disturbed in TBI. The disturbances in the levels of prolactin and glucose are related to the severity of TBI. However, there is no direct relationship between cortisol and severity of TBI. Our results also show that TBI is more common in males and young people.

Keywords: Traumatic Brain Injury, Plasma Glucose, Cortisol, Prolactin

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Introduction

Traumatic Brain Injury (TBI) is a common health problem and is one of the main causes of chronic disability and death among young adults through a variety of mechanisms, and is now recognised as a cause of neuroendocrine dysfunction (Mazaux and Richer, 1998). TBI-induced neuroendocrine dysfunction was previously thought to be a rare occurrence; however, it is now being increasingly diagnosed (Ghigo *et al*., 2005). Recent studies of traumatic head injury patients in the chronic recovery phase from their injuries have indicated specific deficits in their general health, vitality, and mental health with depression and anxiety being particularly common (Colantonio *et al*., 1998; Morton and Wehman, 1995). These psychosocial consequences often become the major impediment to successful rehabilitation (Morton and Wehman, 1995).

However, assessment of pituitary functions in patients with TBI is not a routine procedure in endocrine practice. Hypopituitarism due to TBI may be partial or complete, and 20-50% of patients who were tested several months and years after head trauma have been demonstrated to have some degrees of pituitary dysfunction (Leal-Cerro *et al*., 2005; Tanriverdi *et al*., 2006).

Mortality and morbidity rates are significantly lower in patients treated in a postoperative surgical intensive care unit (ICU) with intensive insulin therapy, titrated to maintain strict blood glucose control (blood glucose levels at 80–110 mg/dl or 4.44–6.11 mmol/l), than in patients receiving conventional therapy (Van den Berghe *et al*., 2005). Strict glycaemic control with low target ranges invariably carries a risk of inadvertent hypoglycemic episodes. One study has documented an association between incidental hypoglycemia and an increase in short-term complications or mortality (Krinsley and Grover, 2007). Several studies have nevertheless reported a potentially higher incidence of hypoglycemia in patients under strict glycaemic control (Thomas *et al*., 2007).

There has not been any study to the best of our knowledge conducted in the North-Central Region of Nigeria to investigate the relationship between stress hormones and plasma glucose in the early phase of TBI. Therefore, we set out to study the stress hormones (cortisol and prolactin) and plasma glucose in the early phase (within 24 hours of trauma) in 25 patients with TBI. Additionally, the relationships between the serum level of the stress hormones and plasma glucose, and severity of the TBI were investigated.

Patients and Method

Patients

Twenty-five patients with TBI (16 men, 9 women; age 42±13.4, range 17-84 years) who were admitted via Accident and Emergency (A&E) Unit and managed by the Neurosurgery Unit of the University of Ilorin Teaching Hospital were included in the study consecutively between January and April, 2013. The study was approved by the Ethical Review Committee of the University of Ilorin Teaching Hospital. The instrument used included semi-structured questionnaire for the clinical details and the laboratory assessments.

The demographic details and time of presentations were noted in the information retrieved. The level of consciousness of the patients was assessed by the same investigators according to Glasgow Coma Scale (GCS) as soon as the patients were admitted to A&E Unit. The post resuscitation GCS score was used to classify TBI into; mild (GCS 14-15), moderate (GCS 9-13) and severe (GCS ≤ 8) (Mena *et al*., 2011). None of the patients had a history of any known pituitary disorder and all the patients were off any drug affecting hypothalamo-pituitary function.

The cause of TBI was road traffic accidents in all the patients: 9 (36%) was due to motorcycle accident and 16 (64%) was due to motor vehicular accident

Basal Hormonal Assay in the Acute Phase

All patients underwent basal hormonal evaluation within the first 24 hours of admission to the A&E. blood samples were taken between 8.00-9.00hr. No patient received glucocorticoids, dopamine, ketoconazole or calcium channel blockers before blood specimen collection. Basal hormonal levels of prolactin and cortisol, and random blood glucose were measured. Menstrual history was obtained from women or their relatives.

Hyperprolactinaemia was defined when basal level is higher than the upper normal level of the reference limit (male: 18ng/ml, premenopausal women: 29ng/ml, postmenopausal women: 20ng/ml). Normal range of cortisol is (Adults: Morning: 5-23µg/dl, Afternoon: 3-13 µg/dl; Children: Morning: 3-21µg/dl, Afternoon: 3-10 µg/dl). Ref limits for glucose: Postprandial of up to 10.0mmol/l.

Analytical Method

All serum hormones were measured by using ELISA

method following the instructions on the commercial kits. Cortisol and prolactin were measured by using AccuBind ELISA kit, (Monobind Incorporated, Lake Forest, CA USA). Glucose was estimated using Accucheck (Rhode Diagnostics, Indianapolis, IN, USA).

Age Range (years)	Number of Patients
10-25	13
26-40	7
41 and above	5

Statistical Analysis

Statistical analysis was performed using the Statistical Package for the Social Sciences (SPSS) version 20.0 for windows. All information retrieved was entered into SPSS version 20.0 and manual corrections for errors were done and data were subjected to Duncan post-hoc test. Data were presented as mean±SD, normally distributed values between two variables were compared by unpaired t-test. More than two variables were compared by using one-way ANOVA test and Duncan's test was performed for post-hoc analysis.

Results

Twelve (48%) patients had mild (mean GCS: 14.4±0.8), 8 (32%) had moderate (mean GCS: 11.1±1.4) and 5 (20%) had severe (mean GCS: 6.1±1.1) TBI. One of the patients, a male, who had severe TBI died within 72 hours of admission. Our results showed that 21 of the patients representing 84% were males and only 4 were females representing 16% of the patients. The age range of the patients in Table 1 shows that 13 (52%) were within the age range of 13-25 years, while 7 (28%) of the patients were within the range of 26-40 years and 5 (20%) were older than 41 years.

Table 1. The age range of the patients

The results of the serum hormones and glucose in Fig. 1, showed that serum prolactin and glucose were significantly ($p<0.05$) higher in the TBI groups compared to the control group. However, serum cortisol was only significantly ($p<0.05$) higher in the moderate TBI group than the control.

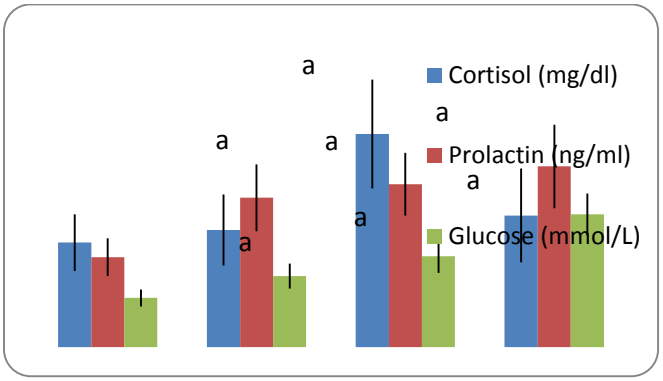

Fig. 1. Changes in Plasma cortisol, prolactin and glucose in the early acute phase of TBI. Data are presented as mean±SD, a indicates $p<0.05$ vs control for the parameters.

Discussion

The results of this study showed that TBI is overwhelmingly a male gender problem with about ratio 5 to 1. This is consistent with earlier reports which demonstrated a ratio of 3:1 (Greenwal *et al.*, 2003). However, our ratio of 5:1, may not be unconnected with the fact that, in our environment, motor cycle is used as a form of public transport and it is an exclusively a male business. The results also demonstrated that more than half of the patients with TBI were in the age range of 10-25 years. It has been reported previously that the highest injury occurs in young men between that age of 15 and 24 years (Murdoch and Theodoros, 2001). Some of the reasons adduced for the preponderance of TBI in young adult is because overall, motor vehicle or related transportation accidents and falls comprise the most common cause of TBI. Transportation accidents, particularly for young males (15 to 24 years), by some estimates account for more than 50% of all head injuries (Murdoch and Theodoros, 2001).

We demonstrated that there were changes in basal stress hormone levels and plasma glucose following traumatic brain injury (TBI). Our research also showed that plasma glucose and stress hormones changes in TBI are related to the severity of the TBI.

The pituitary gland responds to acute traumatic events and several changes in the circulating hormone levels become apparent during the first hours or days after injury, and may continue for the period of acute critical illness (Woolf, 1992). Elevated serum cortisol level during the initial phase of trauma has been previously reported in patients with mild and moderate TBI (Barton *et al.*, 1987). Additionally, a positive correlation between the severity of the injury and cortisol

concentration has been shown in patients with mild or moderate TBI, but not in those with severe injury (Feibel *et al*., 1983). In contrast, primary or secondary adrenal failure has been shown in 15% of patients with moderate to severe injury, 7-60 days after TBI (Dimipoulou *et al*., 2004). In the present study, cortisol levels were positively correlated with mild and moderate injury, whereas cortisol level was negatively correlated with severe TBI. The result of our study is different from that of Tanriverdi *et al*., 2007, which showed negative correlation between cortisol levels and severity of TBI.

Severe injury may give rise to more hypothalamic or pituitary damage, and results in blunted hypothalamic-pituitary axis response to stress (Tanriverdi *et al*., 2007). Also, other factors involve in the control of cortisol secretion may come into play during severe TBI.

In acute phase of TBI hyperprolactinaemia has been reported in more than 50% of the patients who had moderate or severe injury (Bondanelli *et al*., 2005). A positive correlation between severity of trauma and the prolactin levels has been demonstrated in previous studies (Agha *et al*., 2004; Bondanelli *et al*., 2005). In this study prolactin is higher in all the TBI groups than in the control group and this is related to the severity of the injury. Stalk lesions or hypothalamic lesions are generally related to hyperprolactinaemia. Thus the normal prolactin in all our patients was suggestive of pituitary lesion. Therefore, it is tempting to speculate that mild injuries may generally affect pituitary but severe injuries may affect the stalk and hypothalamus. Our result is similar to the findings of Tanriverdi *et al*., 2007, which showed positive correlation between serum prolactin and severe TBI.

Hyperglycaemia is frequent during acute brain injury such as ischaemic stroke, intracranial haemorrhage or traumatic brain injury and is associated with increased morbidity and mortality (Bhalla *et al*., 2003; Bilotta *et al*., 2007). TBI also leads to a profound increase in glucose utilization (hyperglycolysis) that can persist for up to one week and alter the ability to use ketone bodies as energetic substrates (Robertson *et al*., 1991). Our study shows a positive correlation between plasma glucose and severity of TBI. Hyperglycaemia in the trauma patients, as in other critically ill patients, is caused by a hypermetabolic response to stress (Eakins, 2009). Even though cortisol is one of the major stress hormones, our study does not show direct relationship between plasma glucose and cortisol. This may be due to the disruption of hypothalamic-pituitary axis leading to reduced production of corticotrophin-releasing hormone (CRH) and adrenocorticotropic hormone (ACTH) which is essential for the production of cortisol. Severe trauma may give rise to more hypothalamic or pituitary damage, and results in blunted HPA-axis response to stress[27]. In the severe TBI group, our study shows reduced cortisol concentration. The high blood glucose in the severe TBI group could therefore be due to other stress hormones, such as prolactin which shows direct relationship between the severity of TBI and plasma glucose. Holbein and colleagues pointed out in their study that hyperglycaemia following severe TBI down regulates GLUT 1 transporter in the blood-brain barrier thereby decreasing endothelial flux of glucose even at high arterial blood glucose levels, thereby leading to reduced cerebral glucose availability despite an adequate arterial supply (Holbein et al., 2009). This would increase lactate production, decrease intracellular pH and cause cellular distress, which results in impaired metabolic activity and possibly adverse outcome (Vespa et al., 2006; Holbein et al., 2009).

In conclusion, our data clearly demonstrate that TBI is associated with hyperglycaemia and disturbed stress hormones such as prolactin and cortisol. The study also shows the need to institute intensive management of plasma glucose following TBI so as to improve outcome.

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