The role of cortisol and thyroid stimulating hormone in prognosis of acute anticholinesterase pesticides poisoned patients admitted to Tanta Poison Control Center

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Abstract	**Introduction:** Anticholinesterase poisoning is a major global health problem with thousands of deaths each year. Determination of prognosis is a major concern for clinical toxicologists. Previous studies reported that cortisol and thyroid stimulating hormone (TSH) may have prognostic role in patients poisoned by organophosphates. **Aim of the work:** Evaluation of prognostic role of cortisol and TSH in acute anticholinesterase pesticides poisoned patients admitted to Tanta Poison Control Center. **Methodology:** This prospective study included 29 patients of moderate to severe acute anticholinesterase poisoning according to poisoning severity score (PSS) between August 2019 and July 2020. TSH and serial cortisol were assessed by ELISA techniques. **Results:** TSH has no prognostic role, but cortisol has predictive role in mortality, need for ICU admission and intubation. **Conclusion:** Measuring cortisol at admission, after six and twelve hours from admission could predict need for ICU admission, intubation and mechanical ventilator, while measuring it at admission can be predictor for mortality.

Introduction

Anticholinesterase pesticides are common to be used in Egypt due to their wide availability and cheap prices. They are considered to be frequent reasons for admission in hospitals and intensive care units (ICU) in developing countries (Arafa et al., 2017 & Elagamy and Gaber, 2019)

Organophosphorous and carbamates poisoning cause acetylcholinesterase (AChE) inhibition at cholinergic synapses at the central nervous system and autonomic nervous system, as well as at the neuromuscular junction (NMJ) resulting in excess sweating, salivation, bronchospasm, bronchorrhea, bradycardia, NMJ dysfunction and disturbed consciousness (Arafa et al., 2017).

During critical illness, profound changes may occur in the hypothalamic-pituitary-thyroid (HPT) and hypothalamic-pituitary-adrenal axes (HPA) with increase in cortisol level. At the level of the hypothalamus, thyrotropin-releasing hormone (TRH) is released and stimulates the thyrotropic cells in the pituitary to synthesize and secrete thyroid-stimulating hormone (TSH). TSH in turn drives the thyroid gland to synthesize and secrete thyroid hormones (Abo Elfottoh et al., 2020).

Specifically, Rao and Bhavana (2015) reported that human thyroid has cholinergic innervation.

Acetylcholine (Ach) as a neurotransmitter has been detected in the human body including the brain, vascular system, urogenital system, and endocrine system. Anticholinesterase can affect the endocrine system through hormone receptors, synthesis, and transcription factors. They exert their effects on pituitary hormones in the acute and chronic periods by decreasing cholinesterase levels (Şimşek et al., 2019).

Several animal studies revealed that cholinesterase inhibition causes endocrine disruption, affect adrenal gland steroidogenesis and Adrenocorticotropic hormone (ACTH) secretion so, affect cortisol level (Goad et al, 2004).

Determination of prognosis is a major concern for clinical toxicologists managing acutely poisoned patients. Prognostic factors facilitate appropriate disposition to limited ICU beds. (Alizadeh et al., 2014).

Therefore, the aim of the present study was to evaluate the prognostic role of cortisol and thyroid stimulating hormone (TSH) in acute anticholinesterase pesticides poisoned patients admitted to Tanta Poison Control Center.

Patients and Methods

Patients: This study was a prospective cohort study conducted on patients suffering from acute anticholinesterase pesticides poisoning who were admitted to the Poison Control Center of Tanta University Emergency Hospital, Tanta, Egypt, between August 2019 to end of July 2020. The study was approved by the Research Ethics Committee of the Faculty of Medicine, Tanta University. An informed written consent was obtained from each patient (or his attending relatives if unable to do so) after receiving

detailed information about the study (Research ethics committee approval number: 33251/7/19) and data was collected through a standardized checklist. Privacy and confidentiality of patients and results of investigations were maintained by using coding number.

Inclusion criteria:

Patients of both sexes with moderate to severe symptoms of acute anticholinesterase poisoning according to poisoning severity score (PSS) (Persson et al., 1998) with diagnosis made on the basis of:

1. History taking either from patient himself or relatives.
2. Identification of the compound based on the container brought by patient or attendants if possible.
3. Manifestations of anticholinesterase poisoning as excess sweating, salivation, bronchospasm, bronchorrhea, bradycardia, hypotension, neuromuscular junction dysfunction (Tattersall, 2018).
4. Psudocholinesterase activity.
5. (Normal values at 37 ℃: in Children, men of all ages and women over 40 years: 5400- 13200 U/L, Women 18-39 years: 4300- 11500 U/L) (Blawen et al., 1983).

Exclusion criteria:

1. Asymptomatic and mild cases.
2. Patients with history of co-ingestion.
3. Patients with history of thyroid disease.
4. Patients on steroid therapy
5. Pregnant and lactating women.
6. Patients with chronic and psychiatric diseases.
7. Conditions that affect pseudocholinesterase activity as malignancy, liver/kidney disease, pregnancy, burns, obesity, chronic alcoholism and medications as aspirin, metoclopramide, monoamine oxidase inhibitors and oral contraceptives (Lee et al., 2013).

Methodology: all cases were subjected to:

▪ History taking: Sociodemographic data including age and sex, toxicological history includes route of administration either inhalation, ingestion or dermal exposure, amount of pesticides taken (in case of ingestion), mode of poisoning either suicidal or accidental, time delay between pesticides exposure and hospital admission and any prehospital intervention.

▪ Clinical examination: Physical examination as vital signs (pulse, blood pressure, respiratory rate and temperature), level of consciousness assessed by Glasgow coma scale and systemic examination including neurological, respiratory, cardiovascular and abdominal examinations.

The normal values of vital signs are: Pulse ranges between 60 to 100 beat per minute, blood pressure ranges between 90\60 mmhg to 140\90 mmhg, respiratory rate ranges between 12 to 20 breaths per minute (Hoffman et al., 2011) and temperature ranges between 36.5 to 37.5℃ (Nield and Kamat, 2011).

▪ Laboratory investigations: includes arterial blood gases, serum sodium and potassium levels, random blood sugar, pseudocholinesterase activity, serum cortisol level assessed by ELISA technique (serial measurements on admission, after 6 hours and after 12 hours) and serum thyroid stimulating hormone (TSH) level on admission assessed by ELISA technique.

▪ Electrocardiogram (ECG).

▪ Outcome measures (prognosis): Improved or died, need for ICU admission and assisted ventilation, ICU admission duration, total hospital admission duration and total needed amount of antidote therapy.

Criteria needed for ICU admission and assisted ventilation are: respiratory failure, ventricular arrhythmia and unstable hemodynamics (Sungur and Güven, 2001).

▪ Treatment: Started by providing an adequate airway, oxygenation, and ventilation and at stabilizing cardiorespiratory function by reversing excessive muscarinic effects. Once the patient become stable, the administration of an AChE-reactivating oxime drug, such as pralidoxime or obidoxime, can be considered along with the need for skin and/or gastric decontamination (Eddleston, 2019).

Statistical analysis

Statistical analysis was performed using Statistical Package for Social Sciences (IBM SPSS Statistics) for Windows, version 26 (IBM Corp., Armonk, N.Y., USA). For quantitative data, the Shapiro-Wilk test for normality was performed. For data that followed normal distribution, values were expressed as mean ± standard deviation. For data that did not follow normal distribution, median, interquartile range (expressed as 1st and 3rd quartiles), and range (expressed as minimum to maximum) were calculated.

Results

In this study, there were twenty-nine acute anticholinesterase pesticides poisoned patients.

Table (1) shows the sociodemographic and toxicological data of our studied patients. Majority of cases (69%) were below twenty years old (16-19 years) and 58.6% of them came from rural areas. The predominant sex was female (62.1%). Concerning toxicological history, all cases ingested pesticides with suicidal intention and the mean time delay was 3.2 hours.

As regards clinical examination of our included patients presented in table (2), all of them had normal blood pressure. Sixty-five and half percent (65.5%) of patients had normal heart rate and the rest of cases presented with tachycardia on admission. Normal respiratory rate and normal blood sugar were found in 72.4 % and 86.2% of our patients respectively. As regards conscious level, 93.1% of patients were fully conscious. Two patients presented with disturbed conscious level (GCS 7\15). Chest findings showed that four patients had chest crepitation and two patients had wheezy chest. Cardiovascular and abdominal examinations were normal in all cases.

As regards investigations, normal ABG and normal sodium level were found in majority of our patients with percentage of 69% and 93.1% respectively. Abnormalities in ABG results were detected in 31% of patients; in the form of respiratory alkalosis observed in 10.3% and respiratory acidosis in 6.9% of patients. Concerning potassium level,

hypokalemia was observed in majority of studied patients (58.6%). Mean pseudocholinesterase activity was 1100±800 U/L.

Tables (3,4) show the levels of measured hormones of studied patients; median serum TSH was 1.14 mIU/L. Regarding cortisol, by comparing data in the three measurements, there was significant difference when comparing first and second measurements and when comparing first and third measurements *(P value was<0.001).*

Normal ECG was found in 93.1%, of patient and 6.9% of patients had sinus tachycardia.

As regards outcome, only two patients died (6.9%) because of respiratory failure and four patients (13.8%) needed ICU admission, intubation and mechanical ventilation due to bronchorea and respiratory muscles weakness that caused hypoxia. The mean ICU admission duration was 48 hours and the mean of total hospital admission duration was 39± 29 hours. Concerning PSS, only two cases (6.9%) had severe toxicity. Rest of patients had moderate toxicity according to this scale.

Tables (5, 6) show the relationship between levels of TSH, cortisol hormones and mortality, there was no significant difference between survivors and non survivors as regards TSH level *(P value was >0.05).* As regards cortisol, there was significant difference between survivors and non survivors in the first (on admission) estimation only *(P value was<0.05).*

With concern to relationship between measured hormones and need for ICU admission and assisted ventilation, there was no significant difference in patients needed ICU admission and assisted ventilator and patient didn`t need regarding TSH level *(P value was >0.05)* as shown in table (7). Moreover, there was significant difference between them regarding the three serial cortisol estimations *(P value were <0.05).*

As regards relationship between hormones and pseudocholinesterase activity, there was only significant association with cortisol level after 6 hours *(P value <0.05).* While correlation between level of hormones and total antidote therapy given showed that there was only significant association between total number of atropine ampules and second measurement of serum cortisol level *(P value was <0.05)* as mentioned in table (9).

Table (10) and figure (1) show the results of ROC curve of serum cortisol level at admission as predictor for mortality in anticholinesterase pesticides poisoned patients. It had AUC of 1 which is graded as excellent one. The optimum cut-off value was identified at > 80.9 μg/dl. So at this point, cortisol level had a sensitivity and specificity of 100%.

As regards need for ICU admission, intubation and mechanical ventilation, the second and third cortisol measurements had AUC of 1 which is graded excellent. The optimum cutoff value for both measurements were identified at >62.7 and >30.2 μg/dl respectively, so at this level they had 100% specificity and sensitivity as shown in figures (2-4) and table (11).

Table (1): Distribution of sociodemographic and toxicological data of 29 cases of anticholinesterase pesticides poisoning included in the study:

	Age			Sex		Residence		Route of administration		Mode of poisoning		Prehospital intervention		Mean Delay time
	16-19	20-29	30-37	Male	Female	Urban	Rural	Oral	Inhalation	Suicidal	Accidental	Yes	No	3.2 hours
Number of cases / percentages	20 (69%)	8 (27.9%)	1 (3.4%)	11 (37.9%)	18 (62.1%)	12 (41.4%)	17 (58.6%)	29 (100%)	0 (0%)	29 (100%)	0 (0%)	7 (24.1%)	22 (75.9%)	

Table (2): Distribution of vital signs and level of consciousness among 29 cases of anticholinesterase pesticides:

	Pulse		Blood pressure		Respiratory Rate			Random Blood Sugar		Level of Consciousness	
	Normal	tachycardia	Normal	abnormal	Normal	Tachypnea	Bradypnea	Normal	Hyperglycemia	Conscious	DCL
Number of cases / percentages	19 (65.5%)	10 (34.5%)	29(100%)	0 (0%)	21 (72.4%)	6 (20.7%)	2 (6.9%)	25 (86.2%)	4 (13.8%)	27 (93.1%)	2 (6.9%)

Table (3): Thyroid stimulating hormone level (mIU/L) of 29 cases of anticholinesterase pesticides poisoning:

Thyroid stimulating hormone (mIU/L)			
Range	1st quartile	Median	3rd quartile
0.36-3.12	0.96	1.14	1.51

Table (4): Friedman test: statistical analysis to compare serial cortisol levels (µg/dl) for 29 poisoned cases by anticholinesterase pesticides:

Cortisol (µg/dl)	At Admission	After 6 Hours	After 12 Hours	X^2	P
Range	15.1-82.2	9.17-64.50	4.24-84.00	15.600	<0.001*
Median	47.3	28.20	23.50		
Post Hoc Dun Bonferrani	P1: 0.001*	P2: 0.279	P3: 0.001*		

X^2: *Friedman test, *: statistically significant result at P value<0.05, P1: comparing level at admission with level at 6 hours, P2: comparing level at 6 hours with the level at 12 hours, P3: comparing level at admission with the level at 12 hours*

Table (5): Mann whitey U test: statistical analysis to compare between survivors and non-survivors among 29 cases of anticholinesterase pesticides poisoning included in this study regarding TSH level (mIU/L):

TSH (mIU/L)	Outcome		Z	P
	Survivors N= 27	Non-survivors N= 2		
1st quartile	0.96	1.51		
Median	1.14	1.51	-1.126	0.260
3rd quartile	1.67	1.51		

*TSH: thyroid stimulating hormone, Z: Mann whitey U test, *: statistically significant result (P value<0.05)*

Table (6): Mann whitey U test: statistical analysis to compare between survivors and non-survivors among 29 cases of anticholinesterase pesticides poisoning included in this study regarding serial cortisol measurements (µg/dl):

Cortisol (µg/dl)	Outcome		Z	P
	Survivors N= 27	Non-survivors N= 2		
Cortisol at admission				
1st quartile	32.9	82.2		
Median	47.3	82.2	**2.328**	**0.020***
3rd quartile	54.1	82.2		
Cortisol after 6 hours				
1st quartile	19.95	-		
Median	28.20	-		
3rd quartile	39.95	-	**Not Applicable**	
Cortisol after 12hours				
1st quartile	18.20	-		
Median	23.50	-		
3rd quartile	29.40	-		

*Z: Mann whitey U test, *: statistically significant result (P value<0.05)*

Table (7): Mann whitey U test: statistical analysis for comparison between 29 cases of anticholinesterase pesticides poisoning who needed intensive care unit admission, intubation and mechanical ventilator and who didn`t need regarding TSH level (mIU/L):

TSH (mIU/L)	ICU admission		Z	P
	Need N= 4	Not need N= 25		
1st quartile	1.14	0.96		
Median	1.33	1.14	-0.763	0.445
3rd quartile	1.51	1.67		

ICU: intensive care unit, Z: Mann whitey U test

Table (8): Mann whitey U test: statistical analysis for comparison between 29 cases of anticholinesterase pesticides poisoning who needed intensive care unit admission, intubation and mechanical ventilator and who didn`t need regarding serial cortisol measurements (µg/dl):

Cortisol (µg/dl)	ICU admission		Z	P
	Need N= 4	Not need N= 25		
Cortisol at admission				
1st quartile	54.1	32.9		
Median	68.2	45.0	-2.407	0.016*
3rd quartile	82.2	53.0		
Cortisol after 6 hours				
1st quartile	64.50	17.40		
Median	64.50	28.10	-2.304	0.021*
3rd quartile	64.50	31.20		
Cortisol after 12hours				
1st quartile	84.00	18.20		
Median	84.00	21.90	-2.276	0.023*
3rd quartile	84.00	27.40		

*Z: Mann whitey U test, *: statistically significant result (P value<0.05), ICU: intensive care unit, Z: Mann whitey U test*

Table (9): Pearson Correlation between total atropine and oximes ampoles given, cholinesterase activity (U/L) and TSH (mIU/L) and serial cortisol (µg/dl) levels in 29 anticholinesterase poisoned patients:

	Total Atropine	Total Oximes	Cholinesterase Activity (U/L)
TSH (mIU/L)			
R	0.130	-0.084	0.268
P	0.500	0.665	0.160
Cortisol at Admission (µg/dl)			
R	0.002	0.317	0.012
P	0.994	0.094	0.950
Cortisol after 6 Hours (µg/dl)			
R	0.423	0.342	-0.439
P	0.039*	0.102	0.032*
Cortisol after 12 Hours (µg/dl)			
R	-0.367	0.190	-0.186
P	0.178	0.422	0.432

*r: Pearson Correlation, * Statistically significant (<0.05)*

Table (10): ROC curve analysis: Serum cortisol hormone (µg/dl) at admission as predictor of mortality in anticholinesterase pesticides poisoned patients (29 cases):

Parameters	AUC (95% CI)	p - value	Cut-off value	Sensitivity (%)	Specificity (%)
Cortisol at admission (µg/dl)	1.000 (0.884-1.000)	<0.001*	>80.9	100.0	100.0

AUC: area under the curve; CI: confidence interval

Table (11): ROC curve analysis: Comparison between cortisol (µg/dl) at admission, 6 hours and twelve hours as predictors of ICU admission, intubation and mechanical ventilator for anticholinesterase pesticides poisoned cases (29 cases)

Parameters	AUC (95% CI)	p - value	Cut off value	Sensitivity (%)	Specificity (%)
Cortisol at admission (µg/dl)	0.885 (0.715 – 0.972)	<0.001*	>53	100.0	76.9
Cortisol after 6 hours (µg/dl)	1.000 (0.858 – 1.000)	<0.001*	>62.7	100.0	100.0
Cortisol after 12 hours (µg/dl)	1.000 (0.832- 1.000)	<0.001*	>30.2	100.0	100.0
p-value from Pairwise comparisons	Admission cortisol vs 6-hr cortisol = 0.004* Admission cortisol vs 12-hr cortisol = 0.004* 6-hr cortisol vs 12-hr cortisol = 1.000				

*AUC: area under the curve; CI: confidence interval; * significant at p<0.05.*
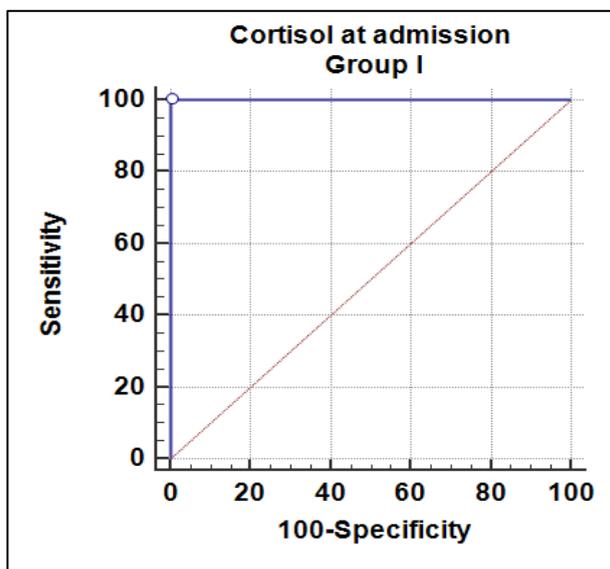

Figure (1): Relationship between outcome and cortisol at admission for 29 cases of anticholinesterase pesticides poisoned patients
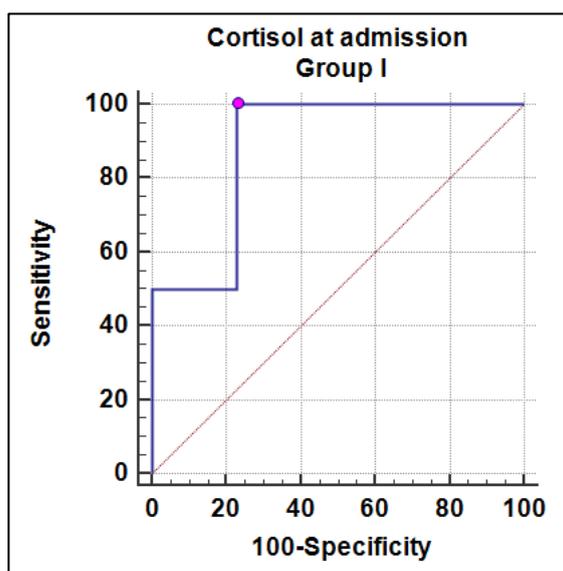

Figure (2): Relationship between cortisol at admission and need for ICU admission for anticholinesterase pesticides poisoned cases (29 cases)
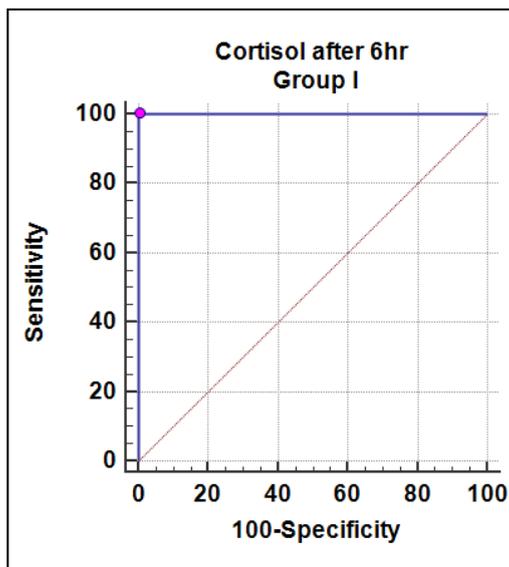
Figure (3): Relationship between cortisol after six hours from admission and need for ICU admission, intubation and mechanical ventilator for anticholinesterase pesticides poisoned cases (29 cases)
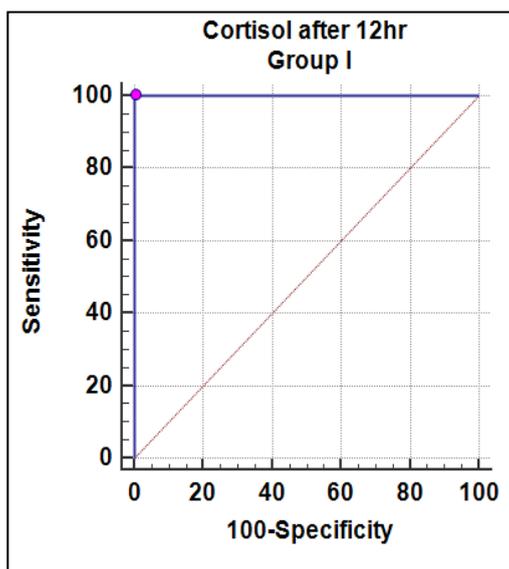

Figure (4): Relationship between cortisol after twelve hours from admission and need for ICU admission, intubation and mechanical ventilator for anticholinesterase pesticides poisoned cases (29 cases)

Discussion

In Egypt, anticholinesterase poisoning constitutes the majority of suicidal cases by pesticides due to their easy availability and low price (Gunnell et al., 2007). Concerning Tanta Poison Control Center, El-Maddah, (2012) and Abo El-Noor, (2013) reported that anticholinesterase pesticides poisoned patients represented 30.4% and 20% of acutely poisoned patients respectively. Furthermore, El-Mansy et al, (2014) revealed that phosphide poisoning represent the most common cause of death followed by anticholinesterase poisoning in the period between 2009 and 2013.

Determination of prognosis may allow more intensive monitoring and favorable outcome in pesticides poisoned patients (El-Sarnagawy, 2017).

Previous studies reported that cortisol and TSH may have prognostic role in organophosphates poisoned patients (Shadnia et al., 2018).

Changes in thyroid profile may occur in critical illnesses through different mechanisms such as the inhibition of thyroxine uptake by the hepatocytes and limiting its conversion to triiodothyronine in the periphery, also circulating cytokines can influence hormones levels. These alterations in thyroid hormones levels are called sick euthyroid syndrome. This syndrome may result from severe illness, physical trauma, physiologic stress and large number of drugs and chemical compounds as some pesticides (Tomescu et al., 2018). The normal TSH in healthy adult ranged from 0.5 to 5 mIU/L (Vadiveloo et al., 2013).

Upon exposure to stressful conditions or in cases of critical illness, activation of hypothalamic-pituitary-adrenal axis (HPA) occurs with subsequent increase in cortisol level (Herman et al., 2016). However in some patients, their cortisol production is not sufficiently increased in response to stress conditions which is known as critical illness-related corticosteroid insufficiency (CIRCI) (Pisano et al., 2017).

According to Kronenberg, (2008), the normal cortisol levels during stress should be more than 34 μg/dl.

In addition, Anticholinesterase pesticides can affect the endocrine system through hormone receptors, hormone synthesis, and transcription factors (Şimşek et al., 2019). Based on that, our study was made to evaluate the prognostic role of and cortisol and thyroid stimulating hormones in acute pesticides poisoned patients.

The present study included 29 patients with acute anticholinesterase pesticides poisoning. All included patients were at middle age ranged between 16 and 37 years old as this age group is the most physically active and more liable to stress and depression during their lives (Farahat et al., 2016). Also, we found that all included patients ingested pesticides with suicidal intension according to their allegation. This could be attributed to many factors such as poverty, financial problems, economic instability, unemployment, marital conflicts, failure of love and breakup in the family support system (Kumar et al., 2010). Besides, many individuals do not seek help for their suicidal thoughts because of the stigma associated with mental illness (Li et al., 2015). These results are similar to El-Gendy et al., (2017) who reported that majority of their patients were at middle age and ingested pesticides with suicidal intention.

As regarding sex, there was female predominance in this study representing 62% of patients. This may be due to sociocultural factors as lower education and lower economic income than males (Arafat, 2019).

These results come in line with Sarhan, (2015) and Ohbe et al., (2018) results. Moreover, this is contradictory to El-Sheikh et al., (2017) who found 83% of patients were males and El-Gendy et al., (2017) who reported that 57.5% were males. They explain that as males work in agriculture more than females.

Regarding residence, 58.6% of patients were from rural areas. This is similar to Elgohary et al., (2013) and El-Gendy et al., (2017) who found 82% and 60% of their patients from rural areas explaining that by wide exposure to these compounds in the Delta agriculture region.

Regarding time delay between pesticides exposure and hospital admission, the median time delay in this study was 3.2 hours. This is due to presence of Tanta Poison Control Center near to rural areas in Gharbia Governorate. This come in line with Oreby and Elmadah (2017) result who made their study in Tanta also. This is different to Phanindra et al., (2020) in India who reported that mean time delay in their patients was 6 hours.

However, according to Liu et al., (2015) time between anticholinesterase exposure and seeking medical advice could be attributed to nature of poisoning, awareness of family by toxicity, availability of transportation and distance of hospitals from poisoning place.

In this study, all patients had normal blood pressure, 34.5% had tachycardia. This is explained by Rabha et al., (2017) as preganglionic nicotinic receptor stimulation was followed by release of adrenaline and noradrenaline from adrenal gland leading to predominance of adrenergic activity on the heart. Moussa et al., (2018) found that 9.5% of patients presented with tachycardia and 1.5% of patients presented with bradycardia. Concerning the blood pressure, they found 5% of their patients had hypotension, 2% of patients had hypertension. Also, Farooqui et al., (2020) and Luo et al., (2020) reported normal blood pressure in majority of their cases. Banerjee et al., (2012) reported occurrence of hypertension in 9%, bradycardia in 38%and tachycardia in 8%. These differences between the studies may be caused by differences in delay time before hospital admission. Gündüz et al., (2015) noted that after exposure to anticholinesterase, initial tachycardia occurs due to sympathetic stimulation followed by bradycardia due to parasympathetic stimulation.

Regarding respiratory rate, abnormalities were recorded in 27.6 % of patients (20.7% had tachypnea, 6.9% with bradypnea). Other studies as Banerjee et al., (2012) and Moussa et al., (2018) reported that tachypnea represented 6%, 35% of cases respectively. Tachypnea may be a sign of respiratory failure (Sungur and Güven, 2001). Carey et al., (2013) reported that accumulated Ach at carotid body chemoreceptors increases respiratory activity.

Chest examination revealed 13.8% of cases had chest crepitations, 6.9% had wheezy chest. This is partially similar to Karki et al., (2004) who found chest abnormalities in 21.6% of their patients. Abedin et al., (2012) reported that 70% of their patients had chest manifestations as wheeze and crepitations. In addition, Elagamy and Gabr, (2019) revealed presence of bronchorhea in 58% in their study group.

Respiratory manifestations are main signs of anticholinesterase pesticides poisoning which are a part of acute cholinergic crisis occurred by acetylcholine accumulation (Hulse et al., 2014).

Regarding serum potassium level, there was hypokalemia in 58.6% of patients, which explained by vomiting and diarrhea which are very common muscarinic manifestations (Roberts and Brett, 2014). This is partially similar to Abd Alkareem and Khater, (2019) who reported hypokalemia in 41.6% of their patients. On the other hand, (Someswar et al., 2015) found hypokalemia in 24% of their patients. They explained the bad prognosis associated with hypokalemia could be explained by muscle weakness, cardiac dysrhythemia and renal failure.

Concerning ECG, it was normal in 93.1% of cases in this study, only 6.9% had sinus tachycardia. Uddin et al., (2020) reported normal ECG findings in 64% of their patients and the commonest change was sinus tachycardia in 14% of cases.

In this study, only 6.9% of cases died and 13.8% were intubated and admitted to ICU. This percentage of

mortality may be explained by early administration to hospital with early intervention with antidotes. In addition, because 93.1% were moderate cases as regards poison severity score. This mortality percentage was lower than El-Gendy et al., (2017), Amin et al., (2018) and Oreby and Elmadah, (2017), also the mean ICU stay duration was 48 hours and total hospital stay time was 39 hours in this study. Same results obtained by Brvar et al., (2018). However, Samprathi et al., (2020) mean hospital stay in their patients was 9.4 days and ICU stay was 5.9 days.

During critical illness, profound changes may occur in the hypothalamic-pituitary-thyroid (HPT) axis. The most consistent change is a decrease in serum tri-iodothyronine (T3) level, but in severe illness, serum thyroxine (T4) and TSH may also decrease (Fliers et al., 2001).

Anticholinesterase compounds affect thyroid hormones through different mechanisms including interfering with their biosynthesis, interrupting the transport of thyroid hormones in the blood circulation, their binding to receptors and disrupting their metabolism in the liver (Yang et al., 2020).

Concerning TSH level, majority of patients had normal level; only one patient had decreased its level. This come in line with Güven et al., (1999), Dutta et al., (2015) and Gundogan et al., (2018). This may be explained by euthyroid sick syndrome which is characterized by normal TSH, T4 levels and decreased T3 level which normalize after treatment (Tomescu et al., 2018).

Furthermore, Hundekari et al., (2012) made a study on 150 organophosphate poisoned patients, they reported that there was a slight and nonsignificant decrease in serum T3 and serum T4 levels in OP poisoned cases without any significant change in serum TSH levels as compared to control and their values didn`t change after treatment. Moreover, Rao and Bhavana (2015) discussed two case reports in which there was decreased TSH measurement and hyperthyroidism at stage of acute poisoning and normalized at time of discharge.

Dutta et al., (2015) revealed that alteration in TSH level during critical illness depend on severity and duration of illness, age of the patient and cytokines level. This didn`t occur in our study may be due to majority of our patients were at middle age and were moderate cases as regard PSS. Also, we selected only acute poisoning with anticholinesterase pesticides.

Another study as Satar et al., (2008) reported histological structural changes in thyroid gland after poisoning with methamidophos (one of OP compounds) suggesting that certain OP compound may have toxic effect on thyroid gland. Furthermore, Huang et al., (2017) concluded increased risk of hypothyroidism after anticholinesterase poisoning especially in age group 40-64 years old. This difference between our study and their study because our patients were at middle age.

Regarding prediction of mortality by TSH level, this study showed no significant difference between survivors and non-survivors. This comes in line with Najari et al., (2018) results. Also, regarding secondary outcome as need for intubation or ICU admission, this study reported that TSH level can`t predict need for intubation or ICU admission.

As regards serum cortisol level, this study revealed that median cortisol level at admission was 47.3μg/dl. This is partially similar to Satar, (2004) who reported median cortisol level at admission was 41.8μg/dl. Other studies as Güven et al., (1999) and Dutta et al., (2015) reported that the mean cortisol level at admission was 25.5± 14 and 34.3 μg/dl respectively. The initial rise in cortisol level is explained by stress or the effect of acetylcholine on corticotropin releasing hormone and ACTH (Kale, 2014).

According to Kronenberg, (2008), if blood cortisol level less than 15 μg/dl is graded as adrenal insufficiency, if between 15 and 33 μg/dl is graded as CIRCI and if more than 34μg/dl is considered adequate adrenal response to stress.

Previous studies reported that cortisol level increased during stressful conditions and that increase is related to severity of illness, loss of circadian level, increased its production and decrease in its half-life and they also reported that loss of AChE activity is similar to a generalized stress reaction, in which the plasma cortisol concentration should elevate (Satar, 2004).

Furthermore, Martin-Reina et al., (2017) reported that acute anticholinesterase poisoning might cause significant elevation of prolactin, adrenocorticotrophic and cortisol. Güven et al., (1999) noted in their study that numerous animal studies were done and reported increased cortisol levels in acute anticholinesterase poisoning and shown that the degree of elevation is related to the severity of illness.

In this study, we measure cortisol level at three stations; first at admission, second estimation after six hours and the last measurement after twelve hours of admission. During this period, first aid was made and patients received their antidote therapy. According to Kronenberg, (2008), majority of cases (74.1%) showed adequate adrenal response to stress at admission, moreover after six and twelve hours incidence of critical illness related corticosteroid insufficiency increased represented 48.1% and 59.3% respectively.

By comparing cortisol level at admission with mortality, we had significant difference between survivors and non-survivors. Also, this study reported that there was significant difference between the three cortisol maesurements and need for ICU admission and intubation.

Conclusion

This study concluded that measurement of cortisol at admission is a predictor for mortality in anticholinesterase pesticides poisoned patients. In addition, measuring cortisol at admission, after six and twelve hours from admission can predict need for ICU admission and intubation and mechanical ventilator but TSH have no prognostic role in organophosphates poisoned patients.

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تقييم دور هرموني الكورتيزول و تحفيز الغدة الدرقية كعوامل للتنبؤ في المرضي المصابين بالتسمم الحاد بمثبطات انزيم الكولين استيريز بمركز طنطا الجامعي لعلاج حالات التسمم

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الملخص العربي

المقدمة: يعتبر التسمم بمضادات الكولينستيراز مشكلة عالمية كبرى تؤدي إلى وفاة الآلاف كل عام. التنبؤ بمصير الحالات امر يهم كل اطباء السموم. حيث أفادت دراسات سابقة أن هرموني الكورتيزول و تحفيز الغدة الدرقية قد يكون لهما دور تنبؤي في المرضى الذين أصيبوا بالتسمم بالفوسفات العضوي.

الهدف: هدفت هذه الدراسة إلى تقييم دور هرموني الكورتيزول و تحفيز الغدة الدرقية للتنبؤ بمصير حالات التسمم بالحاد بالمبيدات المضادة للكولين استيراز الذين تم إدخالهم إلى مركز جامعة طنطا لعلاج حالات التسمم.

الطريقة المستخدمة في البحث: تضمنت هذه الدراسة ٢٩ مريضًا يعانون من التسمم الحاد بمضادات الكولينستيراز والذين كانوا متوسطين أو شديدوا التسمم وفقًا لمقياس شدة التسمم بين أغسطس ٢٠١٩ ويوليو ٢٠٢٠. تم تقييم هرموني تحفيز الغدة الدرقية والكورتيزول التسلسلي بواسطة تقنيات ELISA.

النتائج : كانت نتائج هذه الدراسة أن هرمون تحفييز الغدة الدرقية ليس له دور تنبؤي ولكن للكورتيزول دور تنبؤي في الوفيات والحاجة إلى دخول وحدة العناية المركزة.

الاستنتاج: قياس الكورتيزول عند دخول المستشفى ، بعد ست واثنتي عشرة ساعة يمكن أن يتنبأ بالحاجة إلى دخول وحدة العناية المركزة و الوضع على جهاز التنفس الصناعي، في حين أن قياسه عند الدخول الي المستشفي يمكن أن يكون مؤشرًا للوفيات.

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