Functional Disorders of the Hypothalamic-Pituitary-Adrenal Axis in Patients with Severe Head-Brain-Injury: A Retrospective Study and Review of the Literature

1Munthir Al-Zabin, 2Thomas Kemmer

1Correspondence Author, MD, PhD, Senior Specialist Neurosurgery, Department of Neurosurgery, Khoula Hospital, Sultanate of Oman
2 MD, PhD, Fachkrankenhaus Neresheim gGmbH, HOD of the Department of Internal Medicine and Endocrinology, Hospital for Brain and Head Injuries, (Neresheim), Germany

Abstract: Adrenal insufficiency is common but underdiagnosed. It develops in critically ill patients. Hypotension is a frequent observation caused by adrenal insufficiency in severely cerebro-cranial traumatic and brain-injured patients. This type of hypotension is refractory to fluid substitution, and the application of vasopressors is often required. The investigation of adrenal insufficiency seems to be essential, whereas current data suggest that treatment with glucocorticoids are necessary to improve clinical outcome.

Objectives: Determination of the role of the hypothalamic-pituitary-adrenocortical system (HPAS) after brain injury. Investigation of the relationships between adrenocorticotropic hormone (ACTH), cortisol levels, and clinical condition of the patients.

Materials and Methods: Patients with traumatic brain injury (TBI, n=19), subarachnoid haemorrhage (SAH, n=8), intracerebral haemorrhage (ICH, n=5), cerebral hypoxia (Hypoxia, n=5), other neurological diseases (Others, n=5). Measurement of ACTH and Cortisol values basal and after stimulation with CRH (100 µg i.v.): -15, 0, 15, 30, 45, 60, 90, 120 min. Areas under the curve (AUC) were calculated and ANOVA test was performed for statistical evaluations. P values less than 0.05 were considered as significant.

Results: The evaluation of the measurements of ACTH and Cortisol values basal and after stimulation with CRH has mainly depended on the clinical conditions of the patients. The calculations of the statistical results have been considered, whereas it was ensured, that the patients have passed the eventually complication of brain oedema. Conclusions: Brain injuries mainly exercise influence over the above-mentioned hypothalamic-pituitary-adrenocortical system (HPAS) depending on the severity of the trauma. The results of this study indicate that investigation of HPAS hormones might be useful as an additional method in the common complex of ordinary examinations in establishing an early prognosis and improving the treatment of patients with brain injury.

Keywords: Head-brain-injury, hypopituitarism, HPAS, pituitary gland.

1. INTRODUCTION

After many decades of being considered simply a clinical endocrinology “curiosity”, the long-term endocrine consequences of traumatic brain injury (TBI) have in the past few years been the subject of resurgent interest. First reported almost 100 years ago, chronic pituitary dysfunction following a head injury was originally thought to be a rare occurrence. This viewpoint has been challenged by recent researches on adult survivors of severe brain injury, which
variously report the prevalence of pituitary hormone deficiencies to be between 23% and 69%. Clear from these studies is that one or any number of hypothalamic–pituitary hormone axes may be impaired in the chronic phase following head injury, with the growth hormone (GH; 10–33%), adrenal (5–23%) and gonadal axes (8–30%) apparently the most vulnerable to problems. Further clinical complexity is also evident from prospective, longitudinal observations, which suggest that for many head-injury survivors pituitary hormone dysfunction may not develop until at least 6 to 12 months after TBI, whereas, in others deficiencies can be transient and resolve spontaneously during the year after the trauma. Morbidity following moderate-to-severe head injury is high, and many of the chronic problems and symptoms reported in this group of patients (e.g., fatigue, poor concentration and depression) are common to the clinical phenotype associated with hypopituitarism (1-6).

A third of prospectively studied patients and 45% of a retrospectively identified group had endocrine abnormalities consistent with pituitary dysfunction, Gerard Raverot, MD, of Hospices Civils de Lyon in France, reported at the Endocrine Society meeting (1).

While growth hormone deficiency accounted for the largest proportion of cases, 10% to 20% of patients had evidence of multiple hormonal disorders. (3, 6, 8-10, 12-13)

These results were preliminary, but they confirm the high risk for pituitary disorders after moderate to severe neurologic events, including traumatic brain injury and subarachnoid hemorrhage. (2-5, 11-12, 19, 22). The results supported a recommendation for evaluation of pituitary function in patients with subarachnoid hemorrhage or moderate to severe traumatic brain injury. (1-6, 15-19)

Ischemic strokes probably disturb pituitary function, he added, but the ability to study any associations is complicated by an older patient population that might already be predisposed to endocrine disorders (5, 7, 20-, 21, 27).

In the present study the functional disorders of the hypothalamic-pituitary-adrenal axis in patients with severe brain injury could be demonstrated.

Moderate to severe brain trauma increases the risk of pituitary functional abnormalities and / or disorders, that warrant investigation before the patients become symptomatic (1-6, 11-12, 14, 19, 23).

Objective:

Adrenal insufficiency is a common and underdiagnosed disorder, that develops in critically ill patients. A deficiency of one or more of the hormones regulated by the pituitary gland may have physical and/or psychological effects such as reduced muscle mass, weakness, decreased exercise capacity, fatigue, irritability, depression, impaired memory, reduced sex drive. Hypotension that is refractory to fluids and requires vasopressors is the most common presentation of adrenal insufficiency in severely cerebro-cranial traumatic and brain-injured patients.

The investigation of adrenal insufficiency seems to be necessary, whereas current data suggest that treatment with glucocorticoids improves outcome.

2. METHODS

To determine the role of the hypothalamic-pituitary-adrenocortical system (HPAS) after brain injuries, the relationship between adrenocorticotropic hormone (ACTH), cortisol levels, and clinical condition was examined in 42 patients, who were treated and followed up after severe head – brain – injuries in Hospital for Brain and Head Injuries, Neresheim, Germany in the period of time 1999 and 2011. Age was between 16 and 72 years, Mean was 49 years, 31 male and 11 female. In severely brain-injured patients with cerebro-cranial traumatic brain injury (TBI, n=19), subarachnoid hemorrhage (SAH, n=8), intracerebral hemorrhage (ICH, n=5), cerebral hypoxia (HYP, n=5), and other neurological diseases (OTH, n=5) basal and CRH (100 μg i.v.)-stimulated ACTH and cortisol values were measured at -15, 0, 15, 30, 45, 60, 90 and 120 min, respectively.

Areas under the curve (AUC) were calculated and Anova test was performed, p<0.05 has been considered as significant. The calculations of the statistical results have been considered, whereas it was ensured, that the patients have passed the eventually complication of brain edema.
3. RESULTS

Following measurements of ACTH were obtained (mean+SEM): TBI 5567±557, SAH 4071±564, ICH 6009±1353, HYP 4551±786, OTH 3878±1290 pg/ml x min (not significant, n.s.). The cortisol measurements (mean+SEM) have been: TBI 2046±182, SAH 1975±152, ICH 2704±320, HYP 2439±228, OTH 2305±588 µg/dl x min (n.s.). (Diagrams 1 to 10).
Calculations of ACTH and CORTISOL levels were done for all investigated groups with calculations of Area under the curve (AUC) and ANOVA Test was performed. P was < 0.05 (was considered as significant). See Diagrams 11 and 12.

Patients with hypocortisolism and ACTH dysfunction have been substituted, whereas there clinical outcome could be improved throughout the subacute period.

4. DISCUSSION

Pituitary dysfunction has a recognized association with traumatic brain injury, including subarachnoid hemorrhage. However, the magnitude and nature of the association had not been thoroughly examined. (2-4, 6, 12-15, 19-23)

Seeking a better understanding of brain trauma's impact on pituitary function, investigators in a multicenter French study prospectively evaluated 64 patients with moderate to severe traumatic brain injuries or subarachnoid hemorrhage. They also reviewed records of another 64 patients with a history of brain trauma (7-11, 17-21).

In addition to neurologic and general medical examination, the prospectively studied patients had an extensive endocrinologic workup that included determination of free thyrotropin, prolactin, thyrotropin-stimulating hormone, insulin-like growth factor, testosterone, follicle-stimulating hormone, luteinizing hormone, and evaluation for cortisol and growth hormone deficiencies. (24-27).

In many studies after traumatic brain injuries (1-6, 24-25), it was reported that 36% of prospectively studied patients (23 of 64) had endocrine abnormalities, including growth hormone deficiency in 14 (21%), gonadotrope deficiency in eight (12.5%), and corticotrope deficiency in five (3.1%). Six patients (9.3%) had combined deficiencies. The retrospectively identified patients had a 45.3% prevalence of endocrine disorders (29 of 64), including growth hormone deficiency in 21 (32.8%), gonadotrope deficiency in 11 (17.1%), cortisol deficiency in 6 (9.3%) and combined deficiencies in 11 (17.1%).
5. CONCLUSION

Brain injuries mainly exercise influence over the above-mentioned hypothalamic-pituitary-adrenocortical system (HPAS) depending on the severity of the trauma. The results of this study indicate that investigation of HPAS hormones might be useful as an additional method in the common complex of ordinary examinations in establishing an early prognosis and improving the treatment of patients with brain injury.

REFERENCES


