MORBIDITY AND MORTALITY PREDICTORS IN PATIENTS WITH ACUTE TRICYCLIC ANTIDEPRESSANT TOXICITY

Thesis

Submitted for Fulfillment of MD
Degree in Forensic Medicine and Clinical Toxicology

By

AMRO ABD EL-GHANY ABD EL- GAYD

Assistant Lecturer of Forensic Medicine and Clinical Toxicology
Faculty of Medicine - Fayoum University

Under Supervision of

Prof. Dr. Mervat Hamdy Abd El-Salam

Professor of Forensic Medicine and Clinical Toxicology

Faculty of Medicine, Cairo University

Prof. Dr. Mohey Kadry El-Masry

Professor of Clinical Toxicology

Faculty of Medicine - Ain Shams University

Dr. Ghada Mostafa El-Galad

Assistant Professor of Forensic Medicine and Clinical Toxicology

Faculty of Medicine -Fayoum University

Faculty of Medicine

Fayoum University

2012

SUMMARY

Tricyclic antidepressant drugs are well known classic medications not only for depression but also for other medical indications like nocturnal enuresis and chronic pain. Although SSRI are widely prescribed nowadays for treatment of depression, yet TCA are still prescribed for severe forms of depression and due to their cheaper cost than SSRI.

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). Group III was subdivided into group IIIA which received the treatment protocol of PCC using $NaHCO_3$. Group IIIB received intralipid 20% either alone or plus $NaHCO_3$ when the patients had evident cardiac toxicity.

The aim of this study is to predict the morbidity and mortality factors in patients with acute TCA toxicity, to assess the effect of intralipid 20% on progression of cases presented by coma and cardiac toxicity with comparison with those taking $NaHCO_3$ for cardiac toxicity and to detect early evidence of cardiotoxicity using quantitative analysis of Troponin I.

For each patient the following data were studied:

I- Sociodemographic data: *as age, sex, residence and occupation.*

II- Medical evaluation: Including the patient's medical history, general examination, systemic examination and the poisoning circumstances.

III- Investigation parameters:

A-Laboratory investigations: Including arterial blood gases, Serum electrolytes (Na and K), random blood sugar and serum troponin I level.

B-Electrocardiography (ECG) monitoring:

ECG was recorded to all subjects under the present study .In addition to continued monitoring to detect any cardiac arrhythmia during the patients hospital stay.

IV- Treatment: Including $NaHCO_3$ alone or combined with intralipid 20%.

V- Outcome: include coma grade, ECG findings and duration of hospitalization.

This research studied the effect of some risk factors as age, sex, available ingested dose, type of TCA ingested, previous attempts of suicide, presence of psychiatric disease, coingestion of other drugs, delay time and mode of toxicity, inaddition to clinical presentations like seizures, metabolic acidosis and respiratory failure for which endotracheal intubation was been necessitated. Data were analyzed in relation to outcome toxicity measures.

By the end of the study, the recorded clinical data of all the studied patients were tabulated for statistical analysis.

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). Most patients presented by suicidal ingestion (suicide vs. accidental= 89% vs. 11%).

The age of the studied patients ranged from 2-73 years and the most commonly affected age group ranged from 20-40 years with male: female ratio 1: 2.7.

Type of TCA ingested was an important risk factor, as it showed a highly significant difference between groups (p-value <0.0001). Amitriptyline was the commonest followed by clomipramine/ nortriptyline (not represented in group III), while dothiepin was the least ingested drug (18 patients), most of which (13 patients) presented in severe toxicity group (III).

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 as19.6% and 19.2% in deep coma (coma grade II, III, IV) constituting 37.5% and 12.5% of intubated patients respectively. Patients who were conscious or coma grade I were intoxicated by amitriptyline, clomipramine/nortriptyline and dothiepin as 63.4%, 29.5% and 7.1% respectively.

The dose of TCA had a highly significant effect (p-value <0.0001) on severity of toxicity, coma grade and ECG finding, where patients who had the highest dose were in group III (severe toxicity), deep coma (coma grade II, III, IV) and abnormal ECG findings.

The most presenting complaint in the studied patients was vertigo, while the most common finding in clinical examination was sinus

tachycardia (49%), followed by drowsiness (41%) and agitation (34%). 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) are important indicator for the severity of toxicity. It had a high significant effect (p-value <0.0001) on ECG findings, coma grade and type of TCA ingested. Patients with two or more ADORA criteria had abnormal ECG findings (96.2%) and coma grade II or III or IV (53.8%). Also 88.9% of patients intoxicated by dothiepin presented with two or more ADORA criteria, while 48.2% of patients intoxicated by amitriptyline and 34.6% intoxicated by clomipramine / nortriptyline had two or more ADORA criteria. Altered mental status was the commonest ADORA criterion in 71% of patients followed by dysrhythmias in 50% of patients.

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 indications for intubation in the current study were deep coma, respiratory depression and aspiration of gastric contents constituting 50%, 37.5% and 12.5% of patients respectively.

The most common acid-base disorder in the present study was metabolic acidosis. Coma had a highly significant effect (P-value <0.0001) on the occurrence of metabolic acidosis as 88.9% of patients complicated by metabolic acidosis were in deep coma (grade II, III, IV), while only one patient (11.1%) complicated by metabolic acidosis was conscious or just drowsy (grade 0, I). All patients complicated by metabolic acidosis had significant abnormal ECG findings.

ECG changes were evaluated to be normal in 49% of patients, sinus tachycardia was the most common dysrhythmia observed followed by prolonged QTc interval and wide QRS complex in 44%, 6% and 5% of patients respectively. Other types of dysrhythmias were presented in little proportions of patients.

ECG changes had no relation (P- value >0.05) with all risk factors except for the age and the mode of poisoning. Abnormal ECG findings were present more in suicidal poisoning and old age.

QRS duration is a good predictor for occurrence of seizures. This study showed that most seized patients had abnormal ECG finding in the form of wide QRS >100 ms or ≤ 160 ms (p- value< 0.05).

ECG changes are good outcome toxicity parameter for severeity of TCA toxicity (p-value < 0.001), as all patients in group III (severe toxicity group) had abnormal ECG findings.

Duration of hospitalization had no relation (P- value >0.05) with all risk factors except for the dose of TCA, as patients with higher doses stay in hospital for long duration.

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. All patients in group III (severe toxicity group, ICU admission) had abnormal ECG findings and deep coma ranging between grade II, III and grade IV. The mean DOH for group III, II and I was 47.20 ± 25 hours, 27.60 ± 11.813 hours and 6.89 ± 1.956 hours respectively.

Grade of coma had no relation (P- value >0.05) with all risk factors except for the dose of TCA, as patients with higher doses developed deep grades of coma (II, III, IV).

In the present study coma grade is a good outcome toxicity predictor for endotracheal intubation and ICU admission (p-value < 0.001).

This study revealed that the time to regain consciousness was significantly lower (p-value < 0.05) in group IIIB (12.10 ± 6.674 hours) than group IIIA (21.42 ± 12.163 hours).

The present study reported non significant difference (p-value > 0.05) between group IIIB and group IIIA as regard the duration of hospitalization in ICU, although it was lower in group IIIB than group IIIA.

Patients in group IIIA and group IIIB who had cardiac dysrhythmia treated with $NaHCO_3$ and intralipid infusion plus $NaHCO_3$ respectively, had all improved and reversed, meanwhile the dose of $NaHCO_3$ required for treatment of group IIIB was less than the dose required for the patients in group IIIA.

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