

MORBIDITY AND MORTALITY PREDICTORS IN PATIENTS WITH ACUTE TRICYCLIC ANTIDEPRESSANT TOXICITY

* Mervat H Abd El-Salam, ** Mohey K El-Masry, ***Ghada MA El-Galad,*Abla Abd El-Rhman and *** Amro AA Saleh

Dept. of Forensic Medicine and Clinical Toxicology - Faculty of Medicine - *Cairo, **Ain Shams, and *** Fayoum Universities.

ABSTRACT

Background: Tricyclic antidepressant drugs are well known medications for depression, nocturnal enuresis and chronic pain. The severe morbidity and mortality associated with these drugs is well documented due to their cardiovascular and neurological toxicity.

Objective: The aim of this study is to predict the morbidity and mortality factors in patients with acute TCA toxicity in relation to outcome toxicity measures (coma grade, ECG findings and duration of hospitalization) and to detect early evidence of cardiotoxicity using quantitative analysis of Troponin I.

Patients and Methods: The present study was conducted on 100 patients presented to the PCC of Ain Shams University hospitals during the period from October 2009 to March 2011 with acute TCA toxicity of both sex and different ages. Patients were divided into 3 groups according to poisoning severity score (PSS) into group I (mild toxicity), group II (moderate toxicity) and group III (severe toxicity). All subjects were examined for: **I)** sociodemographic data **II)** medical evaluation **III)** Investigation: Including arterial blood gases, Serum electrolytes (Na and K), random blood sugar, serum troponin I level and Electrocardiography (ECG) monitoring **IV)** Outcome: include coma grade, ECG findings and duration of hospitalization.

Results: Risk factors (sex, coingestion, time delay and previous attempts) had no effect on difference between groups, while age and mode of toxicity were significantly different (p-value <0.05) between groups. It is found that age has a direct relation with the severity of toxicity, as it was higher in severe group (34.03± 15.016 years). Type of TCA ingested had significant effect (p-value <0.05) on both coma grade and endotracheal intubation. Patients with dothiepin toxicity were presented as 72.3% in deep coma (coma grade II, III, IV) constituting 50% of intubated patient, while amitriptyline and clomipramine / nortriptyline were presented as 19.6% and 19.2% in deep coma (coma grade II, III, IV) constituting 37.5% and 12.5% of intubated patients respectively. The dose of TCA had a highly significant effect (p-value <0.0001) on severity of toxicity, coma grade and ECG findings. The commonest cause of ICU admission was CVS complications especially severe hypotension, dysrhythmia and conduction block. ADORA criteria (QRS interval >100 msec, cardiac dysrhythmias, altered mental status, seizures, respiratory depression and hypotension) had a high significant effect (p-value <0.0001) on ECG findings, coma grade and type of TCA ingested. The risk factors for intubation in the present study were evident in patients with dothiepin or amitriptyline ingestion, old age, abnormal ECG, deep coma, seizure and two or more ADORA criteria. The most common acid-base disorder in the present study was metabolic acidosis. ECG changes had no relation (P-value >0.05) with all risk factors except for the age and the mode of poisoning. Duration of hospitalization (DOH) had a highly significant (p-value < 0.001) relation with the severity of toxicity in the studied groups, ECG findings and coma grade. Grade of coma had no relation (P-value >0.05) with all risk factors except for the dose of TCA. Level of troponin I was non evident in predicting cardiotoxicity except for occurrence of IHD.

Conclusion: Reed's coma scale is an indicator either for evaluation of poisoning severity in individual TCAs or for assessment of relative toxicity between different types of TCAs. Severity of toxicity in studied groups had a highly significant effect on the duration of hospitalization, ECG findings and coma grade. ECG findings especially QRS duration is an easy, cheap and available diagnostic tool in Emergency Room (ER) to help not only in diagnosing TCA poisoning but also in predicting its severity and occurrence of other complications. No case fatalities recorded in the current study.

KEYWORDS: TCA; Cardiotoxicity; Electrocardiogram; Reed's coma scale; Duration of hospitalization.

INTRODUCTION

Tricyclic antidepressants (TCAs) are a class of psychoactive drugs used primarily as antidepressants. They are named after their chemical structure, which contains three rings of atoms ⁽¹⁾.

Tricyclic antidepressants (TCAs) were one of the most important causes of mortality resulting from poisoning until 1993 and continue to be responsible for more deaths per prescription than all other antidepressants put together. In 2006, about 6000 cyclic antidepressant overdoses were reported with 4% resulting in serious adverse outcomes including death ⁽²⁾.

Tricyclic antidepressant (TCA) overdoses had higher rates of hospitalization (78.7% vs. 64.7%) and much higher fatality rates (0.73% vs. 0.14%) than did SSRI overdose reports ⁽³⁾.

SUBJECTS AND METHODS

This study was carried out at the Poison Control Center (PCC), Ain Shams University Hospitals during the period from October 2009 to March 2011. The cases were diagnosed as TCA poisoning through accurate history taking.

Subjects:

The selected patients were of both sexes in different ages with acute TCA poisoning. The diagnosis was based mainly on accurate history taking about accidental, suicidal or homicidal exposure to TCA, in addition to clinical manifestation of TCA poisoning.

Patients with TCA and polymedication poisoning were included. The study was conducted on one hundred patients who were classified according to **Persson et al., 1998** ⁽⁴⁾ into;

Group I: 40 patients with mild TCA poisoning, presented with nausea, vomiting, vertigo, normal ECG, normal laboratory finding and discharged 6 hours after observation .

Group II: 30 patients with moderate acute TCA poisoning, presented with palpitation, coma grade I and sinus tachycardia in ECG.

Group III: 30 patients with severe acute TCA poisoning, presented with coma grade II or more, unstable vital signs and cardiac arrhythmias or respiratory depression.

Group IV: No fatal cases recorded in the study.

Exclusion criteria

Patients with history of other medical disorder as cardiac, pulmonary disease or renal impairment are excluded.

-In each patient, the following were studied;

A-Sociodemographic data: It included data regarding age, sex, occupation and residence.

B-Poisoning data: It included;

- Type of ingested TCA drug.
- Mode of poisoning.
- Amount of ingested dose.
- Number of previous attempts.
- Coingestion of other drugs.
- Time passed since poisoning.

C- Clinical evaluation:

❖ **Medical history:**

- ❖ **Physical Examination**
- ❖ **Antidepressant Overdose Risk Assessment criteria (ADORA criteria):** dysrhythmias, altered mental status, conduction block, respiratory depression, hypotension, seizures ⁽⁵⁾.

D-Investigation parameters:

I-Laboratory investigations:

The laboratory work of the study was conducted at the laboratory of Ain-Shams university hospitals.

-One milliliter of arterial blood is freshly drawn from femoral or radial artery for immediate blood gas analysis using Rapid lab 855 of Bayer Company.

-Five milliliters of venous blood were collected for estimation of the following parameters:

- **Random blood sugar** was determined by colorimetric method using glucose oxidase.
- **Serum electrolytes** (Na and K) were determined by ion selective electrode technique using easylyte analyzer Chairon model.
- **Third sample:** was collected from Group III patients 6 hours after admission and kept for quantitative analysis of troponin I. cTnI was studied with immunoassay method using Tosoh AIA600 II cTnI second generation-2005 (AIA-PACK cTnI 2nd-Gen). Levels >0.1 ng/ml were accepted as indicating myocardial damage.

II. Electrocardiogram (ECG)

Electrocardiographic recording was done for every patient on admission then repeated for those admitted to ICU using FuKuda denshi Cardimex (model Fx-2111, Japan). ECG recordings aimed to check rate, conduction blocks or ST – T wave changes.

E- Patient's outcome

(A) Duration of hospitalization in the PCC.

(B) Grade of coma.

(C) ECG findings.

Analysis of the data included studying the relation between risk factors in patients with TCA overdose (age, sex, type of TCA ingested, dose, mode of poisoning, coingestion of other drugs and delay time of poisoning either within or more than 6hours) in relation to outcome toxicity measures (Reed coma scale, ECG abnormalities and duration of hospitalization in the PCC).

Statistical analyses

Data were checked, coded, and analyzed by using SPSS (version 11.0 software package. Numerical data were expressed as mean \pm SD. All qualitative data were expressed as frequencies (number of cases) and percentage. Comparison of quantitative variables between the study groups was done using student t- test for independent samples for two groups.

ANOVA was used for Comparison of quantitative variables for more than two groups.

Qualitative variables were compared using the Chi-square (χ^2) test. Fisher exact test was used instead of the Chi-square (χ^2) test when the expected frequency is less than 5. Non-parametric tests as Mann-Whitney test or Kruskal-Wallis test were used for comparison of quantitative variables instead of t-test and ANOVA respectively when appropriate. P-value was considered significant if < 0.05, highly significant if < 0.01 and non significant if > 0.05 for all tests.

RESULTS

I- Sociodemographic criteria

The majority of patients (49%) lied in age group of 20-40 years, followed by patients under the age of twenty years (32%), while patients in the age group of 41-60 years age were represented as 13%. Females (73%) predominated in this study with male to female ratio 1:2.7. Residence distribution patterns showed that 92% were from urban areas. Acute tricyclic

antidepressant poisoning was commonly found in unemployed (40%), followed by housewives (30%).

There was significant difference in age distribution between groups and non significant difference in sex distribution, where the mean age of the studied patients in group I (mild poisoning), group II (moderate poisoning) and group III (severe poisoning) was 23.78 ± 13.789 years, 25.57 ± 10.919 years and 34.03 ± 15.016 years respectively, with male/female distribution was 9/31, 9/21 and 9/21 respectively.

II- Poisoning data:

In 89% of patients, suicide attempts history was traced while 11% resulted from accidental exposure. No significant difference between groups was shown as regard coingestion of other drugs or history of psychiatric disease. There was a high significant difference as regard the dose of ingested TCA as in group I, group II and group III the mean dose was 66.61 ± 51.517 mg, 435.71 ± 90.784 mg and 592.39 ± 199.635 mg respectively. The mean duration of hospitalization was significantly different among different groups. In group I, group II and group III the mean duration of hospitalization was 6.89 ± 1.956 hours, 27.60 ± 11.813 hours and 47.20 ± 25 hours respectively. Time delay was non-significant in different severity groups.

III. Clinical manifestations:

Normal clinical examination was evident in 19%. Dyspnea was noticed in 10%, tachycardia in 49% and hypotension in 15% of patients. The neurological manifestation included agitation in 34% and hallucination in 29%. Majority of patients were conscious (grade 0) (40%), followed by coma grade I and coma grade II in 31% and 22% of patients respectively, while 5% were in coma grade III and (2%) were in coma grade IV. The commonest

ADORA criterion was altered mental status in 71%, followed by dysrhythmia in 50% of patients, while conduction block and hypotension were observed in 13% and 15% respectively. Seizures and respiratory depression were the least observed ADORA criterion and occurred in 8% of patients. The most common indication for intubation was deep coma (Reed's classification) in 4 patients (50%), followed by respiratory center depression in 3 patients (37.5%), while aspiration of gastric contents was the reason in only 1 patient (12.5%). There was highly significant difference between intubated and non intubated group of patients as regard ECG findings and coma grade. A significant difference between both groups was evident regarding type of TCA, occurrence of seizures and number of ADORA criteria, there was non significant difference between both groups in sex distribution and number of suicidal attempts (table 1).

IV-Electrocardiographic changes (ECGs) (table 2):

Interpretation of ECGs showed that: sinus tachycardia was the most common ECG abnormality found in 44% of patients, followed by prolonged QTc interval found in 6% (Fig.1), while wide QRS complex, prolonged PR interval, sinus bradycardia, Right bundle branch block (RBBB) and premature ventricular contractions (PVCs) (Fig.2) were found in 5%, 3%, 2%, 2% and 1% of patients respectively. In addition ST-T changes were observed in the form of depressed ST segment in 2% of patients, while normal ECG findings were found in 49% of patients.

There was a high significant difference in patients with normal/abnormal ECG as regard their group, while there was a significant difference regarding occurrence of seizures and

mode of poisoning, but there was non significant difference regarding sex and coingestion of other drugs (table 3). There was a highly significant difference between patients with normal and abnormal ECG finding as regard both the dose of TCA ingested and duration of hospitalization. There was a significant difference regarding their age, as patients with abnormal ECG were older (30.55 ± 14.082 years) than patients with normal ECG finding (24.10 ± 13.232 years) (table 4).

V-Duration of hospitalization in PCC as outcome toxicity measure.

There was a highly significant difference in patients as regard grade of coma, where the mean duration of hospitalization in patients with coma grade 0, I (n=71) and patients with coma grade II, III, IV (n=29) was 15.75 ± 12.249 hours and 48.93 ± 24.675 hours respectively (table 5).

VI- Grade of coma as outcome toxicity measure.

There was a significant difference between patients as regard the type of TCA ingested, while there was non significant difference in patients regarding mode of poisoning, delay time, coingestion of other drugs and number of suicidal attempts (table 6). There was a high significant difference in patients as regard dose of TCA ingested. It was found that patients presented by coma grade II, III, IV ingested significantly larger dose of TCA (609.78 ± 177.856 mg) than patients presenting with coma grade 0, I (172.56 ± 174.661 mg).

Biochemical changes

There was significant difference in the level of troponin I between patients complicated by IHD and those not complicated by IHD (table 7).

Table (1): Endotracheal intubation rates in relation to the presentation characteristics of acute tricyclic antidepressant toxicity ingestion.

presentation characteristics	Intubated (N=8)		Not intubated (N=92)		X ²	P- value
	N	%	N	%		
Sex *						> 0.05 NS
Male	2	25%	25	27.1%		
Female	6	75%	67	72.9%		
No. of suicidal attempts *						> 0.05 NS
0, 1	4	50%	75	81.5%		
>= 2	4	50%	17	18.5%		
Type of TCA					6.088	< 0.05 S
Amitriptyline	3	37.5%	53	57.6%		
Clomipramine / Nortriptyline	1	12.5%	25	27.2%		
Dothiepin	4	50%	14	15.2%		
Coma grade *						< 0.0001 HS
0, I	0	0%	71	77.2%		
II, III, IV	8	100%	21	22.8%		
ECG *						< 0.0001 HS
Normal	0	0%	49	53.3%		
Abnormal	8	100%	43	46.7%		
Seizures *						< 0.05 S
Yes	3	37.5%	5	5.4%		
No	5	62.5%	87	94.6%		
No. of ADORA criteria *						< 0.05 S
0, 1	0	0%	48	52.2%		
>= 2	8	100%	44	47.8%		

Table (2): ECG changes of the studied patients.

ECG findings	Number	Percent (%)
Normal finding	49	49%
Sinus tachycardia	44	44%
Sinus bradycardia	2	2%
Premature ventricular contractions (PVCs)	1	1%
Right bundle branch block (RBBB)	2	2%
Wide QRS complex	5	5%
Prolonged QTc interval	6	6%
Prolonged PR interval	3	3%
Depressed ST segment	2	2%

* Fisher exact test was done N= number of cases X²: Chi square statistical analysis
P: > 0.05 insignificant difference (NS) P: < 0.05 significant difference (S) P: < 0.0001 highly significant (HS)

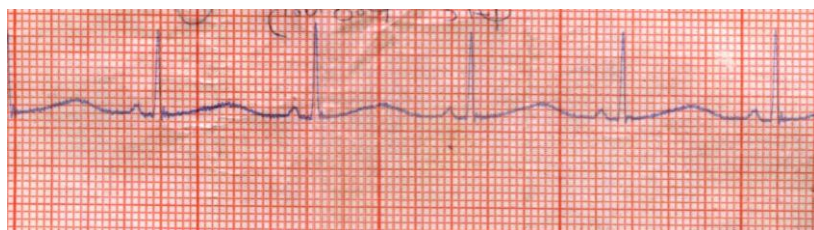


Figure (1): ECG rhythm strip showing prolongation of QTc interval in TCA intoxicated patient

Table (3): Relation between ECG findings and some qualitative parameters.

Parameters	Normal ECG findings (N=49)		Abnormal ECG findings (N=51)		X ²	P- value
	N	%	N	%		
Sex					3.633	> 0.05 NS
Male	9	18.4%	18	35.3%		
Female	40	81.6%	33	64.7%		
Seizures *						<0.05 S
Yes	0	0%	8	15.7%		
No	49	100%	43	84.3%		
Group					74.790	<0.0001 HS
I	40	81.6%	0	0%		
II	9	18.4%	21	41.2%		
III	0	0%	30	58.8%		
Mode of poisoning					5.327	<0.05 S
Accidental	9	18.4%	2	3.9%		
Suicide	40	81.6%	49	96.1%		
Coingestion of other drugs.					2.121	> 0.05 NS
Negative	43	87.8%	41	80.4%		
Positive	6	12.2%	10	19.6%		

* Fisher exact test was done N= number of cases X²: Chi square statistical analysis
P: > 0.05 insignificant difference (NS) P: < 0.05 significant difference (S)

Table (4): Relation between ECG findings and some quantitative parameters

P: < 0.05 significant difference (S). * = student's t-test
P: < 0.0001 highly significant (HS).

Parameter	Normal ECG findings (N=49)	Abnormal ECG findings (N=51)	t*	P- value
Age (years) Mean± SD	24.10 ±13.232	30.55 ±14.082	2.357	< 0.05 S
Dose(mg) Mean± SD	101.91 ±126.017	538.97±188.815	8.407	< 0.0001 HS
Duration of hospitalization (hours) Mean± SD	10.55 ± 9.160	39.41±22.582	11.226	< 0.0001 HS

Table (5): Relation of duration of hospitalization (hours) of acute tricyclic antidepressant intoxicated patients with different ages and different groups.

Parameters	Duration of hospitalization (hours) Mean ± SD	F *	P- value
Age		1.76	>0.05 NS
<20 years (n=32)	20.52 ± 18.495		
20-40 years (n=49)	25.33 ± 21.138		
41-60 years (n=17)	35.65 ± 31.561		
>60 years (n=2)	24 ± 000		
Group		58.354	<0.0001 HS
I (n=40)	6.89 ± 1.956		
II (n=30)	27.60 ± 11.813		
III (n=30)	47.20 ± 25		

* ANOVA test was done N = number of patients.
P: > 0.05 insignificant difference (NS).
P: < 0.0001 highly significant (HS).

Table (6): Relation between grades of coma of acute tricyclic antidepressant intoxicated patients and some poisoning data.

	Grade of coma 0, I (n=71)		Grade of coma II, III, IV (n=29)		X ²	P-value
	N	%	N	%		
Type of TCA					14.783	<0.05 S
Amitriptyline	45	63.4 %	11	38 %		
Clomipramine / Nortriptyline	21	29.5 %	5	17.2 %		
Dothiepin	5	7.1%	13	44.8 %		
Mode *						
Accidental	10	14.1 %	1	3.6 %		> 0.05 NS
Suicidal	61	85.9 %	28	96.4 %		
Coingestion *						
Negative	61	85.9 %	23	82.1 %		> 0.05 NS
Positive	10	14.1 %	6	17.9 %		
Delay					0.849	> 0.05 NS
< 6 hours	59	83.1 %	21	72.4 %		
> 6 hours	12	16.9 %	8	27.6 %		
Number of suicidal attempts *						
0, 1	59	83 %	20	69 %		> 0.05 NS
>= 2	12	17 %	9	31 %		

* Fisher exact test was done N= number of cases X²: Chi square statistical analysis
P: > 0.05 insignificant difference (NS) P: < 0.05 significant difference (S)

Table (7): Comparison of level of troponin I in group III of acute tricyclic antidepressant intoxicated patients as regard presence of ischemic heart disease or not

	Troponin I (ng/ml) median (IQR)	P
ST-T wave changes	0.046 (0.036- 0.076)	< 0.05
No ST-T wave changes	0.099 (0.083- 1.3)	S

IQR = Inter Quartile Range.
P: < 0.05 significant difference (S).
IHD: ischemic heart disease.



Figure (2): ECG rhythm strip showing Premature ventricular contractions (PVCs) in TCA intoxicated patient

DISCUSSION

The present study revealed that the studied patients were males (27%) and females (73%) with male: female ratio was 1: 2.7; most of patients were unemployed (40%) and housewives (30%). The study also showed non significant difference between groups as regard **sex** distribution (p-value >0.05). These findings were in agreement with **Unverir et al., 2006⁽⁶⁾** who conducted a retrospective analysis of antidepressants poisoning in 356 patients for antidepressant ingestion from January 1993 to June 2004, where female constituted 77.8% of patients and male represented 22.2%. **Soghoian et al., 2009⁽⁷⁾** stated that the incidence of cyclic antidepressants poisoning is higher in women than in men. This most likely reflects a higher rate of depression and suicide attempts among women.

In the present study, the age ranged between 2-73 years with the mean age was 27.39 ± 13.983 years, with relatively high frequency of poisoning cases between 20 and 40 years (49%). These findings were in agreement with **Unverir et al., 2006⁽⁶⁾**, and also with **Aslan et al., 2011⁽⁸⁾**, The study also showed significant difference between groups as regard their **age** (P-value < 0.05) as the advance in the age directly related to the severity of the toxicity.

The current study showed that 27% of patients were suffering from **previous psychiatric diseases** while 73% of patients had negative history. **Aslan et al., 2011⁽⁸⁾**, recorded 22.5% of patients had history of **psychiatric diseases**, where **Unverir et al., 2006⁽⁶⁾**, found such patients constituted 40% in his study.

Coingestion of other drugs was non significant between groups. These findings were in disagreement with **Caravati and Bossart 1991⁽⁹⁾** and **Unverir et al., 2006⁽⁶⁾** who

recorded 61% and 70.9% of patients with coingestion of other drugs were presenting with severe toxicity respectively. This difference between the current study and other studies may be related to the type and dose of coingested drugs and their effects on different systems of the body.

There was a significant relation between the **type of TCA overdose** and **coma grade**

Results showed that dothiepin and amitriptyline are more toxic than clomipramine or nortriptyline. Consistent with the present study results, **Buckley et al., 1994⁽¹⁰⁾** & **Gillman, 2007⁽¹¹⁾**, While **Crome and Newman 1979⁽¹²⁾** found most common case is amitriptyline.

The current study showed that the time of presentation after intoxication didn't play any role in the severity of symptoms. This was consistent with the study by **Callaham and Kassel 1985⁽¹³⁾**,

The higher the dose, the more severe was the presenting picture, which was in agreement with a study performed by **Bramble et al., 1985⁽¹⁴⁾**.

The most common clinical finding was sinus tachycardia (49%), followed by drowsiness (41%) and agitation (34%). This was in agreement with **Unverir et al., 2006⁽⁶⁾**. On the other hand **Hazim Olgun et al., 2009⁽¹⁵⁾**, reported that the most common finding is lethargy followed by sinus tachycardia.

The present study revealed similarly a highly significant difference between **number of ADORA criteria** and both **ECG findings** and **grade of coma**, Consistent with **Unverir et al., 2006⁽⁶⁾** the number of ADORA criteria, coma grade and ECG findings showed high significant differences between studied groups

The risk factors for intubation in the present study were present in patients who ingested dothiepin or

amitriptyline, old age, had abnormal ECG findings, deep coma, seized and had two or more ADORA criteria. These findings were in agreement with **Unverir et al., 2006**⁽⁶⁾ who determined that 9.6% required endotracheal intubation. He also reported that abnormal ECG findings, general tonic clonic seizures, a GCS score of 8 and < 8 and poisoning cases with two or more ADORA criteria had a reasonably higher frequency of intubation when compared to the cases didn't require endotracheal intubation. Consistent with this study, **Bateman, 2005**⁽¹⁶⁾ stated that Clinical progress, hemodynamic instability, and GCS are important parameters in decision-making of endotracheal intubation.

The indications for intubation in the current study were mostly deep coma in 50% of patients, followed by respiratory depression and aspiration of gastric contents in 37.5% and 12.5% of patients respectively. Our findings were in accordance with **Unverir et al., 2006**⁽⁶⁾. On the contrary, **Hazim Olgun et al., 2009**⁽¹⁵⁾ reported 48% of the patients were in coma and only 1 patient (1.92%) required mechanical ventilation because of respiratory depression.

It was found that risk factors; sex and coingestion of other drugs had no effect on ECG findings, while **age and mode of poisoning** had significant effect on ECG findings, abnormal ECG findings were more frequent in suicidal ingestion (96.1%) and in old age than normal findings.

This study revealed as well a highly significant relation between **ECG findings and severity of toxicity in studied groups**, where all patients in group III (severe toxicity group) had abnormal ECG findings. In agreement with this study, **Boehnert and Lovejoy 1985**⁽¹⁷⁾ reported that QRS complex duration was useful as a predictor of TCA cardiac and

neurological toxicity. Contrary to the present study, **Foulke and Albertson 1987**⁽¹⁸⁾ found the QRS duration to be an unreliable indicator of seizures and ventricular dysrhythmias, concluding that a QRS complex interval less than 0.10 seconds does not exclude serious toxicity.

This study showed highly significant difference between **duration of hospitalization** and the following; **severity of toxicity in studied groups, ECG findings and coma grade**, this finding is highly logic and acceptable as The mean DOH for group III (severe toxicity, abnormal ECG finding and deep coma) was higher than the other 2 groups. This was in agreement with a study by **Unverir et al., 2006**⁽⁶⁾ and **Karcioglu et al., 2000**⁽¹⁹⁾. Contrary to the present study, **Aslan et al., 2011**⁽⁸⁾ and **Hazim Olgun et al., 2009**⁽¹⁵⁾, reported that the mean length of hospitalization for intoxication was 1.8 ± 1.7 days (range: 1-10 days) and 2.3 ± 2.3 days (range: 1-7 days) respectively.

The present study revealed that majority of patients (71%) were conscious or coma grade I, while 29% of patients were in deep coma which was in agreement with **Unverir et al., 2006**⁽⁶⁾. On the other hand **Hazim Olgun et al., 2009**⁽¹⁵⁾, reported 48% of patients presented by deep coma in his study.

It was found that risk factors; age, sex, coingestion of other drugs, delay time and mode of poisoning had no effect on grade of coma. On the other hand both of **the type of TCA** and **the dose of TCA** had significant relation with grade of coma.

Level of troponin I in group III, showed significant difference between patients had ST-T wave changes and those didn't have these changes. On the other hand there was insignificant difference in the level of troponin I between patients presented by different

types of conduction block. So troponin I had no role in predicting different types of cardiotoxicity caused by TCA overdose.

Conclusion:

Type and dose of tricyclic antidepressants are important risk factors in predicting severity of TCA toxicity, where amitriptyline and dothiepin proved to be the most toxic members.

The most common finding in clinical examination was sinus tachycardia followed by drowsiness and agitation.

The risk factors for respiratory assistance and intubation were dothiepin or amitriptyline, old age, abnormal ECG changes, deep coma, seizures and two or more ADORA criteria.

The indications for respiratory assistance were mostly deep coma followed by respiratory depression and aspiration of gastric contents.

The studied risk factors (age, sex, ingested dose, mode of poisoning, delay time, coingestion of other drugs and type of TCA ingested) had variable effects according to the measured outcome toxicity parameters.

Level of troponin I was non evident in predicting cardiotoxicity except for presence of IHD.

REFERENCE

- 1- **Glauser J. (2000):** Tricyclic antidepressant poisoning. *Cleve Clin J Med*; 67:704-719.
- 2- **Bronstein AC, Spyker DA, Cantilena LR Jr, et al. (2007):** 2006 Annual Report of the American Association of Poison Control Centers' National Poison Data System (NPDS). *Clin Toxicol Phila*; 45(8):815-917.
- 3- **Busch SH, Frank RG, Leslie DL, Martin A, Rosenheck RA, Martin EG, et al. (2010):** Antidepressants and suicide risk: how did specific information in FDA safety warnings affect treatment patterns? *Psychiatr Serv*; 61(1):11-6.
- 4- **Persson HE, Sjoberg GK, Haines JA, et al. (1998):** Poisoning severity score. Grading of acute poisoning. *J Toxicol Clin Toxicol*; 36(3):205-213.
- 5- **Foulke GE. (1995):** Identifying toxicity risk early after antidepressant overdose. *Am J Emerg Med*; 13:123-126.
- 6- **Unverir P, Atila R, Karcioglu O, Topacoglu H, Demiral Y, Tuncok Y. (2006):** A retrospective analysis of antidepressant poisonings in the emergency department: 11-year experience. *Human & Experimental Toxicology*; 25: 605 –612.
- 7- **Soghoian Samara, Christopher I Doty, Frank A Maffei, Janet Weis, Heidi Connolly. (2009):** Toxicity, Tricyclic Antidepressant. www.e-medicine.com Updated: Oct 22.
- 8- **Aslan S, Müahit Emet, Zeynep Cakir, Ayhan Aköz, Sultan Tuna, Akgöl Gür. (2011):** Suicide attempts with amitriptyline in adults: a prospective, demographic, clinical study. *Turk J Med Sci*; 41 (2): 243-249.
- 9- **Caravati EM, Bossart PJ. (1991):** Demographic and electrocardiographic factors associated with severe tricyclic antidepressant toxicity. *J Toxicol Clin Toxicology*; 29(1):31-43.
- 10- **Buckley NA, Dawson AH,**

- Whyte IM, Henry DA. (1994):** Greater toxicity of dothiepin in overdose than of other tricyclic antidepressants. *Lancet*; 343:159-162.
- 11- Gillman PK. (2007):** "Tricyclic antidepressant pharmacology and therapeutic drug interactions updated". *British Journal of Pharmacology*; 151 (6): 737-748.
- 12- Crome P, Newman B. (1979):** Fatal tricyclic antidepressant poisoning. *J Roy Soc Med*; 72:649-653.
- 13- Callaham M, Kassel D. (1985):** Epidemiology of fatal tricyclic antidepressant ingestion: Implications for management. *Ann Emerg Med*; 14:1-9.
- 14- Bramble MG, Lishman AH, Purdon J, Diffey BL, Hall RJ. (1985):** An analysis of plasma levels and 24-hour ECG recordings in tricyclic antidepressant poisoning: implications for management. *Q J Med*; 56:357-366.
- 15- Hazim Olgun, Zuhul Keskin, Mehmet Karacan, Naci Ceviz. (2009):** Clinical, Electrocardiographic, and Laboratory Findings in Children with amitriptyline intoxication. *Pediatr Emerg Care*; 25: 170-173.
- 16- Bateman DN. (2005):** Tricyclic antidepressant poisoning: central nervous system effects and management. *Toxicol Rev*; 24: 181-186.
- 17- Boehnert MT, Lovejoy FH. (1985):** Value of the QRS duration versus the serum drug level in predicting seizures and ventricular arrhythmias after an acute overdose of tricyclic antidepressants. *N Engl J Med*; 313: 474-479.
- 18- Foulke GE, Albertson TE. (1987):** ORS complex interval in tricyclic antidepressant overdose: Inaccuracy as a toxicity indicator in emergency settings. *Ann Emerg Med*; 16:160-163.
- 19- Karcioğlu O, Ayrik C, Tomruk O, Topacoglu H, et al. (2000):** Retrospective analysis of adult poisoning cases in the Emergency Department. *J Ondokuz Mayıs Univ School Med*; 17: 156-162.

المؤشرات الدالة على المرض والوفاة فى المرضى المعرضين للتسمم الحاد بمضادات الأكتئاب ثلاثية الحلقات

مرفت حمدى عبد السلام * - محي قدرى المصرى ** - غادة مصطفى عبد العظيم الجلال *** - عبلة عبد

الرحمن * - عمرو عبد الغنى عبد الجيد صالح ***

أقسام الطب الشرعى و السموم الإكلينيكية - كلية الطب - جامعة القاهرة * - جامعة عين شمس ** - جامعة
الفيوم ***

يعتبر الاكتئاب من الأمراض المزمنة التي تؤثر على الملايين من المرضى لأسباب شتى. ومضادات الاكتئاب
ثلاثية الحلقات (TCAS) تعتبر من أهم أسباب الوفيات الناجمة من التسمم وقد يرجع ذلك إلي تأثيرها على القلب
والأوعية الدموية والجهاز العصبى المركزى والجهاز العصبى الارادى.

يهدف البحث الى تقييم حالات التسمم الحاد بمضادات الأكتئاب ثلاثية الحلقات واستخراج عوامل التنبؤ بشدة
المرض والوفاة وذلك من خلال الدراسة الإكلينيكية والمعملية للمرضى مع عمل تحليل لنسبة التروبونين I فى
المصل وبيان ما اذا كان يمكن استخدامه مبكرا للتنبؤ بالإصابة السمية لعضلة القلب.

قد أجريت هذه الدراسة على 100 مريضا فى مركز علاج السموم (PCC) ، مستشفيات جامعة عين شمس خلال
الفترة من أكتوبر 2009 الى مارس 2011. وتم اختيار المرضى من كلا الجنسين فى مختلف الأعمار. وأُعدت
تشخيص هذه الحالات على التاريخ الدقيق لأخذ هذه الادوية سواء من المرضى أو من ذويهم وكذلك على
أعراض التسمم بمضادات الاكتئاب ثلاثية الحلقات.

و تم تقسيم المرضى موضع الدراسة الى ثلاثة مجموعات:

المجموعة الأولى: أربعون مريضا يعانون من التسمم الحاد الخفيف بمضادات الاكتئاب ثلاثية الحلقات وكانوا
يعانون من الغثيان والدوار ، والتقيؤ ، وتخطيط القلب العادي ، و الفحوص المعملية الطبيعية.

المجموعة الثانية: ثلاثون مريضا يعانون من التسمم الحاد متوسط الخطورة بمضادات الاكتئاب ثلاثية
الحلقات وكانوا يعانون من خفقان القلب ، و غيبوبة من الدرجة الاولى مع تسارع فى معدل دقات القلب على رسم
القلب الكهربائى (ECG).

المجموعة الثالثة: ثلاثون مريضا يعانون من التسمم الحاد الشديد بمضادات الاكتئاب ثلاثية الحلقات وكانوا
يعانون من غيبوبة من الدرجة الثانية أو أكثر، عدم استقرار فى العلامات الحيوية وعدم انتظام ضربات القلب أو
هبوط فى الجهاز التنفسى.

و قد شملت هذه الدراسة:

1. البيانات الديمغرافية الاجتماعية : وتشمل البيانات المتعلقة بالعمر والجنس ومحل السكن.
2. البيانات الطبية: طريقة التسمم ، وتسجيل الفاصل الزمني بين التعرض للعقار والوصول الى
مركز علاج التسمم، نوع المركب، الجرعة المستخدمة، تناول أدوية أخرى، عدد محاولات
الانتحار السابقة.
3. الفحص السريرى: نتائج الفحص العام والفحص التفصيلى الذى تضمن الجهاز التنفسى،
الجهاز القلبي الرئوي، الجهاز العصبى و الجهاز المعدى المعوي.
4. الفحوص المعملية: قياس غازات الدم الشرياني ونسبة السكر العشوائى فى الدم وقياس
الصوديوم والبوتاسيوم فى المصل وكذلك عمل تحليل لمستوى التروبونين I فى المصل (فى
المجموعة الثالثة فقط) بالإضافة الى عمل رسم قلب كهربائى.

تم تدوين البيانات الشخصية والطبية و كذلك نتائج الفحوص المعملية والعلاج. وتم عمل تحليل إحصائى
للمعطيات.

تراوحت أعمار المرضى ما بين 2-73 سنة ، وكان غالبية المرضى (49 %) فى الفئة العمرية من 20-40 سنة.
أظهرت النتائج أن هناك علاقة ذات دلالة احصائية بين المجموعات الثلاث من حيث نوع المركب المستخدم
والجرعة وطريقة التسمم، حيث تبين ان دوتيبين هو الاعلى استخداما فى المجموعة الثالثة ذات التسمم الشديد
وان هذه المجموعة تسمت بالجرعة الاعلى من مضاد الاكتئاب ثلاثية الحلقات مقارنة بباقي المجموعات.

أظهرت النتائج أن هناك علاقة ذات دلالة احصائية بين النتائج غيرالطبيعية برسام القلب الكهربائى والعمر،
وطريقة التسمم، والجرعة المستخدمة، بينما أظهرت النتائج أن هناك علاقة ذات دلالة احصائية بين معدل ريد
للغيبوبة و نوع المركب المستخدم وكذلك الجرعة المستخدمة، أظهرت النتائج أن نسبة المرضى الذين احتاجوا
تركيب أنبوبة حنجرية هو 8% مع وجود علاقة ذات دلالة احصائية بين هؤلاء المرضى و معدل ريد للغيبوبة، و
نتائج رسام القلب الكهربائى. أظهرت النتائج عدم وجود علاقة ذات دلالة احصائية بين مدة الاستشفاء فى
مركز علاج السموم وكلا من العمر والجنس، بينما كان هناك علاقة ذات دلالة احصائية بينها وبين معدل ريد
للغيبوبة.