Original Research Paper

Volume -10 | Issue - 5 | May - 2020 | PRINT ISSN No. 2249 - 555X | DOI : 10.36106/ijar

Endocrinology

A STUDY OF CLINICAL AND HORMONAL EVALUATION OF HYPOTHALAMO PITUITARY DYSFUNCTION AFTER TRAUMATIC BRAIN INJURY AND SUBARACHNOID HEMORRHAGE

Mounika Guntaka	Associate Proffessor Biochemistry, biochemistry, Maheshwara Medical College, Chitkul (V), Near Isnapur X Roads, Patancheru, Telangana 502307
Babulreddy Hanmayyagari*	Assistant Professor, Department of Endocrinology, Sapthagiri Institute of Medical Sciences & Research Centre. 15, Hesarghatta Main Rd, Navy Layout, Chikkasandra, Chikkabanavara, Bengaluru, Karnataka 560090 *Corresponding Author
Manoj Gopinath Mengade	Senior Resident, Department of Endocrinology, KIMS Hospital, Secunderabad, India.
Arun Mukka	Consultant Endocrinologist, Yashoda Hospital, Somajiguda, Hyderabad, India.

ABSTRACT Hypopituitarism is one of the common complication following traumatic brain injury or aneurysmal subarachnoid hemorrhage and potentially can contribute to morbidity and poor recovery after brain injury.

Materials and methods: Our study included 15 patients following TBI or SAH in whom hormonal evaluation was performed at baseline, 3 months, 6 months following the injury. Study also attempted correlation of hormonal values with that of clinical scoring (GCS), and with radiological findings (CT/MRI). At baseline, 7 out of 15 patients had evidence of hormonal derangement.

Results: Pituitary dysfunction persisted in 4 patients at the end of 6 months from baseline. Hypocortisolism was the most common disorder at the baseline where as GHD was the most common at 6 months.

Conclusion: Evaluation of intactness of hypothalamo-pituitary axis is of paramount clinical importance in subjects following TBI & SAH at baseline and in the followup, as hormonal derangements are common and correcting the same can improve the clinical outcomes.

KEYWORDS : Hypopitutarism, Hypocortisolism, Growth hormone deficiency (GHD), Traumatic brain injury (TBI), Sub arachnoid hemorrhage (SAH).

INTRODUCTION:

Traumatic brain injury (TBI) is a significant public health problem either in the form of morbidity and mortality or due to its chronic sequelae. Traumatic brain injury (TBI) is a non-degenerative, non-congenital insult to the brain from an external mechanical force, possibly leading to permanent or temporary impairment of cognitive, physical, and psychosocial functions with an associated diminished or altered state of consciousness. The major causes of SAH are ruptured aneurysm (85%) and Perimesencephalic hemorrhage (10%). Hypopituitarism is a common complication of both traumatic brain injury and aneurismal subarachnoid hemorrhage and potentially contribute to morbidity and poor recovery after brain injury[1,2,3]. The signs and symptoms of Hypopituitarism are subtle and overlap with the neurological and psychiatric sequelae of TBI and SAH. Hence the diagnosis of Hypopituitarism is often missed or delayed in the affected individuals[4].

Hypopituitarism caused by TBI was first reported in 1918[5], only 4 years after the initial clinical description of Hypopituitarism. Aneurismal SAH has been considered a rare cause of Hypopituitarism with almost no published data until recent times[6]. The prevalence of reported Hypopituitarism following TBI varies widely among published studies ranging from 15-90%[7,8,9].

We hereby undertook the study to understand the association of hypopitutatrism following TBI & SAH and to assess the pituitary reserve in these patients. Objectives of this study were 1) To perform hormonal evaluation at baseline, 3 months, 6 months following TBI 2) To correlate hormone values with recovery and 3) To assess the incidence of hypothalamo pituitary hormonal dysfunction after TBI and to correlate the CT/MRI findings with increased risk of hormonal dysfunction in TBI.

MATERIALS AND METHODS:

This Prospective study was done on 15 patients, at a single tertiary care centre from December 2014 to December 2016 at Krishna institute of medical Sciences (KIMS), Secunderabad. All patients with moderate to severe traumatic brain injury or subarachnoid hemorrhage (GCS<12) who are admitted in neurosurgical ICU were included in the study. Patients were classified in to mild, moderate and severe injury categories based on clinical (Glasgow Coma Scale) and radiological (Marshall CT classification and Rotterdam CT classification) findings. Only patients with moderate to severe traumatic brain injury were included in the study.

Routine clinical examination and hormonal evaluation was performed at Baseline, 30th and 180th day following traumatic brain injury and/or subarachnoid hemorrhage. Baseline evaluation was done between within 10 days of sustaining the head injury. Baseline hormonal values were compared with the values after 6 months. Findings of CT/MRI were correlated with the hormonal outcomes of the patients.

Endocrine axis	Baseline Tests
Pituitary- Adrenal axis	Morning Cortisol (8 a.m.)
Pituitary- Thyroid axis	Free T4
Pituitary- Gonadal axis	FSH, LH and Testosterone(men), Estradiol (women)
Growth Hormone Assessment	GH, IGF-1

Hypocortisolism defined as basal (8.00 am) cortisol value less than 7 mcg/dl and GHD if IGF-1 levels are less than laboratory reference value. secondary hypothyroidism diagnosed when free T4 levels are lower than normal and secondary hypogonadism when testosterone or oestrogen are lower than the normal in the presence of low or normal FSH, LH.

The exclusion criteria were patients with any known pituitary dysfunction prior to traumatic brain injury or subarachnoid hemorrhage. Also excluded were the patients with severe structural deformity and/ or vegetative state, patients not compatible for long term follow up and those who were on any form of hormonal therapy prior to TBI, which are likely to interfere with the interpretation.

RESULTS:

A total of 15 patients (10 males, 5 females) aged (mean 40.7 ± 6.5 years, range 20–60 years) were identified as eligible for the study. At baseline, a total of 7 out of 15 patients had evidence of hormonal dysfunction. Most common hormonal derrangement observed was hypocortisolism which was seen in 5 patients followed by secondary hypothyroidism in 2 patients. Secondary hypothyroidism and hypogonadism was noticed in one patient which was associated with hypocortisolism. In the acute phase Growth hormone deficiency

(GHD) was not seen as IGF-1levels take longer time to get diminished. At 3 months, 4 patients had persistent hormonal deficiencies with GHD seen in 2 patients, hypocortisolism in 1 patient, combined GHD and hypocortisolism seen in 1 patient and combined hypogonadism and hypothyroidism in 1 patient. Hypocortisolism which was the most common hormonal deficiency in the acute state was resolved in the follow up. All these hormonal deficiencies persisted of 6 months following TBI. The severity of GCS score correlated with the persistence of hormonal deficiencies, where as CT severity did not correlate with hypopitutarism.

DISCUSSION:

The pathphysiology of hypopituitarism following TBI is not fully understood, and several factors were proposed for its development. Some investigators proposed vascular damage with subsequent ischemia or infarction is the mechanism for hypopitutarism[10] yet few others proposed autoimmunity for the development of hypopituitarism[11]. The occurrence of pituitary hormone deficits after TBI also varied among studies. Though any of the pituitary hormonal axis has a potential to get affected, most commonly reported one is growth hormone deficiency (GHD)[8,12], but some reported central hypogonadism as the most frequent pituitary deficiency after TBI[9,13]. This is because difference between assays used diagnostic criteria & time interval between TBI and hormonal assessment. The presence of pituitary dysfunction in the early acute phase (first 24 hr) or acute phase (up to 2-3 wks) following TBI was not related to hypopituitarism after 12 months[9], as the pituitary function was recovered in many patients. Early posttraumatic pituitary dysfunction can be transient in many cases and conversely, hypopituitarism can evolve over several weeks or months after injury[9,14]. This is also evident in our study, hence periodic assessment of pituitary hormones is necessary in the first 12 months of TBI.

The assessment of the growth hormone and adrenocorticotropic hormone axis require dynamic stimulation test like the insulin tolerance test to distinctly separate normal from deficient responses. However, it cannot be performed in patients with severe cardiovascular disease and uncontrolled epileptic seizures, limiting its use in patients with TBI and SAH. Hence some others used alternative tests to assess these hormonal reserves[9,15,16]. The diagnosis of adrenal insufficiency should not be missed as it can be life threatening one[17]. Cortisol is generally increased in the acute phase after TBI, low or low normal baseline free cortisol could still be proposed as potential early marker for the development of chronic ACTH deficiency in TBI. Acute phase morning cortisol level of less than 7.2 µg/dL (200 nmol/L) may be suggestive of adrenal insufficiency in acutely ill patients with TBI or SAH, and glucocorticoid replacement should be instituted accordingly[18]. However, values between 7.2and 18 µg/dL (200-500 nmol/L) in the presence of features suggestive of adrenal insufficiency such as hyponatremia, hypoglycemia, hypotension, or unexpected slow recovery may still be inappropriately low and a trial of glucocorticoid therapy should be considered. For the thyroid, gonadal and prolactin axes basal levels are enough for establishing diagnosis[9,14]. Low levels of fT4 with normal or low TSH diagnosed as central hypothyroidism and low levels of testosterone or oestrogen with normal or low LH/FSH are diagnostic of central hypogonadism[8,19]. Abnormal prolactin is also diagnosed when basal prolactin levels are not within normal range[8,19]. In most patients prolactin levels were mildly elevated and it doesn't have clinical significance. So we have not measured prolactin in our study.

Limitations of the study include lack of performing dynamic studies like Insulin tolerance test or synacthen stimulation test in our patients partly because of financial constraints and in accordance to institutional ethics committee protocols.

CONCLUSIONS:

The derangement of hypothalamo pituitary axis in the setting of TBI and SAH is common & it is associated with poor clinical outcomes. Though recovery happens in some patients in the follow up, the evaluation and treatment of the hypopitutarism is necessary to improve outcomes of these patients.

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