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ASSESSMENT OF HORMONAL LEVELS IN TRAUMATIC HEAD INJURY

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ABSTRACT

Traumatic head injury (THI) is one of the main causes of death and disability in young adults with consequences ranging from physical disabilities to long term cognitive, behavioral, psychological and social defects. Acute THI leads to pituitary dysfunction. 80 patients were analyzed and divided according to the Glasgow coma scale into mild, moderate and severe categories .Medical history was obtained and a physical examination was performed. Age and sex was recorded of each patient. These patients were analyzed for their serum prolactin and serum testosterone levels. The study was conducted over of 18 months in the Goa Medical College. The standard deviation for prolactin was 7.24±1.19 for severe patients and 10.77 ± 2.2 for moderate patients and for testosterone it was 0.22± 0.03 for severe patients and 0.65±1.13 in moderate patient all of which are statistically significant. A statistically significant increase in serum prolactin levels and decrease in serum testosterone in patients of THI was observed.

KEY WORDS: Traumatic head injury, Testosterone, Prolactin.

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INTRODUCTION

Traumatic brain injury is a non-degenerative, non-cognitive insult to the brain from an external mechanical force causing temporary or permanent neurological dysfunction which may result in impairment of cognitive, physical and psychological functions[1]. The incidence of TBI has been reported as 200 per 100,000 of the population suffer from traumatic brain injury. TBI is a major cause of death and disability worldwide, especially in children and young adults[2]. Causes include falls, vehicle accidents, and violence. Approximately 80,000 to 90,000 persons per year experience some permanent disability as a result of TBI, although the extent and severity of that disability are highly variable[3]. Among the most common sequel of TBI are cognitive impairments, disturbances of emotion and behavior, and somatic symptoms, such as headache, dizziness, visual disturbance, and mobility deficits[4]. Secondary complications of TBI in the acute post injury are frequent and often include reconditioning, altered nutritional status, weight loss, and infection; the complications are particularly common after TBI of moderate or greater severity, and adversely affect recovery from TBI. In light of the critical role of endocrine axis on the response to injury/stress, the effects of neuroactive hormones on neuronal repair, and the implications of neuroendocrine dysfunction on cognitive, emotional, behavioral, and physical function, the integrity of these systems is essential for optimal neurological and neurobehavioral recovery after TBI[4]. Head injuries can be classified into mild, moderate, and severe categories. The Glasgow Coma Scale (GCS), the most commonly used system for classifying TBI severity, grades a person's level of consciousness on a scale of 3–15 based on verbal, motor, and eye-opening reactions to stimuli[5]. It is generally agreed that a TBI with a GCS of 13 or above is mild, 9–12 is moderate, and 8 or below is severe.

Glasgow Coma Scale[6]

Eye Opening	**E**
spontaneous	4
to speech	3
to pain	2
no response	1
Best Motor Response	**M**
To Verbal Command:	
obeys	6
To Painful Stimulus:	
localizes pain	5
flexion-withdrawal	4
flexion-abnormal	3
extension	2

no response	1
Best Verbal Response	**V**
oriented and converses	5
disoriented and converses	4
inappropriate words	3
incomprehensible sounds	2
no response	1

E + M + V = 3 to 15

- 90% less than or equal to 8 are in coma
- Greater than or equal to 9 not in coma
- 8 is the critical score
- Less than or equal to 8 at 6 hours - 50% die
- 9-11 = moderate severity
- Greater than or equal to 12 = minor injury

Testosterone is synthesized in the testes. It begins with the formation of pregnenolone from cholesterol by the action of cholesterol side chain cleavage enzyme. Testosterone circulates in the plasma freely or bound to plasma proteins[7]. The binding protein includes the specific sex hormone binding globulin and non specific proteins like albumin. It exhibits a rhythmic variation in its circulation. Prolactin (PRL) is a hormone of the adenohypophysis. It is also a pituitary lactogenic hormone (23KD) that is synthesized as preprolactin. PRL is formed when an N-terminal signal peptide is cleaved from the preprolactin. PRL is a 198 amino acid peptide secreted by pituitary lacto tropic cells with a structure similar to that of growth hormone. During pregnancy and in the fetal pituitary the relative number and PRL content of lacto tropic cells increases as a result of elevated circulating estrogens during pregnancy.

MATERIALS AND METHODS

The study was conducted in the Department of Biochemistry, Goa Medical College during the period from September 2011 to March 2012. The total number of subjects involved in this study was 130 and the subjects were divided according to the Glasgow coma scale

STUDY GROUP:

The study group comprised of 80 male subjects in different groups divided according to their Glasgow coma scale.

CONTROL GROUP

Comprised of 50 normal healthy subjects who were non-hypertensive, didn't suffer from any brain tumours especially prolactinomas or any hormonal imbalance or any cerebrovascular accidents.

All the patients or relatives were informed and explained about the study being undertaken; in detail and their informed consent was taken. An Institutional Ethics Committee clearance was obtained and since this is a cross-sectional study, there was no follow up.

EXCLUSION CRITERIA:

Subjects suffering from any hormonal imbalance, prolactinomas or from any cerebrovascular accidents such as stroke were excluded from this study. Sample Collection;

5 milliliter of blood was collected from the patients in vacutainers without an

anticoagulant to test the serum for the above tests.

The following parameters were analysed

1. Blood urea[8]
2. Serum creatinine[9]
3. Serum sodium
4. Serum potassium
5. Serum chloride
6. Serum magnesium
7. Serum prolactin
8. Serum testosterone
9. Serum Follicle stimulating hormone

All the above tests will be carried out on the autoanalyzer-architect ci 8200 system.

Principle for Electrolytes estimations:
Using gravimetric methods, each level of the protein based calibrator is prepared with ACS grade sodium chloride, potassium chloride and sodium nitrate. The concentration of sodium and potassium is determined using flame photometry calibrated against NIST SRM 909. The concentration of chloride is determined using titration with silver calibrated against NIST SRM 2202. Serum electrolytes will be tested using the Integrated Chip Technology.

Principle for estimation of serum Magnesium:
This method utilizes arsenazo dye which binds preferentially with magnesium. The absorbance of the arsenazo-magnesium complex is measured at 572 nm and is proportional to the concentration of magnesium present in the sample. Calcium interference is prevented by using calcium chelating agents.

Principle for Hormonal levels:
It is a 2 step immunoassay using serum and plasma by CMIA referred to as chemiflex. In the first step sample and anti-hormonal (mouse, monoclonal) coated paramagnetic micro particles are combined Hormones present in the sample binds to this. After washing, the anti-hormone for example anti-prolactin acridium labeled conjugate is added to the second step. Pre-Trigger and Trigger solutions are then added to the reaction, the resulting chemiluminescent reaction is measured as relative light units (RLUs). A direct relationship exists between the amount of hormones in the sample and the RLUs detected by the architect i optical system. Hormonal levels will be assessed by Chemiluminescent Microparticle Immunoassay.

RESULTS

A total of 80 patients suffering from acute traumatic head injury were evaluated. They were divided into mild, moderate and severe categories based on their Glasgow coma scale.

Table 1
Results of blood urea in the three categories of THI.

Report					
Blood urea					
gcs	Mean	N	Std. Deviation	Minimum	Maximum
severe	20.21622	37	6.110715248	10	41
moderate	25.86957	23	12.04651722	11	59
mild	21.8	20	9.220115309	11	53
Total	22.2375	80	9.147516437	10	59

Table 2
Results of the serum creatinine in the three categories of THI

Report					
Serum creatinine					
gcs	Mean	N	Std. Deviation	Minimum	Maximum
severe	1.148649	37	0.195251	0.7	1.5
moderate	1.004348	23	0.322601	0.2	1.5
mild	1.4535	20	1.800813	0.6	9
Total	1.183375	80	0.924483	0.2	9

Table 3
Results of the serum sodium in the three categories of THI

Report					
Serum Sodium					
gcs	Mean	N	Std. Deviation	Minimum	Maximum
severe	135.8108	37	6.522771	110	149
moderate	137.8261	23	5.499191	128	156
mild	133.2	20	8.563079	110	144
Total	135.7375	80	6.953269	110	156

Table 4
Results of the serum potassium in the three categories of THI

Report					
Serum potassium					
gcs	Mean	N	Std. Deviation	Minimum	Maximum
severe	3.745946	37	0.597027	2	4.9
moderate	3.678261	23	0.645232	2.9	5.2
mild	3.61	20	0.417889	2.9	4.2
Total	3.6925	80	0.568759	2	5.2

Table 5
Results of the serum chloride in the three categories of THI

Report					
Serum chloride					
gcs	Mean	N	Std. Deviation	Minimum	Maximum
severe	102.7297	37	4.706076	89	116
moderate	102.4348	23	5.392133	91	119
mild	100.75	20	5.045842	89	108
Total	102.15	80	4.998987	89	119

Table 6
Results of the serum magnesium in the three categories of THI

Report					
Serum magnesium					
gcs	Mean	N	Std. Deviation	Minimum	Maximum
severe	2.275676	37	0.394691	1.1	3
moderate	2.126087	23	0.546241	1	2.9
mild	1.925	20	0.639798	1	3.1
Total	2.145	80	0.522385	1	3.1

Table 7
Results of the serum prolactin in the three categories of THI

Report					
Serum prolactin					
gcs	Mean	N	Std. Deviation	Minimum	Maximum
severe	38.27027	37	7.244341	30	56
moderate	22.73913	23	10.40637	16	67
mild	32.6	20	38.71543	10	133
Total	32.3875	80	21.39827	10	133

Table 8
Results of the serum testosterone in the three categories of THI

Report					
Serum testosterone					
gcs	Mean	N	Std. Deviation	Minimum	Maximum
severe	0.034324	37	0.022918	0.01	0.1
moderate	0.501739	23	0.658529	0.01	3
mild	0.959	20	1.032075	0.01	3
Total	0.399875	80	0.722453	0.01	3

Table 9
Results of the Serum FSH in the three categories of THI

Report					
Serum FSH					
gcs	Mean	N	Std. Deviation	Maximum	Minimum
severe	5.802973	37	6.460956	36.88	1.37
moderate	3.234348	23	2.252955	8.49	0.61
mild	6.0405	20	6.628915	29.51	0.28
Total	5.123875	80	5.698481	36.88	0.28

ANNOVA TEST OF SIGNIFICANCE

		Sum of Squares	**df**	**Mean Square**	**F**	**Sig.**
SERUM CREATININE	Between Groups	20.174	6	3.362	88.820	0.000
	Within Groups	7.685	203	0.038		
	Total	27.858	209			
BLOOD UREA	Between Groups	16,553.001	6	2,758.833	74.297	0.000
	Within Groups	7,537.904	203	37.133		
	Total	24,090.904	209			
CYSTATIN C	Between Groups	26.160	6	4.360	281.604	0.000
	Within Groups	3.143	203	0.015		
	Total	29.303	209			
FBSL	Between Groups	2,03,422.198	6	33,903.700	128.138	0.000
	Within Groups	52,388.364	198	264.588		
	Total	2,55,810.562	204			
HbA1c	Between Groups	1,787.531	6	297.922	452.115	0.000
	Within Groups	129.813	197	0.659		
	Total	1,917.344	203			

[*] ***The mean difference is significant at the .05 level.***

Table 5
Significance between groups – BONFERRONS TEST

Descriptives								
	N	Mean	Std. Deviation	Std. Error	95% Confidence Interval for Mean		Min	Max
					Lower Bound	Upper Bound		
Serum testosterone								
severe	37	0.034	0.02	0.00	0.02	0.042	0.01	0.1
Moderate	23	0.502	0.65	0.13	0.2	0.786	0.01	3
Mild	20	0.959	1.0	0.23	0.4	1.442	0.01	3
Total	80	0.4	0.7	0.07	0.2	0.560	0.01	3
Serum prol actin								
Severe	37	38.27	7.24	1.19	35.85	40.68	30	56
Moderate	23	22.74	10.40	2.16	18.23	27.29	16	67
Mild	20	32.6	38.71	8.65	14.48	50.94	10	133
Total	80	32.39	21.39	2.39	27.62	37.14	10	133
Serum magnesium								
Severe	37	2.27	0.39	0.06	2.1	2.40	1.1	3
Moderate	23	2.126	0.54	0.1	1.8	2.36	1	2.9
Mild	20	1.92	0.6	0.14	1.62	2.22	1	3.1
Total	80	2.14	0.52	0.05	2.02	2.26	1	3.1
Serum chloride								
Severe	37	102.7	4.70	0.77	101.1	104.2	89	116
Moderate	23	102.4	5.39	1.12	100.1	104.76	91	119
Mild	20	100.8	5.04	1.12	98.38	103.11	89	108
Total	80	102.2	4.9	0.55	101.0	103.26	89	119
Serum pot tasium								
Severe	37	3.74	0.59	0.09	3.54	3.94	2	4.9
Moderate	23	3.67	0.64	0.13	3.39	3.95	2.9	5.2
Mild	20	3.61	0.41	0.09	3.41	3.80	2.9	4.2
Total	80	3.69	0.56	0.06	3.56	3.81	2	5.2
Serum sodium								
Severe								
Moderate	37	135.8	6.52	1.07	133.6	137.9	110	149

Mild	23	137.8	5.49	1.14	135.4	140.2	128	156
Total	20	133.2	8.56	1.91	129.1	137.2	110	144
	80	135.7	6.95	0.7	134.1	137.2	110	156
Serum creatinine								
Severe								
Moderate	37	1.14	0.19	0.03	1.08	1.2	0.7	1.5
Mild	23	1.0	0.3	0.06	0.86	1.1	0.2	1.5
Total	20	1.4	1.80	0.40	0.6	2.2	0.6	9
	80	1.1	0.92	0.10	0.97	1.3	0.2	9
Blood urea								
Severe								
moderate	37	20.22	6.11	1.00	18.1	22.0	10	41
mild	23	25.87	12.04	2.51	20.6	31.0	11	59
Total	20	21.8	9.22	2.06	17.4	26.1	11	53
	80	22.24	9.14	1.0	20.2	24.27	10	59

**The mean difference is significant at the .05 level.*

DISCUSSION

Head injury is any trauma that leads to injury of the scalp, skull, or brain. The injuries can range from a minor bump on the skull to serious brain injury[2, 10]. Head injuries may be closed or open. A closed (non-missile) head injury is one in which the skull is not broken[1]. A penetrating head injury occurs when an object pierces the skull and breaches the dura mater[6]. Brain injuries may be diffuse, occurring over a wide area, or focal, located in a small, specific area.

Secretion of PRL is under hypothalamic control and is unique because the main control of its secretion is inhibitory rather than stimulatory. Dopamine is believed to be the principal inhibitor factor that regulates PRL secretion. Thyroid releasing hormone, the releasing factor that controls the Thyroid stimulating hormone release, functions as a PRL –releasing factor (PRF) and stimulates PRL secretion within minutes when injected intravenously into human subjects.

Circulating testosterone serves as a precursor for the formation of two active metabolites: dihydrotestosterone and estrogens. Through the action of 5 alpha reductase, testosterone is converted to dihydrotestosterone. Alternatively testosterone and androstenedine can be converted to estrogens with the help of aromatase. Dihydrotestosterone is metabolised to 3 alpha androstanediol and 3 alpha androstanediol glucoronide, metabolites used for markers of dihydrotestosterone production in the peripheral tissues.

This study was conducted to evaluate the abnormalities in hormonal levels following head injury. In the present study, a statistically significant rise in serum prolactin levels and a subsequent decrease in serum testosterone levels in patients compared to the controls. The more severe the head injuries, the higher the levels of serum prolactin were noted. Pituitary dysfunction following traumatic events can be due to functional alterations during the acute phase of a traumatic head injury or alterations in pituitary hormone secretion that leads to permanent damage. This may be due to haemorrhage and necrosis of the pituitary

gland as this is highly vulnerable to mechanical compression.[11]

CONCLUSION

In conclusion serum prolactin levels are altered significantly following acute traumatic head injury and as a result a decrease in serum testosterone was observed.

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