EVALUATION OF POSTMORTEM SERUM INSULIN-LIKE GROWTH FACTOR 1 LEVELS IN TRAUMATIC DEATHS WITH REGARD TO THE SURVIVAL TIME AND SEVERITY OF TRAUMA

BY

Mona M. Abo El-Noor, Fatma M. Elgazzar, Ghada H. El-Shafy*

*Forensic Medicine and Clinical Toxicology, and Clinical Pathology**

Departments, Faculty of Medicine, Tanta University, Tanta, Egypt

ABSTRACT

Several clinical studies showed reduced levels of circulating insulin-like growth factor 1(IGF-1) in patients with acute trauma. The aim of this study was to investigate postmortem serum IGF-1 levels in traumatic deaths with special regard to the survival time and severity of trauma. This study was carried out on eighty cases of mechanical traumatic deaths subjected to medicolegal autopsy in El-Mansura Department of Forensic Institute during the period from the start of January 2014 to the end of October 2015. Only adult males aged 18 years or more were included. Decomposed bodies and/or those with no confirmed survival period were excluded. For each case, the age, cause and site of trauma, survival period and the cause of death were reported. Additionally, Rt cardiac blood samples were taken using sterile syringes for determination of IGF-1 levels. According to the affected body region, cases were grouped in to: group1 (isolated head trauma, n=20), group 2 (body trauma without head trauma, n=30), and group 3 (combined head and other regional body trauma, n=30). A control group of ten male cases with non-traumatic natural deaths matched for age were selected. There was significant decrease in IGF-1 levels in all the studied groups of traumatic deaths compared to the control group. Additionally, mean IGF-1 levels in group 3 were significantly lower compared to groups 1 and 2. In all the studied groups, there was significant negative correlation between serum IGF-1 levels and the survival time (hs) and prediction of survival time (hs) was determined by simple linear regression analysis. A significant negative correlation was also detected between IGF-1 levels and the total abbreviated injury scale (AIS). In conclusion, this study demonstrated for the first time low postmortem serum IGF-1 levels in males died from mechanical trauma with significant negative correlation with the survival time and trauma severity.

Keywords: *Serum insulin-like growth factor 1, mechanical traumatic deaths, survival time, medicolegal autopsy, abbreviated injury scale.*

INTRODUCTlON

Worldwide, there is an observed increase in the incidence of traumatic deaths (Rhee et al., 2014). Precise estimation of post-injury survival time and the association of injury to death is an important but difficult task for the forensic pathologist (Quan et al., 2010). However, there are only few published autopsy studies on length of survival time, and they are limited to specific types of wounds (Cros et al., 2013). Another frequently asked question to the forensic pathologist is the evaluation of the severity of traumatic injuries and whether the trauma is severe enough to be lethal and considered as the cause of death (Mimasaka et al., 2006).

Postmortem biochemistry has become a potent ancillary procedure in forensic death investigation which complements the conventional autopsy procedures. Measuring biochemical markers in tissues or peripheral body fluids could provide essential information about survival period, the cause of death, postmortem interval, and pathophysiological conditions of diseases and injuries (Maeda et al., 2011).

Insulin-like growth factor 1(IGF-1) is a potent growth factor primarily produced by the liver and to a lesser extent, locally by many types of peripheral cells under basal conditions and in response to inflammatory stimuli (Mangiola et al., 2015). Insulin-like growth factor 1 has variable effects including metabolic insulin-like effects and stimulation of different cells proliferation, differentiation and survival (Walsh et al., 2002).

Several earlier clinical studies showed reduced levels of circulating IGF-1 in patients with acute trauma (Byrne et al., 1993; Jeevanandam et al., 1995; Wojnar et al., 1995). However, limited previous published data regarding the practical analysis of postmortem IGF-1 levels in humans were detected in the literature.

The aim of this work was to investigate postmortem serum IGF-1 levels in traumatic death cases with special regard to its relationship with the survival time and severity of trauma in forensic autopsies.

MATERIALS AND METHODS

Forensic autopsy cases and blood samples:

This cross sectional study was carried out on eighty cases of mechanical traumatic deaths subjected to medicolegal autopsy in El-Mansura Department of Forensic Institute during the period from the start of January 2014 to the end of October 2015.

Only male cases were included in this study due to insufficient number of female cases during the study period allowing statistical analysis of both genders.

The bodies had been preserved in refrigerated morgues for several hours or overnight after police inspection and before the autopsy. To fulfill the inclusion criteria of the study, each case had to meet the following conditions: (a) adults of 18 years old or more, (b) postmortem period less than 48h, (c) no significant decomposition, (d) cases where a witness and/or circumstantial evidence was well established to confirm survival, and (e) sufficient volume of the serum for biochemical analysis. Exclusion criteria included (a) decomposed bodies, (b) cases with no confirmed survival times in the traumatic cases.

The following information were recorded for each case: age, cause and site of trauma, types and descriptions of injuries, survival period and cause of death that was determined on the basis of medical records and full autopsy examination including macropathology, histopathology, toxicology, biochemistry, and postmortem radiography.

According to the affected body region, the studied cases were divided into the following groups:

- Group 1: cases with isolated head trauma (20 cases).
- Group 2: cases with regional body trauma without head trauma (30 cases).
- Group 3: cases with combined head and other regional body trauma (30 cases).

As regards cause of trauma, it was either:

- Blunt trauma including road traffic accidents, fall from height, and other blunt injuries.
- Sharp instrument trauma.
- Firearm injuries.

A control group of ten male cases with non-traumatic natural deaths matched for age were selected.

The survival time (time interval between the onset of fatal traumatic event and the time of death) was divided as follows: 0.1-6h, > 6h-24h, and > one day up to seven days. Cases with longer survival time included those underwent medical care involving critical cardiopulmonary support, surgery to the site of injury, fluid infusion, shock therapy, and blood transfusion.

According to Mimasaka et al. (2006), total abbreviated injury scale (AIS) is the most suitable scoring system for the evaluation of trauma severity in postmortem cases. Hence, the total AIS was calculated only for forty cases from the studied traumatic deaths; in whom death occurred within 6h after sustaining trauma (survival period: 0.1-6 h) and description of injuries in the medicolegal reports were sufficiently detailed. Traumatic deaths with long survival (> 6 h) were not included because injuries in these cases were often complicated, medically treated, and their autopsy description was often not detailed.

The abbreviated injury scale for each traumatic injury was determined using the 1985 protocol of the American Association for Automotive Medicine (Civil and Schwab, 1988). The AIS score of each injury ranges from1 to 6, and the total AIS is the sum of all AIS scores in each of the following six body regions: head and neck, face, chest, abdomen, extremities, and the exterior skin.

For determination of IGF-1 levels, cardiac blood samples (right side of the heart in all the cases) from individual cases were taken using sterile syringes. They were centrifuged at 3000g for 10 min, and the sera were stored at -30 ºC until the time of analysis.

Determination of serum IGF-1 levels:

The Assay Max Human IGF-1 ELISA kit (Assaypro Company, Newyork, USA) is designed for the detection of human IGF-1 in plasma, serum, and cell culture supernatants. This assay uses a quantitative sandwich enzyme immunoassay technique that takes 5hs to measure IGF-1 levels. A monoclonal antibody specific for human IGF-1 is precoated onto a microplate. The human IGF-1 in standards and samples is sandwiched by the immobilized antibody and biotinylated polyclonal antibody specific for the human IGF-1, which is recognized by a streptavidin-peroxidase conjugate. All unbound material is then washed away, and a peroxidase enzyme substrate is added. The color development is stopped, and the intensity of the color is measured. Insulin-like growth factor 1 levels were evaluated according to the age dependent reference ranges of the used kits for human serum.

Statistical analysis:

A statistical software package, SPSS (version 20) was used to perform statistical analysis. Categorical variables were analyzed using Chi Square goodness of fit test. Continuous data were tested for normality and homogeneity of variance and one way ANOVA followed by post hoc Tukey's test were used for comparison of IGF-1 levels between the different studied groups. Pearson's correlation coefficient was used to investigate the association between IGF-1 levels and the survival time (h) followed by simple linear regression analysis to establish regression equations between them. Spearman's rank correlation coefficient was used to evaluate the correlation between IGF-1 levels and the total AIS. The association between IGF-1 levels and the chronological age of the studied cases was tested in the different studied groups using Pearson's correlation coefficient.

RESULTS

All the studied cases were males died from mechanical trauma. Their ages ranged from 18-50 y with a mean age of 31.38 ± 6.37 y. The age group of 30 - <40 y showed significantly higher percentage of cases compared to other age groups. No significant differences between the three studied groups of traumatic deaths (isolated head trauma, regional body trauma without head trauma and combined head with other regional body trauma). Blunt trauma was the most common (70%) cause of mechanical trauma in the studied cases compared to sharp instrument trauma (12.50%) and firearm injuries (17.50%) with a statistically significant difference. As regards the survival time, significantly higher percentage (55%) of cases died 0.1-6 h after trauma compared to those died after 6hs and up to 7days (Table 1).

Table (2) shows that post mortem insulin-like growth factor 1 levels in the studied cases ranged from 50–150 ng/ml. There was significant decrease in IGF-1 levels in all the studied groups of traumatic deaths compared to the control group (natural death cases). Additionally, the mean IGF-1 level was significantly lower in group1 (104 ± 20.49 ng/ml) in comparison with group 2 (118.10 ± 20.46 ng/ml) (p=0.029). Moreover, combined head and other body trauma group (group 3) showed significantly lower mean IGF-1 level (83.60 ± 15.34 ng /ml) in relation to groups 1 and 2.

Table (3) demonstrates that mean IGF-1 level was significantly lower in cases with long survival (died after 24hs post trauma up to 7 days) compared to its level in those who died earlier (0.1 -6 h and >6-24 h post trauma) in all the studied groups. Additionally, post hoc Tukey's test per each studied group revealed rapid decline in IGF-1 levels in both groups 1 and 3 with significant differences between the three survivals time periods (In group 1, mean IGF-1 levels were 118.53 ± 14.39, 99.66 ± 3.78, and 77.00 ± 6.68 respectively while in group 3 they were 109.00 ± 8.01, 84.36 ± 4.10, and 61.25 ± 12.50 ng/ml respectively). On the other hand, group 2 showed no significant differences between IGF-1 levels in those died 0.1-6 h post trauma and the cases died in the time period 6h post trauma up to 24 h (p = 0.701).

Figure (1) demonstrates absence of significant association between IGF-1 levels (ng/ml) and the chronological age (years) in all the studied cases of traumatic deaths (r= 0.031, p=0.786). Figures (2, 3, and 4) illustrate significant negative correlation between IGF-1 levels and the survival time (hours) in the different studied groups of traumatic deaths. In group 1 ($r = -.810$, $p < 0.001$), in group 2 ($r = -.838$, $p < 0.001$), and lastly in group 3 ($r = -.907$, $p < 0.001$).

Prediction of survival time (h) by the detection of post mortem serum IGF-1 level was determined by simple linear regression analysis between IGF-1 levels and the survival time (h) in each studied group. In group 1; survival time (h) = 193.685 + (-1.619x IGF-1 level ng/ml) with accuracy of 65.6%. In group 2; the survival time (h) = 256.028 + (-1.887 x IGF-1 level ng/ml) with higher accuracy of 70.2%. Regarding the combined head and body trauma group (3), the survival time (h) = 123.340 + (-1.283 x IGF-1 level ng/ml) with higher accuracy of 82.3% (Table 4).

The autopsy description of the injuries was sufficiently detailed in only forty cases from all the studied mechanical traumatic deaths (80 cases), in whom death occurred within 6 h post trauma. The total AIS could be calculated to evaluate the severity of trauma. In these cases, the total AIS ranged from six to 36 with a median score of 17 and the interquartile range (25^{th} –75^{th} percentile) was 13 - 28.75 respectively. The IGF-1 levels in these cases ranged from 85-150 ng/ml with a median level of 111 ng/ml and the interquartile range was 95ng/ml (25^{th} percentile) – 131.25 ng/ml (75^{th} percentile). Spearman's rank correlation coefficient was used to evaluate the relationship between IGF-1 levels and the total AIS and revealed significant negative correlation ($r = -0.653$, p value < 0.001) as illustrated in figure (5).

Table (1) : Base line characteristics of the studied cases of mechanical traumatic deaths (n=80).

Characteristics		n	Percentage	Chi-Square X^2	p value
Age groups (years)	18-<30	35	43.75	21.92	< 0.001*
	30-<40	38	47.50		
	40-50	7	8.75		
Region of trauma	Group 1	20	25	2.50	0.287
	Group 2	30	37.5		
	Group 3	30	37.5		
Cause of trauma	Fall from height	11	13.75	52.12	< 0.001*
	Road traffic accidents	4	5.00		
	Other blunt trauma	41	51.25		
	Sharp instrument trauma	10	12.50		
	Firearm injuries	14	17.50		
Survival time	0.1-6h	44	55.00	16.97	< 0.001*
	>6-24h	19	23.75		
	>1d-7d	17	21.25		
Total		80	100		

n: number, *: significant at p ≤ 0.05, group (1): isolated head trauma cases, group (2): regional body trauma with intact head cases, group (3): combined head and other regional body trauma cases, h: hour, d: days.

Table (2) : Comparison of insulin- like growth factor 1(IGF-1) in the different studied groups of mechanical traumatic deaths and the control group (n=90).

		Traumatic deaths			Control group n=10
		Group (1) n =20	Group (2) n = 30	Group (3) n= 30	
		Range mean ± SD	Range mean ± SD	Range mean ±SD	Range mean ±SD
IGF1 level (ng/ml)		70 - 143 104± 20.49	80 – 150 118.10 ±20.46	50-115 83.60± 15.34	139 -270 190.50 ± 45.59
ANOVA	F	25.71			
	P value	< 0.001*			
	Post hoc Tukey's test	All groups are significant to each other. Group 1 versus group 2 (p=0.029*) Group 1 versus group 3 (p =0.001*) Group 2 versus group 3 (p < 0.001*)			

n: number, *: significant at p ≤ 0.05, group (1): isolated head trauma cases, group (2): regional body trauma with intact head cases, group (3): combined head and other regional body trauma cases, control group: non-traumatic natural death.

Table (3) : Comparison of insulin- like growth factor 1 (IGF-12) levels in the different survival time periods in each studied group of mechanical traumatic deaths (n =80).

Survival time periods		Traumatic deaths		
		Group1 n= 20	Group2 n= 30	Group 3 n= 30
		IGF1 level (ng/ml) mean ±SD	IGF1 level (ng/ml) mean ± SD	IGF1 level (ng/ml) mean ±SD
0.1-6h		118.53 ± 14.39	129.93 ± 14.54	109.00 ± 8.01
>6-24h		99.66 ± 3.78	124.80 ± 2.86	84.36 ± 4.10
>1-7d		77.00 ± 6.68	93.33 ± 10.88	61.25 ± 12.50
ANOVA	F	17.62	25.94	76.24
	p value	< 0.001*	< 0.001*	< 0.001*
	Post hoc Tukey's test	All are significant to each other [a]	All are significant to each other except 0.1-6 h vs >6-24 h (p = 0.701)	All are significant to each other p < 0.001*

n: number, *: significant at p ≤ 0.05, group (1): isolated head trauma cases, group (2): regional body trauma with intact head cases, group (3): combined head and other regional body trauma cases, h: hour, d: day.

a 0.1-6 h versus >6-24h: p = 0.017*

0.1-6 h versus >1-7d: p < 0.001*

>6-24 h versus >1-7d: p = 0.015*

Table (4) : Simple linear regression between insulin-like growth factor1 (IGF-1) levels and survival time (hs) in the different mechanical traumatic studied groups (n = 80).

	B coefficient	Standard Error	Beta	Unpaired t- test		R^2 (accuracy)
				T	p-value	
Group 1						
Constant	193.685	29.268		6.618	<0.001*	65.6%
IGF1	- 1.619	.276	-.810	-5.859	<0.001*	
Group 2						
Constant	256.028	27.836		9.198	<0.001*	70.2%
IGF1	-1.887	.232	-.838	-8.122	<0.001*	
Group 3						
Constant	123.340	9.543		12.925	<0.001*	82.3%
IGF1	-1.283	.112	-.907	-11.419	<0.001*	

n: number, *: significant at p ≤ 0.05, group (1): isolated head trauma cases, group (2): regional body trauma with intact head cases, group (3): combined head and other regional body trauma cases.

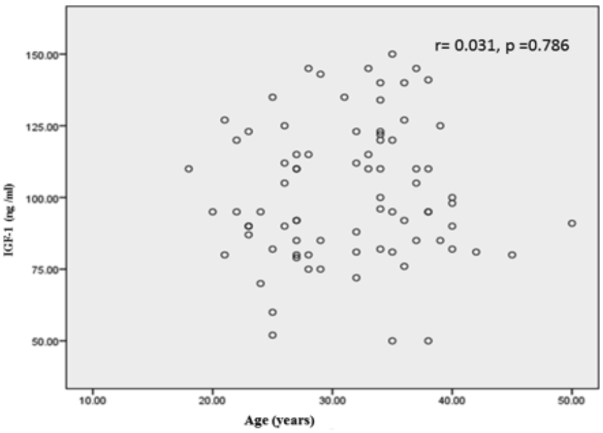

Fig. (1) : Correlation between IGF-1 level (ng/ml) and the chronological age of the studied cases (years).

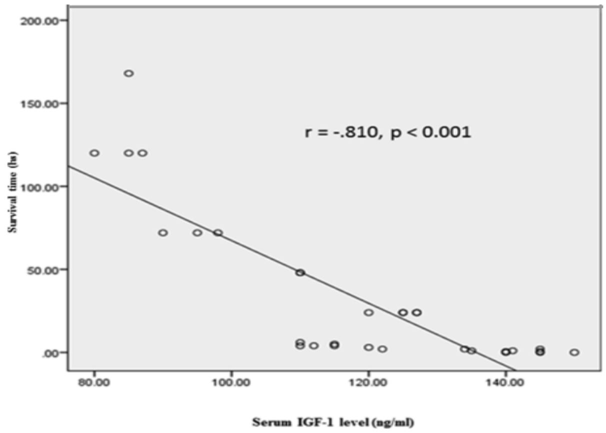

Fig. (2) : Correlation between IGF-1 level (ng/ml) and the survival time (h) in isolated head trauma cases (group 1).

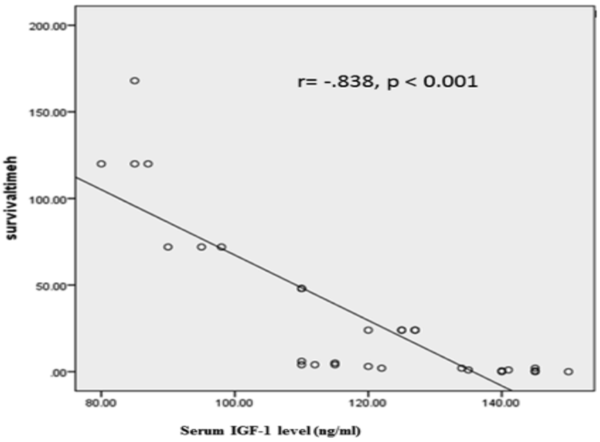

Fig. (3) : Correlation between IGF-1 level (ng/ml) and the survival time (h) in regional body trauma with intact head cases (group 2).

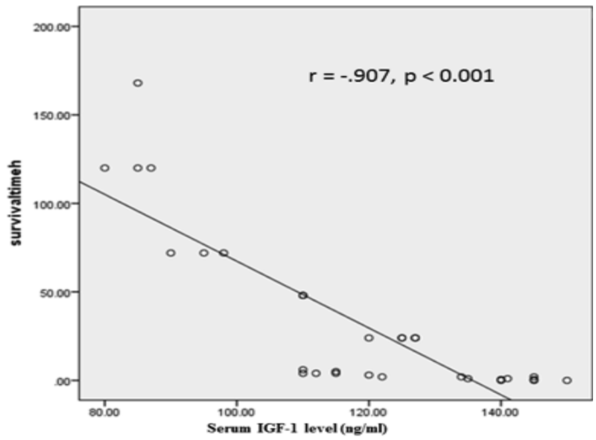

Fig. (4) : Correlation between IGF-1 level (ng/ml) and the survival time (h) in combined head and other regional body trauma cases (group 3).

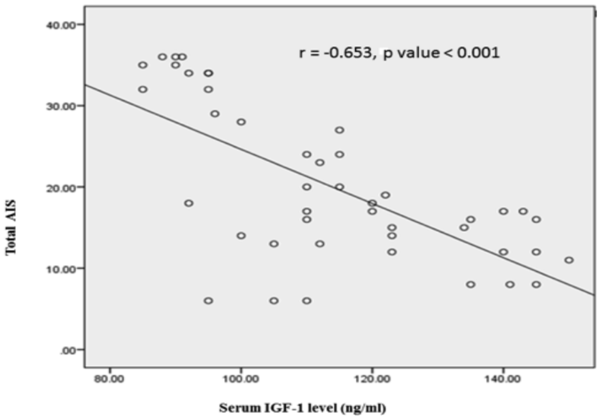

Fig. (5) : Correlation between postmortem serum insulin like growth factor 1 levels (ng/ml) and the total abbreviated injury scale (AIS) in forty cases of mechanical traumatic deaths.

DISCUSSION

Medicolegal investigation of traumatic deaths requires the determination of important issues like cause of death, post mortem interval, and survival time by the forensic pathologist (Jalalzadeh et al., 2015).

The question of victim's survival time with the possibility of physical activity and the association of injury to the event of death is often raised in homicidal cases (Cros et al., 2013). Besides gross and histologic examination of the injury, post mortem biochemistry is considered one of the important tools in the forensic work (Maeda et al., 2009).

In this study, postmortem serum IGF-1 levels in males died from mechanical trauma were studied with special regard to its relationship with the survival time and the severity of trauma.

This study demonstrated low postmortem serum IGF-1 levels in males died from mechanical trauma compared to the matched control group of nontraumatic natural deaths and age-related reference values reported in the literature (Blum, 1996). The possible effect of age of the studied cases on the measured IGF-1 values was statistically tested and revealed non-significant correlation between serum IGF-1 levels and the chronological age of all the studied cases. Therefore, all the analyzed IGF-1 values in this study are not confounded by the deceased age.

Regarding the differences between the involved body regions, postmortem serum IGF-1 levels were lower in both the isolated head trauma and combined head with other regional body trauma cases compared to those with regional body trauma without head trauma. To the best of our knowledge, this is the first study to measure postmortem serum levels of IGF-1 in cases with fatal mechanical trauma. However, several previous studies investigated IGF-1 levels in patients with acute trauma; in head injury patients with or without femoral fractures, Beeton et al. (2002) reported lower circulating IGF-1 levels in head injury and combined head injury and fractures patients than those with only fractures. Additionally, Sanus et al. (2007) reported significant decrease in IGF-1 levels in patients with severe head injury when compared with controls. Other earlier studies showed reduced serum IGF-1 levels in patients with severe polytrauma (Jeevanandam et al., 1992; Jeevanandam et al., 1995; Houston-Bolze et al., 1996).

In traumatic brain injuries, IGF-1 is considered an endogenous neuroprotective agent that helps to limit the injury (Guan and Gluckman, 2009). In experimental animals, studies of traumatic brain injuries including cortical compact injury (Madathil et al., 2010) and penetrating injury (Kazanis et al., 2003; Kazanis et al., 2004) reported induced IGF-1expression and increased IGF-1 levels in the injured brain tissue. This is explained by selective passage of IGF-1 across the blood brain barrier via transcytosis in to the injured brain tissues (Davila et al., 2007) with subsequent decline in the circulating IGF-1 levels.

Growth hormone deficiency, the main regulator of IGF-1 secretion from the liver, is another suggested mechanism of the reported low IGF-1 in head trauma cases (Berryman et al., 2013). Growth hormone deficiency was reported to be the most common pituitary deficit in acute and long-term pituitary insufficiency due to moderate to severe traumatic brain injury (Schneider et al., 2005; Klose et al., 2007; Alavi et al., 2015; Prasanna et al., 2015). Forensic autopsy of subjects who survived 12 h after traumatic brain injury showed that 35% of them have infarction involving approximately 70% of the anterior pituitary in the peripheral region that is responsible for growth hormone secretion (Kornblum and Fisher, 1996; Urban, 2006). This could be explained by two proposed mechanisms: compression of the pituitary gland and/or the hypothalamic nuclei due to oedema, skull fracture, haemorrhage, increased intracranial pressure, hypoxic insult, or direct mechanical injury to the hypothalamus, pituitary stalk or the pituitary gland (Kelly et al., 2000; Bondanelli et al., 2005).

The observed low IGF-1 levels in cases with body trauma without head involvement may be attributed to hypoxia and acidosis that complicates trauma (Dinleyici et al., 2006). This is supported by Hannon et al. (2011) who stated that patients with acute critical illness are usually associated with hormonal changes including low IGF-1 levels that most likely attributed to physiological adaptation to severe physiological stress. In addition, Jeevanandam et al. (1995) reported a hyper catabolic state in those acute polytraumatic patients who survived for days. This hypercatabolic state reduces growth hormone secretion or actions on its receptors which in turn reduces IGF-1 levels. Moreover, reduced IGF-1 levels with long survival could be attributed to the involvement of IGF-1in wound healing phases including proliferative and/or migratory response of the epithelial cells, deposition of various components of extracellular matrix as well as angiogenesis (Ando and Jensen, 1993; Aghdam et al., 2012).

There is a need for precise determination of survival time in the medicolegal investigation of traumatic deaths. This may help to confirm or refute a witness and statements (Itabashi et al., 2011). This was considered in this study and there was a significant negative correlation between IGF-1 levels and the survival time with time dependent decrease in IGF-1 levels. Cases with long survival (died after 24 h post trauma up to 7 days) showed significant lower levels compared to those who died earlier in all the studied groups of traumatic deaths. This decline in IGF-1 levels occurred early in response to the mechanical trauma even in cases of rapid death in the scene (0.1 h) and the time course of it was observed to be rapid in both isolated head trauma cases and combined head with other regional body trauma cases that remained significant when all the studied time points were considered.

On the other hand, isolated body trauma cases with intact head region showed early but gradual decline with no significant differences between IGF-1 levels in the first 24h following trauma. This agrees with Schwab et al (1997) who demonstrated progressive decline in plasma IGF-1 levels over a period of 10 days in patients with acute cerebral ischemia. In contrast, Olivecrona et al. (2013) found a relatively transient decrease in serum IGF-1 level after severe traumatic brain injury that was restored towards normal on day 4. This has been attributed to a state of acquired peripheral growth hormone resistance in the critical illness phase of trauma (Van den Berghe et al., 2000). It is worth to mention that gradual increase in IGF-1 concentrations in the weeks following trauma was only demonstrated in survivor patients with healing bony fractures and traumatic brain injuries (Wildburger et al., 2001).

The potential predictive value of the post mortem serum IGF-1 level for the survival time (h) was studied by simple linear regression analysis. This revealed regression equations with increasing accuracy according to the involved body region (65.6%, 70.2%, and 82.3% in isolated head trauma, other regional body trauma with intact head, and combined head and other regional body trauma respectively). Insulin-like growth factor 1 as a biochemical predictor of survival time as demonstrated in these equations is a new helpful tool supportive to the hisopathological and immunohistochemical procedures of time dependent changes of the injury site (Kondo et al., 1999; Hausmann and Betz, 2002; Kagawa et al., 2009). However, the severity of tissue damage is a confounder factor which may have an effect on the time and pattern of IGF-1 response to trauma. Unfortunately, this could not be analyzed in all the studied cases of mechanical traumatic deaths due to limitations in describing details of trauma. In forty out of the total studied cases with survival period up to 6 h post trauma, total AIS was calculated and there was significant negative correlation between IGF-1 levels and the severity of anatomical traumas represented by the total AIS.

In clinical practice, many trauma scoring systems are available to evaluate the severity of trauma and its outcome (Chawda et al., 2004). However, most of them include physiological variables such as blood pressure, heart rate, coma level, respiratory rate, etc., and are, therefore, unsuitable for postmortem applications. The simple AIS scoring system seems to be the most appropriate system in forensic conditions because it evaluates the anatomical severity of injuries.

In conclusion, this study demonstrated for the first time low postmortem serum IGF-1 levels in males died from mechanical trauma with significant negative correlation with the survival time and trauma severity. Insulin- like growth factor 1 response to trauma differed by the involved body region where postmortem IGF-1 levels were lower in the isolated head trauma and combined head and other body regions trauma cases compared to regional body trauma other than head cases.

ACKNOWLEDGEMENT

The authors wish to convey their full appreciation to Hanan Farouk El-Faresy, a forensic pathologist at El Mansoura Department, Medicolegal Institute, Ministry of Justice, Egypt for her kind help in data collection.

REFERENCES

Aghdam, S.Y.; Eming, S. A.; Willenborg, S.; et al. (2012): "Vascular endothelial insulin/IGF-1 signaling controls skin wound vascularization". Biochem. Biophys. Res. Commun., 421(2):197-202.

Alavi, S. A.; Tan, C. L.; Menon, D. K.; et al. (2015): " Incidence of pituitary dysfunction following traumatic brain injury: A prospective study from a regional neurosurgical center". Br. J. Neurosurg., 1-5.

American Association for Automotive Medicine (1985): "The abbreviated injury scale (AIS)-1985 revision". Des. Plans Illinois.

Ando, Y. and Jensen, P.J. (1993): "Epidermal growth factor and insulin-like growth factor I enhance keratinocyte migration". J. Invest. Dermatol., 100(5):633-639.

Beeton, C. A.; Brooks, R. A.; Chatfield, D.; et al. (2002): "Circulating levels of insulin-like growth factor-1 and insulin-like growth factor binding protein-3 in patients with severe head injury". J. Bone

Joint Surg. Br., 84(3): 434-439.

Berryman, D. E.; Glad, C. A.; List, E. O.; et al. (2013): "The GH/IGF-1 axis in obesity: pathophysiology and therapeutic considerations". Nat. Rev. Endocrinol., 9 (6): 346-356.

Blum, W. (1996): Insulin-like growth factors and their binding proteins. In: Diagnostics of Endocrine Function in Children and Adolescents. Ranke MB, ed., Heidelberg, Germany, Barth. Verlag., P.P. 190-218.

Bondanelli, M.; Ambrosio, M.R.; Zatelli, M.C.; et al. (2005): "Hypopituitarism after traumatic brain injury". Eur. J. Endocrinol., 152: 679-691.

Byrne, T.A.; Morrisey, T.B.; Gatzen, C.; et al. (1993): "Anabolic therapy with growth hormone accelerates protein gain in surgical patients requiring nutritional rehabilitation". Ann. Surg., 218:400-418.

Chawda, M. N.; Hildebrand, F.; Pape, H. C.; et al. (2004): "Predicting outcome after multiple trauma: which scoring system"? Injury, 35(4): 347-358.

Civil, I.D. and Schwab, C.W. (1988): "The abbreviated injury scale, 1985 revision: a condensed chart for clinical use". J. Trauma, 28:87-90.

Cros, J.; Alvarez, J. C.; Sbidian, E.; et al. (2013): "Survival time estimation using Injury Severity Score (ISS) in homicide cases". Forensic Sci. Int., 233(1): 99-103.

Davila, D.; Piriz, J.; Trejo, J. L.; et al. (2007): "Insulin and insulin-like growth factor I signaling in neurons". Front. Biosci., 12: 3194-3202.

Dinleyici, E.C.; Tekin, N.; Colak, O.; et al. (2006): "Cord blood IGF-1 and IGFBP-3 levels in asphyxiated term newborns". Neuro. Endocrinol. Lett., 27(6): 745-747.

Guan, J. and Gluckman, P. D. (2009): "IGF-1 derived small neuropeptides and analogues: a novel strategy for the development of pharmaceuticals for neurological conditions". Br. J. Pharmacol., 157(6), 881-891.

Hannon, M.J.; Sherlock, M. and Thompson, C.J. (2011): "Pituitary dysfunction following traumatic brain injury or subarachnoid haemorrhage - In: Endocrine Management in the Intensive Care Unit." Best Pract. Res. Clin. Endocrinol. Metab., 25(5):783-798.

Hausmann, R. and Betz, P. (2002): "The course of MIB-1 expression by cerebral macrophages following human brain injury". Legal Med., 4:79-83.

Houston-Bolze, M.S.; Downing, M.T.;

Sayed, A. M.; et al. (1996): "Gender differences in the responses of serum insulin-like growth factor-1 and transthyretin (prealbumin) to trauma". `Crit. Care Med., 24(12):1982-1987.

Itabashi, H. H.; Andrews, J. M.; Tomiyasu, U. (2011): Dating/aging of common lesions in neuropathology. In: Forensic Neuropathology: A Practical Review of the Fundamentals. Itabashi, H.H.; Andrews, J.M.; Tomiyasu, U.; Erlich, S.S.; Sathyavagiswaran, L.; Eds. Amsterdam, Netherlands: Elsevier. P. 49.

Jalalzadeh, H.; Giannakopoulos, G. F.; Berger, F. H.; et al. (2015): "Post-mortem imaging compared with autopsy in trauma victims-A systematic review". Forensic Sci. Int., 257: 29-48.

Jeevanandam, M.; Holaday, N. J. and Petersen, S. R. (1995): "Plasma levels of insulin-like growth factor binding protein-3 in acute trauma patients". Metabolism, 44 (9): 1205-1208.

Jeevandam, M.; Holaday, N. J.; Shamos, R. F.; et al. (1992): "Acute IGF-1 defeciency in multible trauma victims"'. Clin. Nutr., 11: 352-357.

Kagawa, S.; Matsuo, A.; Yagi, Y.; et al. (2009): "The time-course analysis of gene expression during wound healing in mouse skin". Legal Med., 11: 70-75.

Kazanis, I.; Bozas, E.; Philippidis, H.; et al. (2003): "Neuroprotective effects of insulin-like growth factor-I (IGF-I) following a penetrating brain injury in rats". Brain Res., 991: 34-45.

Kazanis, I.; Giannakopoulou, M.; Philippidis, H.; et al. (2004): "Alterations in IGF-I, BDNF and NT-3 levels following experimental brain trauma and the effect of IGF-I administration". Exp. Neurol., 186: 221-234.

Kelly, D.F.; Gonzalo, I.T.W.; Cohan, P. et al. (2000): "Hypopituitarism following traumatic brain injury and aneurysmal subarachnoid hemorrhage: a preliminary report". J. Neurosurg., 93: 743-752.

Klose, M., Juul, A., Struck, J., Morgenthaler, N. G.; et al. (2007): "Acute and long-term pituitary insufficiency in traumatic brain injury: a prospective single-centre study". Clin. Endocrinol., 67(4): 598-606.

Kondo, T.; Ohshima, T. and Eisenmenger, W. (1999): "Immunohistochemical and morphometrical study on the temporal expression of interleukin-1alpha (IL-1alpha) in human skin wounds for forensic wound age determination". Int. J. Legal Med., 112: 249-252.

Kornblum, R.N. and Fisher, R.S. (1996): "Pituitary lesions in craniocerebral injuries". Arch. Pathol., 88: 242-248.

Madathil, S. K.; Evans, H. N. and Saatman, K. E. (2010): "Temporal and regional changes in IGF-1/IGF-1R signaling in the mouse brain after traumatic brain injury". J. Neurotrauma, 27(1): 95.

Maeda, H.; Ishikawa, T. and Michiue, T. (2011): "Forensic biochemistry for functional investigation of death: concept and practical application". Leg. Med. (Tokyo), 13:55-67.

Maeda, H.; Zhu, B. L.; Ishikawa, T.; et al. (2009): "Significance of postmortem biochemistry in determining the cause of death". Leg. Med., 11: S46-S49.

Mangiola, A.; Vigo, V.; Anile, C.; et al. (2015): "Role and importance of IGF-1 in traumatic brain injuries". Biomed. Res. Int. 2015:1-12.

Mimasaka, S.; Ohtsu, Y.; Tsunenari, S.; et al. (2006): "Postmortem cytokine levels and severity of traumatic injuries". Int. J. Legal Med., 120(5): 265-270.

Olivecrona, Z.; Dahlqvist, P. and Koskinen, L. O. (2013): "Acute neuroendocrine profile and prediction of outcome after severe brain injury". Scand. J. Trauma Resusc. Emerg. Med., 21: 33.

Prasanna, K. L.; Mittal, R. S. and Gandhi, A. (2015): "Neuroendocrine dysfunction in acute phase of moderate-to-severe traumatic brain injury: A prospective study". Brain Inj., 29(3): 336-342.

Quan, L.; Zhu, B. L.; Ishikawa, T.; et al. (2010): "Postmortem serum erythropoietin level as a marker of survival time in injury deaths". Forensic Sci. Int., 200(1): 117-122.

Rhee, P.; Joseph, B.; Pandit, V.; et al. (2014): "Increasing trauma deaths in the United States". Ann. Surg., 260:13-21.

Sanus, G. Z.; Tanriverdi, T.; Coskun, A.; et al. (2007): "Cerebrospinal fluid and serum levels of insulin-like growth factor-1 and insulin-like growth factor binding protein-3 in patients with severe head injury". Ulus. Travma. Acil. Cerrahi Derg., 13(4):281-287.

Schneider, M.; Schneider, H. J. and Stalla, G. K. (2005): "Anterior pituitary hormone abnormalities following traumatic brain injury". J. Neurotrauma, 22(9): 937-946.

Schwab, S.; Spranger, M.; Krempien, S. et al. (1997): "Plasma insulin-like growth factor I and IGF binding protein 3 levels in patients with acute cerebral ischemic injury". Stroke, 28(9): 1744-1748.

Urban, R.J. (2006): "Hypopituitarism after acute brain injury". Growth Hormone

& Insulin Growth Factor Research, 16: 25-29.

Van den Berghe, G. (2000): "Increased mortality associated with growth hormone treatment in critically ill adults". N. Engl. J. Med., 2(2):135.

Walsh, P.T.; Smith, L. M.; O'Connor, R. (2002): "Insulin-like growth factor-1 activates Akt and Jun N-terminal kinases (JNKs) in promoting the survival of T lymphocytes". Immunology, 107: 461-471.

Wildburger, R.; Zarkovic, N.; Leb, G.; et al. (2001): "Post-traumatic changes in insulin-like growth factor type 1 and growth hormone in patients with bone fractures and traumatic brain injury". Wien. Klin. Wochenschr., 113(3-4): 119-126.

Wojnar, M. M.; Fan, J.; Frost, R. A.; et al. (1995): "Alterations of the insulin-like growth factor system in trauma patients". Am. J. Physiol., 268: 970-977.

تقييم مستوى عامل النمو مثيل الإنسولين ١ فى المصل فى الوفيات الإصابية وعلاقته بفترة البقاء على قيد الحياة وشدة الإصابة

المشتركون فى البحث

د. منى محمد أبو النور د. فاطمة محمد الجزار
د. غـــادة الشافعــى

من أقسام الطب الشرعي والسموم الإكلينيكية - الباثولوجيا الإكلينيكية*

كلية الطب - جامعة طنطا - مصر.

أظهرت العديد من الدراسات السريرية إنخفاض في مستويات IGF-1 في مرضى الإصابات الحادة. وكان الهدف من هذه الدراسة هو دراسة مستوى IGF-1 في مصل الدم في حالات الوفاة الاصابية وخاصة علاقته مع فترة البقاء على قيد الحياة وشدة الإصابة. وقد أجريت هذه الدراسة على ثمانين حالة توفيت من أثر الإصابة الميكانيكية والتي خضعت للتشريح بمصلحة الطب الشرعي بمدينة المنصورة خلال الفترة من بداية يناير ٢٠١٤ إلى نهاية أكتوبر ٢٠١٥. وقد شملت الدراسة فقط حالات الذكورالبالغين ذوى ثمانية عشر عاما أو أكثر. بينما تم استبعاد الحالات المتحللة وكذلك الحالات التي لم يتم التأكد من فترة بقائها على قيد الحياة. وقد تضمنت بيانات كل حالة العمر وسبب الإصابة وموضعها من الجسم، و فترة البقاء على قيد الحياة وسبب الوفاة، بالإضافة إلى ذلك تم أخذ عينات دم من الناحية اليمنى للقلب لتحديد مستوى IGF-1. وقد تم تصنيف الحالات محل الدراسة وفقا للمنطقة المصابة من الجسم إلى ثلاث مجموعات :المجموعة الأولى والتي شملت إصابة في الرأس فقط (٢٠ حالة) المجموعة الثانية والتي شملت إصابة في الجسم بينما منطقة الرأس سليمة (٣٠ حالة) والمجموعة الثالثة والتي شملت إصابات مجمعة في الجسم شاملة الرأس (٣٠ حالة) حالة وقد تم اختيار مجموعة ضابطة من عشر حالات من الذكور من الوفيات الطبيعية الغير اصابية متطابقة في العمر مع الحالات الاصابية. وقد لوحظ انخفاض ذو دلالة إحصائية في مستوى IGF-1 في كل مجموعات الوفيات الاصابية محل الدراسة مقارنة مع المجموعة الضابطة. بالإضافة إلى ذلك كان مستوى IGF-1 فى المجموعة الثالثة منخفضا بدرجة كبيرة مقارنة بالمجموعتين الأولى والثانية. فى جميع الحالات محل الدراسة كان هناك إرتباط سلبى ذو دلالة إحصائية بين مستويات IGF-1 فى المصل ومدة البقاء على قيد الحياة (ساعة) وقد تم استخدم تحليل الانحدار الخطي للتنبؤ بوقت البقاء على قيد الحياة. كان هناك أيضا إرتباط سلبى ذو دلالة إحصائية بين مستويات IGF-1 فى المصل وشدة الإصابة. يمكن أن نخلص إلى أنه أظهرت هذه الدراسة للمرة الأولى انخفاضا فى مستوى IGF- 1 في المصل فى وفيات الذكور الإصابية مع وجود إرتباط سلبى مع فترة البقاء على قيد الحياة وشدة الإصابة.