SERUM CORTISOL LEVELS- A STUDY IN ACUTE HEAD INJURY PATIENTS

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Abstracts: **Introduction:** Adrenal insufficiency (AI) has a great impact on the prognosis of patients with traumatic brain injury. In the healthy persons during normal day to day activity the concentration of plasma cortisol is high in the morning, decreases during the day and rises again during night. But this diurnal rhythm is abolished in long- term unconscious patients and in those with disturbed sleep cycles. Also patients with central nervous system disease, who are conscious but have lesions in the temporal lobe, the pretectal or hypothalamus area demonstrate abnormal rhythms. **Material and methods:** This cross-sectional study recruited 33 consecutive patients attending emergency medical departments of Prathima Institute of Medical Sciences Hospital between July 2017 to April 2018 with mild to severe traumatic head injury within six hours of injury. Selected patients were mainly divided into three groups depending on the Glascow coma scale (Mild head injury (14-15); Moderate head injury (9-13); Severe head injury (3-8)). In each group 11 patients were selected. GCS was calculated at the time of admission. The adrenal function of the patients was assessed by using the serum cortisol tests. **Results:** In this comparative study of acute head injury among three groups males are more prone to injured than females , with the % of 81,90, 72 in mild , moderate & severe injuries respectively. The result mainly shows that the mean cortisol levels estimated were significantly increased in mild head injury & were with greater increase in cases of moderate & severe head injuries. Statistically significant positive correlation was observed between serum cortisol & GCS levels. **Conclusions:** In this study of serum cortisol levels in head injury patients, we observed that there is increase in the serum cortisol level immediately after trauma. The increase is linearly related with the severity of head injury. Hence performing serum cortisol test is recommended for the assessment of adrenal function in patients with traumatic head injury.

Key Words: Traumatic head injury, Adrenal function, Serum cortisol .

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INTRODUCTION: When an animal or human is exposed to any immense variety of noxious or potentially noxious stimuli, there is an increased secretion of Adrenocorticotrophic hormone (ACTH) and consequent rise in the circulating cortisol. Thus this cortisol is known as stress hormone. This rise is essential for survival [1]

Cortisol levels respond within minutes to stress, whether physical (trauma, surgery and exercise), psychological (anxiety & depression) or physiologic (hypoglycaemia & fever). The reasons why glucocorticoid levels protect the organism under stress are not understood but in conditions of cortisol deficiency, such stresses may cause hypotension, shock & death [2]

Cortisol is synthesised in adrenal cortex. The daily secretion of cortisol ranges between 40-80µmol with a pronounced circadian cycle. The plasma cortisol tends to rise and fall. The bursts are more frequent in the morning & less frequent in the evening (circadian rhythm). ACTH is a polypeptide hormone secreted by anterior pituitary & stimulates adrenal cortex for the synthesis of corticosteroids. ACTH also related to the circadian rhythm in many animals including human beings [3]

In the healthy persons during normal day to day activity the concentration of plasma cortisol is high in the morning, decreases during the day and rises again during night. But this diurnal rhythm is abolished in long- term unconscious patients and in those with disturbed sleep cycles. Also patients with central nervous system disease, who are conscious but have lesions in the temporal lobe, the pretectal or hypothalamus area demonstrate abnormal rhythms[4,5].For this reasons the present study is design to examine the serum cortisol levels in head injury patients in acute phase (i.e.) below six hours of trauma.

Traumatic brain injury (TBI) is one of the main causes of death and disability in young adults, with consequences ranging from physical disabilities to

long-term cognitive, behavioural, psychological and social defects [6, 7] these long-term consequences make TBI a public health problem [8].

Closed head injury has reached epidemic proportions in western countries and also in India due to poorly controlled vehicular traffic and to rising in violence of citizens. The total injury produced by mechanical trauma depends not only on the primary mechanical damage but also on the complex interaction of patho physiological events. Head injuries include skull fractures, focal injuries & diffuse injuries. Head injuries are due to fall, road transport accidents (RTA). For our study the Glasgow coma scale classification was accepted for grading the clinical severity of head injuries.

The main aim of the study is the estimation of serum cortisol in acute phase of head injury i.e., within six hours of trauma.

MATERIAL AND METHODS:

The study was conducted with head injury patients attending emergency medical departments of Prathima Institute of Medical Sciences Hospital between July 2017 to April 2018. A total of 33 head injury patients were selected for this study.

Selected patents were mainly divided into three groups depending on the Glasgow coma scale (Mild head injury (14-15); Moderate (9-13); Severe (3-8)). In each group 11 patients were selected. . GCS was calculated at the time of admission to assess the injury severity.

The following is the scoring system of the Glasgow coma scale. [9].

Eye opening Test(E)	**SCORE**
Spontaneous	4
To verbal command	3
To pain	2
None	1

Best motor response(M)	
Obeys commands	6
Localization of painful stimulus	5
Flexion withdrawal response to pain	4
Abnormal flexion response to pain	3
Extension response to pain	2
None	1

Best verbal response(V)	
Oriented conversation	5
Diaoriented conversation	4
In appropriate words	3
In comprehensible words	2
None	1

Maximum scores (E+M+V)= 15

Head injury severity scale

CATAGORY	**GCS-Score**
Minimal	15(no loss of consciousness)
Mild	14 (brief loss of consciousness)
Moderate	9-13(loss of consciousness > 5 min)
Severe	5-8
Ctritical	3-4

GCS Score:

Mild	14-15
Moderate	9-13
Severe	5-8

The study protocol was approved by ethical committee of Prathima Institute of Medical Sciences (Ref number: IEC/PIMS/2017/004.

Inclusion criteria:

1. Patients with history of traumatic head injury within six hours of injury
2. Patients selected should have only pure brain injury without any injuries of long bones.
3. All modes of injuries were taken viz., road traffic accidents, falls & others.
4. Both male & female patients were included.

Exclusion criteria:

1. Patients with polytrauma including abdomen and chest were not taken up for the study
2. Patients with history metabolic syndrome & alcohol intoxication were not included
3. Patients suffering with chronic diseases like diabetes, hypertension, coronary arterial diseases & cerebrovascular diseases were not included in this study.

Blood samples were collected from the selected patients in the emergency medical department only for the estimation of serum cortisol. For each patient, the following information was recorded: age, sex, vital signs, mechanisms of trauma (road accidents, falls, etc.), before collection of the sample because study is focused in acute phase of head injury i.e., within six hours of injury. The blood samples were taken at 8:00 AM & 4 PM for estimation of basal serum cortisol. The serum from blood samples were instantly separated and kept frozen at –70°C until they were assayed. All the cortisol levels were measured via the enzyme radioimmunoassay (RIA)[10,11] with the coat -A-Count @ In-vitro Diagnistic test kit

STATISTICAL ANALYSIS:

Data was expressed as Mean±SD. Analysis of Variance (One-way ANOVA) was used for comparison between mild, moderate & severe head injury patients using SPSS statistical package version 20. p< 0.05, p< 0.01 was considered statistically significant, p< 0.001 was considered highly significant (HS) and p> 0.05 was considered as not Significant. Serum cortisol levels were correlated with injury severity (GCS score) using Pearson's co- relation co-efficient (r) method.

RESULT:

Table:1 Comparison between Sex, type of injury in mild, moderate & severe head injuries.

Table 1 shows sex,type of injury in mild,moderate & severe head injuries.

In present study males are more prone to injured than females, with the % of 81, 90, and 72 in mild, moderate & severe injuries respectively.

The type of accident which resulted in head injuries were grouped as road traffic accidents (RTA), fall and others. In this study majority of Mild head injuries were due to RTA (45.4%) than fall (36.3%) & others(18.1%). Where as in moderate & severe injuries greater number of cases were due to RTA(45.4%,38.3%) and fall(36.3% & 36.3%) than others(18.1%.27.2%)was observed.

Table:2 : Comparsion of age, GCS & serum cortisol in mild, moderate & severe head injury

	Group I	Group II	Group III
Parameter	Mild Head Injury patients N=11	Moderate Head Injury patients N=11	Severe Head Injury patients N=11
Male %	9(81%)	10(90%)	08(72%)
Female %	02(19%)	01(10%)	03(28%)
RTA% (Road Traffic Accidents)	05(45.4%)	05(45.4%)	04(38.3%)
Fall%	04(36.3%)	04(36.3%)	04(36.3%)
Other%	02(18.1%)	02(18.1%)	03(27.2%)

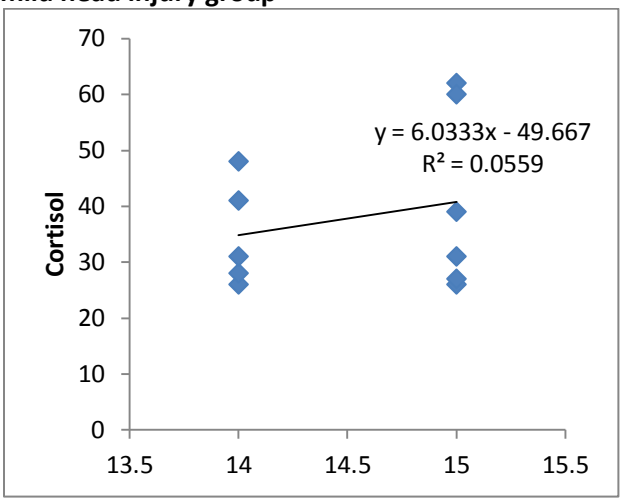
Parameters	Group-I Mean± SD (n=11)	Group-II Mean± SD (n=11)	Group-III Mean± SD (n=11)	F-Value	P Value
Age(years)	30.45± 11.72	34.54± 15.70	32.18± 8.41	0.300	0.74(NS)
Cortisol in µg/dl	38.09± 13.33	56.72± 16.34	57.90± 25.39[b]	3.741	0.03*
GCS	14.5	11.8[a]	6.0[a,b]	98.03	<0.001***

p>0.05: Not Significant (NS), *p: <0.05: Significant(S), **p: <0.01: Highly significant(HS), ***p: <0.001: Very highly significant.

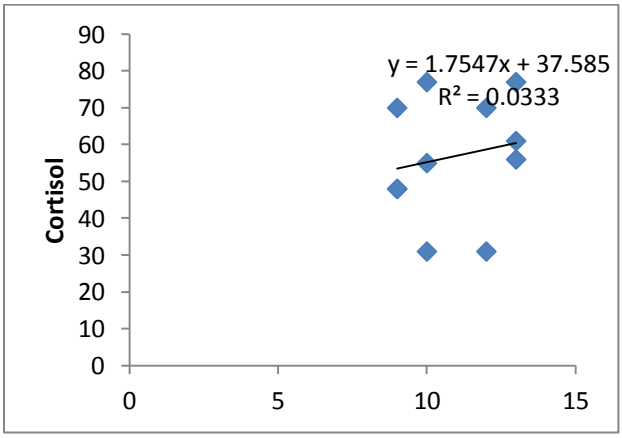
Table 3: Correlation Analysis between serum cortisol & GCS score

GROUPS	Correlation Co efficient	R	P Value
Mild head injury patients	Cortisol & GCS	0.236	0.04*
Moderate head injury patients	Cortisol & GCS	0.183	0.5
Severe head injury patients	Cortisol & GCS	0.273	0.4
Correlation is significant at 0.05 level (p); r-regression.			

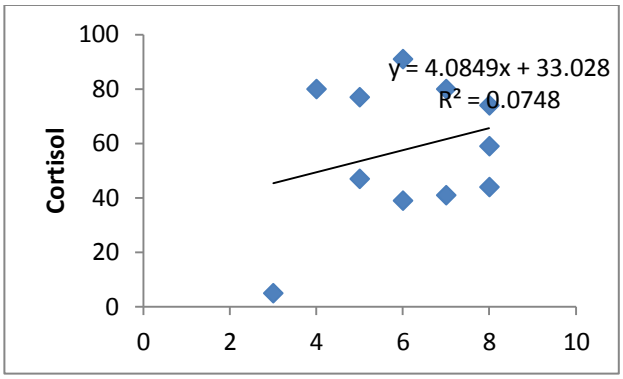
Graph- 1: Correlation between Cortisol and GCS mild head injury group



Graph -2: Correlation between Cortisol and GCS in moderate head injury group



Graph-3: Correlation between Cortisol and GCS in severe head injury group



Graphs 1,2 and 3 shows that a positive correlation existed between the Serum Cortisol and GCS levels which was statistically significant in mild head injury group. But in moderate & severe head injury groups statistically not significant correlation was existed between cortisol & GCS level. Our study showed that the association between Cortisol and GCS was stronger among mild head injury patients than in moderate & severe head injury patients.

DISCUSSION: A total 33 head injury patients were selected & studied for the cortisol level by collecting blood samples within six hours of head injuries. These patients were grouped into three groups depending upon Glasgow Coma Scale Score.

In each group 11 patients were studied. The accidents which caused head injuries were grouped into road traffic accidents, fall & others. In all three groups of head injury it has been observed that the serum cortisol levels were significantly increased above the normal with a mean serum cortisol levels of 38.09ug/dl,56.72ug/dl,57.90ug/dl in mild, moderate & severe head injuries respectively.

Stress is a physiological condition which can increase the cortisol levels. So we tried to study increase in the cortisol level which is due to the trauma, which can be either concussion haemorrhage or injury to brain structures.

The increase of cortisol in case of trauma is due to stimuli from the injured area which traverse to the reticular formation & the limbic areas, these impulses then travel to the median eminence which release CRH (Cortisol Releasing Hormone). This stimulate anterior pituitary to secrete ACTH. This in turn stimulates the adrenal cortex to release cortisol. Hence in traumatic brain injury the cortisol levels are elevated during acute phase. Similar reports were given by Feibel Jet al., &

Chesnokova V et al., [12, 13].

It is also noted that there is loss of normal circadian pattern of ACTH secretion after head injury & loss of responsiveness in the negative feedback mechanism. There is usually an increase in the production of cortisol but it fails to create a sufficient response to stress. This may be the cause from increase levels of serum cortisol after injury. Similar reports were given by Kozyra EF et al., [14].

Trauma including head injury is associated with increased sympathetic activity & increased levels of circulating catecholamines due to adrenal medullary stimulation. The magnitude of the catecholamines is directly related to the severity of the brain injury. It is presumed that increased blood catecholamine's are responsible for the hyper metabolic state observed after head injury manifested by hypotension, tachycardia, increased cop & excessive caloric consumption with development of negative nitrogen balance. This observation was supported by Cohan et a., [15]

According to Barton RN et al.,[16] there is a positive correlation between cortisol concentrations and injury severity has been demonstrated in patients with mild or moderate head injury, but not in those with severe injury . This is in agreement with ths study of Barton RN, et. al[16] our study also revealed that there was a strong positive correlation between cortisol concentrations and GCS levels has been observed in patients with mild head injury , but not in those with moderate & severe injury .

But on the contrary[17], adrenal insufficiency has been found in patients during the early phase of head injury, suggesting post-traumatic damage at the hypothalamic–pituitary level . Damage at the hypothalamic–pituitary level decreases ACTH there by cortisol levels. These data highlight the importance of an early recognition of adrenal insufficiency that may lead to a worse outcome.

There was no much difference in the serum cortisol in moderate & severe head injuries. This is probably one case in the severe head injury showed very low level of serum cortisol of 5ug/dl. She had a low GCS score & the injury was severe including brain stem & hypothalamus indicating the low cortisol levels immediately following severe head injury. In this case low cortisol may be due to failure of hypothalamohypophyseo adreno cortical failure [18].

In relation to age there was no specific relationship noted with serum cortisol levels & also serum cortisol levels do not have much relation with sex also.

CONCLUSION:

In the present study we have studied the serum cortisol levels in the head injury cases, which is a form of stress, resulting in secretion of increased levels of serum cortisol immediately after trauma i.e., with in six hrs of injury. In the above study it has been observed in the mild head injury cases there was a moderate increase in serum cortisol levels. Where as in moderate & severe head injuries there was a much greater increase in the serum cortisol.

To conclude it has been observed that there is increase in the serum cortisol level immediately after trauma. The increase in the serum cortisol has been attributed to increased stimulation of anterior pituitary, adrenal cortex.

So we concluded that there is a linear relationship between severity of head injury & cortisol level. Hence performing serum cortisol test for the assessment of adrenal function in patients with traumatic brain injury is recommended.

Limitations:

In this study follow up was not possible because the study participants were from small cities and rural areas. Future studies with a larger sample size including patients with mild head injury and their follow-up after improvement are required for a concise conclusion on the diagnostic and therapeutic management of this population.

ACKNOWLEDGMENT:

Iacknowledge the cooperation of all the participants in the study. I would also like to thank central lab of Prathima Institute of Medical Sciences, Karimnagar for their valuable support and cooperation.

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Conflict of Interest : None