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Original Research Article

A PROSPECTIVE STUDY: ASSESSMENT OF ENDOCRINE ABNORMALITIES IN SEVERE TRAUMATIC BRAIN INJURY

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Abstract

Background: The prevalence and pattern of endocrine disorders among individuals with traumatic brain injury (TBI) has been the subject of very few investigations. **Materials and Methods:** This study was meant to investigate the pattern of endocrine disruption following a severe head injury. Severe head injury patients admitted to the Department of Neurosurgery, Government Medical College and Government General Hospital, Mahabubabad, from June 2023 to May 2024 in 12 months duration of study. All patients underwent NCCT of the skull upon admission, in addition to a clinical assessment. We conducted a comprehensive anterior pituitary hormone investigation after 24 hours of damage and repeated it at 2 weeks, 3 months and 6 months for the patients who survived. **Results:** A total of 50 patients were included in the study. Forty of our patients succumbed in the hospital. Rest of the patients were followed up for 6 months. Elevations of cortisol followed by prolactin were the most common hormonal derangements at admission. On CT images, the midline shift was negatively associated with cortisol elevation and directly related to GH increase. On CT scans, infarcts were negatively associated with increases in cortisol and LH. A significant change was identified in the declining trend of the mean T4 values and normalization, or a decreasing tendency from initially increased mean cortisol and GH levels over follow- up ($p<0.05$). **Conclusion:** This study demonstrates that alterations in hormone profiles appear to be quite prevalent in severe TBI and fluctuate dramatically over at least 6 months. there is a link between age and radiological results. Performance of hormonal analysis evaluation should be addressed in patients with severe brain damage so that adequate hormone replacement may be done to optimize the clinical outcome.

INTRODUCTION

The considerable improvement in life support methods for patients suffering traumatic brain injury (TBI) has kept more patients alive after damage than was true before.[1] It's important to note that many people who have suffered serious head injuries still have ongoing neurobehavioral problems and quality of life complaints, which are sometimes similar to those people who have adult- onset hormone problems.[2,3] However, we rarely address pituitary dysfunction as a potential source of the aforementioned difficulties, instead implicating primary brain damage and secondary cerebral insults.[4,5] Head injury poses a significant risk to pituitary function because of the gland's bony encasement inside the Sellaturcica, fragile in funicular hypothalamic structures and susceptible vascular supply.[6] The prevalence and pattern of endocrinal disorders among individuals with TBI have received little systematic attention until recently.[7,8] The aim of this study was to identify the incidence and risk factors of pituitary dysfunction following severe head injury, as well as to examine the temporal pattern of hormonal impairment and the clinical- radiological risk variables that impact these endocrine derangements.

MATERIALS AND METHODS

The research group consisted of severe brain injury patients hospitalized within 24 hours after damage to the Department of Neurosurgery, Government Medical College and Government General Hospital,

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Mahabubabad, from June 2023 to May 2024 in 12 months. We measured the degree of trauma using the Glasgow Coma Scale (GCS) and all patients included in the research had a score of <8. The research excluded patients over 60 years old, girls under 16 years old and those with a history of endocrine problems. Furthermore, the study excluded individuals with cardiac, pulmonary, or metabolic diseases. All patients underwent a non- contrast computed tomography (NCCT) scan upon arrival. Within 24 hours of damage, we conducted a comprehensive anterior pituitary hormone study, measuring T3, T4, thyrotropin (TSH), prolactin (PRL), growth hormone (GH), cortisol, luteinizing hormone (LH) and follicle- stimulating hormone (FSH). The patients who survived underwent the following tests at 2 weeks, 3 months and 6 months. Centrifuged blood samples within 2 hours of collection and stored separate plasma aliquots at- 20 °C until we measured all the hormones, except cortisol, using ELISA kits from Genix Technology. Cortisol wasmeasured by ELISA test using kits by BiochemImmunosystems. We recorded and examined the derangement of endocrine parameters and also explored the temporal pattern of hormonal derangement. We evaluated the correlation of clinical data, such as age, GCS at admission and radiological characteristics, with hormonal derangement. We used the SPSS program for statistical analysis. We explored the association of categorical variables using the chi- square test. We performed a two- tailed Student's t- test to compare the means of two independent samples. We used repeated measures ANOVA to compare the sample means at various time points. Statistical significance was determined as $p<0.05$.

RESULTS

The research included 50 patients with a mean age of33.50 years (range 5- 65 years). There was a tendency towards younger age, with 72% of patients being under 38 years old and 82% being male. The ratio of males and females is 5.25:1. The research only included individuals with a GCS of <8. (Tables 1 and 2) present the distribution based on GCS and radiological characteristics, respectively. 23 individuals died during the hospital stay and follow- up (21 during the hospital stay and 6 during follow- up).

Table 1: Distribution of Patients as Per GCS.

GCS on admission	No. (%)
3	8 (16)
4	18 (36)
5	4 (8)
6	2 (4)
7	10 (20)
8	8 (16)

Table 2: Radiological Features

CT finding	No. (%)
Subdural hematoma and/or contusion	26 (52)
Extradural hematoma	4 (8)
Diffuse axonal injury	9 (18)
Subarachnoid hemorrhage	11 (22)
Midline shift (mm)	
0- 5	27 (54)
5–10	7 (14)
>10	13 (26)
Infarct	3 (9)

Among the survivors, there was a varying level of neurological recovery as determined by Glasgow Outcome Score (GOS) during follow- up at 6 months [GOS 2 (4%)., GOS 3 (6%)., GOS 4 (8%)., GOS 5 (10%)].
We followed up the survivors for 6 months, assessing their hormone profile on postoperative days 0, 2 weeks, 3 and 6 months. [Table 3] reports the patients' hormone profiles compared to the reference range over the 6- month period.

Table 3: Hormone Profile in Follow- Up Patients with Severe Head Injury

Hormone		Day 0 (n=27)	2 Week (n=20)	3 month (n=18)	6 months (n=15)
T3	Normal	26	20	17	13
	Low	1	-	-	2
	High	-	-	1	-
T4	Normal	26	17	18	14
	Low	-	1	-	1
	High	1	2	-	-
TSH	Normal	23	16	14	13
	Low	1	-	-	-
	High	3	4	4	2
PRL	Normal	22	15	13	14

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	Low	-			-
	High	5	5	5	1
GH	Normal	23	16	17	14
	Low	-	-	-	-
	High	4	4	1	1
Cortisol	Normal	18	13	12	10
	Low	-		2	2
	High	9	7	4	3
LH	Normal	24	17	16	13
	Low	-	-	-	-
	High	3	3	2	2
FSH	Normal	25	18	17	13
	Low	-	-	-	-
	High	2	2	1	2

*Normal range: T3 (70- 170ng/dl), T4 (4.5- 12.5 µg/dl), TSH (0.4- 4 µIU/ml), PRL(5- 20ng/dl)GH (0.06- 5ng/dl), cortisol (5- 25 µg/dl), LH (0.8- 7.6mIU/ml), FSH (0.7- 11 mIU/ml).

Table 4: Trends of Hormone Abnormality in Follow- Up Patients with Severe Head Injury

		T3	T4	TSH	PRL	GH	Cortisol	LHFSH
Age	<20 years	-	-	-	+	-	-	-
	20- 40 years	-	-	-	-	-	-	-
	>40 years	+	-	-	+	-	-	-
CT- midline shift	0- 5 mm	-	-	-	-	-	-	-
	>5 mm	-	-	+	-	-	+	-
CT- infarct	Present	-	-	-	-	-	-	-
	Absent	-	-	-	-	-	-	+
GOS	Fatal	-	-	-	-	-	-	+
	Survived	-	-	+	-	-	-	-

*+: Significant correlation (p< 0.05), - : not significant (p=NS)

DISCUSSION

All the hormones tested abnormal at various follow- up phases. Though TSH abnormalities were the most prevalent amongst the thyroid hormones, hyper cortisolemia and hyperprolactinemia were the most common hormonal abnormalities shortly after head injury. When assessing the hormone trends in the follow- up period, a significant alteration was found in the decreasing trend of the mean T4 values (p<0.005), normalization, or a decreasing trend from initially elevated mean cortisol (0<0.001) and GH levels (p<0.001) as compared to the normal reference range. During follow- up. Age groups <20 years and more than 40 years were more likely to have elevated PRL than those in the 20- 40- year group. Midline shift was related to a reduced degree of increases in blood cortisol (p<0.001) and a higher rise in GH levels (p<0.05). Infarct was negatively correlated with an increase in blood cortisol and LH levels (p<0.001) [Table 4].

Following TBI, post- traumatic neuroendocrine pathology may be a clinically relevant outcome. Various authors have documented occasional case reports of endocrine abnormalities following headinjury for the last decade, ever since they first established the link between head injury and the development of hypopituitarism. Increased detection of post- traumatic endocrine abnormalities may be attributable to various factors: knowledge of the disorder, increased incidence of traffic accidents and extended life with enhanced critical care.[9,10] In our study, we analyzed the hormonal patterns over a 6- month period among individuals with serious brain injuries.

Pituitary Thyroid Axis Abnormalities: Wartofsky,[11] have addressed the consequences of severe illness on thyroid function. The same sickness has gone by several names, including euthyroid unwell syndrome, non- thyroidal illness and low T3 and normal T4 syndrome.[12] In our investigation, there was a declining trend of serum T4 levels between 2 weeks and 6 months following injury. At 6 months, 4 of the 48 patients had low T3 levels, which previously had been normal, suggesting a tendency towards hypo pituitaries. We discovered TSH values to be high amongst individuals who survived as opposed to thosewho perished from their injuries. Chiolero,[13] observed significantly lower serum TSH levels in non- survivors. According to Beck- Peccoz,[14] the TSH, in situations of severe TBI, has a lower biological activity because of poor receptor binding. This may be one explanation for higher TSH in situations where thyroid hormone metabolism is enhanced.[15]

Pituitary- Adrenal Axis: The head injury patients in our study had plasma cortisol levels that were higher and stayed elevated for a prolonged period of time. 14 of the 27 individuals experienced an increase in cortisol levels within 24 hours of damage. They steadily fell over a 6- month period, becoming low in 2 of the 48 individuals at 6- month follow- up. Higher ACTH levels prolong the maximal cortisol secretion rate over time.[16] This sustained high level of adrenal secretion may contribute to the strong catabolic response and substantial tissue loss seen in head injury patients. In their investigation on plasma

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cortisol levels after head injury, King,[17] observed abnormally increased levels of cortisol as late as 4 months after the injury. Certain investigations have demonstrated an acceptable releasing mechanism, yet high levels of plasma cortisol fail to regulate the release of ACTH.[18,19] In our study, we observed that those patients who succumbed to the damage had a poor rise in cortisol levels as opposed to those who survived the accident, demonstrating not just the predictive value of the hormone but also its role in assisting the body to overcome the negative consequences of head injury. We have established associations between injury severity and pituitary- adrenal activity. Desai et al. discovered significant relationships between the Glasgow Coma Score and cortisol concentrations in individuals with head injuries.[20] However, our study did not find a significant link between GCS and cortisol. However, we did observe a midline shift on a CT scan of the head, performed within 24 hours of the damage, which showed an inverse association with cortisol concentration. As the midline shift increased, the cortisol level blunted, leading to a statistically significant difference.

Growth Hormone Abnormalities: Contradictory literature is present on the GH levels following TBI as reported by several authors, precluding definitive conclusions.[21,22] A group of patients with severe head injuries reported a GH rise following a glucose load, while patients with less severe damage did not differ in their GH response from normal participants.[23] This aberrant GH rise remained for up to 2 months following injury. We also reported higher GH levels following trauma. As compared to day 0, the GH levels steadily rose till 15 days, following which a slow drop towards normalization occurred. In the very earlystages of trauma, changes in GH dynamics may be caused by problems in the central aminergic or peptidergic pathways that control GH.[24] In our study, mean values of GH were significantly higher in patients who survived than in those who perished from their injuries.

Prolactin Abnormalities: Following a head injury, most investigations have found elevated baseline prolactin levels.[25,26] The hypothalamus tonically blocks prolactin, the only pituitary hormone. An elevated plasma prolactin level might signal hypothalamus injury.[27] Edwards and Clark, in their review on post- traumatic hypopituitarism, have identified increased prolactin in the majority of patients. In their study, four of the twelve female patients experienced galactorrhea. Given the location of the prolactin- releasing lactotrophs in the gland's periphery, the death of other pituitary cells could lead to anterior pituitary necrosis, leaving the lactotrophs relatively intact.[28] In our series, prolactin was high in the majority of the patients but was significantly greater in patients aged <20 years or above 40 years. Prolactin levels remained high throughout a 6- month period, with no statistically significant difference between levels immediately after injury and 6 months after injury. Few authors have observed low baseline prolactin levels with no response to TRH, indicating damage to lactotrophs with widespread anterior pituitary necrosis.[29]

Pituitary Gonadal Axis: Various study publications have described hypogonadism following a head injury. Clark,[30] reported a transitory rise in LH concentration, which quickly decreased to subnormal levels and an exaggerated response to exogenous GnRH stimulation. Acineri,[31] identified gonadotropin insufficiency as the most prevalent hormonal abnormality following traumatic brain injury in children. In our investigation, though, we did not come across low levels of gonadotrophs, but in keeping with the preceding study, we discovered a temporary spike in LH and FSH following damage, which progressively normalized. We also demonstrated that infarcts on CT scans following head injuries attenuated this temporary rise. Some writers have proposed a link between primary gonadal malfunction and hypogonadism following trauma, suggesting that higher levels of catecholamines and cortisol directly inhibit Leydigcells.[32]

CONCLUSION

This is a prospective investigation that explores the relationship between endocrine markers and the clinical prognosis in cases of severe TBI. In severe TBI, abnormalities in hormone profiles frequently occur, fluctuating over a period of at least 6 months, as ourresearch has established and these swings are linked to both age and radiological results. Patients with severe brain damage should undergo hormonal analysis evaluations to ensure adequate hormone replacement, thereby optimizing their clinical outcomes.

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