

Evaluation of Copeptin Level and Peradeniya Score as Predictors of Severity and Outcome in Acute Organophosphorus Pesticides Poisoned Patients Admitted to the Poison Control Center Ain Shams University Hospitals

(A Prospective Study)

Thesis

Submitted for Partial Fulfillment of Master Degree in Clinical Toxicology

Presented by

Manar Yehia Ali El-Khashab

Demonstrator in Forensic Medicine and Clinical Toxicology Department Faculty of Medicine – Ain Shams University

Under Supervision of

Prof. Dr. Manal Ali Abd Al-Kareem

Professor of Clinical Toxicology Forensic Medicine and Clinical Toxicology Department Faculty of Medicine-Ain Shams University

Assist. Prof. Dr. Aya Shawky Khater

Assistant Professor of Clinical Toxicology Forensic Medicine and Clinical Toxicology Department Faculty of Medicine-Ain Shams University

بسم الله الرحمن الرحيم

وقُلِ اعْمَلُواْ فَسَيْرَى اللهُ عَمَلُكُ مُ وَقُلِ اعْمَلُواْ فَسَيْرَى اللهُ عَمَلُكُ مُ وَقُلِ اللهُ عَمَلُكُ مُ اللهُ عَمَلُوا فَسَيْرَى اللهُ عَمَلُوا فَسَيْرَى اللهُ عَمَلُكُ مُ اللهُ عَمَلُوا فَسَيْرَى اللهُ عَمَلُوا فَسَيْرَى اللهُ عَمَلُوا فَسَيْرَى اللهُ عَمَلُوا فَسَيْرَى اللهُ عَمَلُوا فَاللهُ عَمَلُوا فَسَيْرَى اللهُ عَمَلُوا فَسَيْرَا اللهُ عَمَلُوا فَسَيْرَا اللهُ عَمْلُوا فَسَيْرَا اللهُ عَمْلُوا فَسَيْرَا اللهُ عَمْلُوا فَسَيْرَا اللهُ عَمْلُوا فَاللهُ عَمْلُوا فَسَيْرَا اللهُ عَمْلُوا فَسَيْرَا اللهُ عَمْلُوا فَاللّهُ عَمْلُوا اللهُ عَمْلُوا فَاللّهُ عَمْلُوا اللهُ عَمْلُوا اللهُ عَلَيْ اللّهُ عَمْلُوا اللهُ عَمْلُوا اللهُ عَمْلُوا اللهُ عَلَيْ اللهُ عَمْلُوا اللهُ عَلَيْ اللّهُ عَلَيْ اللّهُ عَلَيْكُوا اللّهُ عَمْلُوا اللّهُ عَلَيْ اللّهُ عَلَيْكُولُ اللّهُ عَمْلُوا اللّهُ عَلَيْكُولُ اللّهُ عَمْلُوا اللّهُ عَلَيْكُولُ اللّهُ عَلَيْكُولُ اللّهُ عَلَيْكُولُ اللّهُ عَلَيْكُولُ اللّهُ عَلَيْكُولُ اللّهُ عَلَيْكُ عَلَيْكُولُ اللّهُ عَلَيْكُ اللّهُ عَلَيْكُولُ اللّهُ عَلَيْكُولُ اللّهُ عَلَيْكُولُ اللّهُ عَلَيْكُولُ اللّهُ عَلَيْكُولُ عَلَيْكُولُ اللّهُ عَلَيْكُولُ اللّهُ عَلَيْكُولُ اللّهُ عَلَيْكُولُ اللّهُ عَلَيْكُولُ اللّهُ عَلَيْكُ عَلَيْكُولُ اللّهُ عَلَيْكُولُولُ اللّهُ عَلَيْكُولُ اللّهُ عَلَيْكُولُ اللّهُ عَلَيْكُولُ اللّهُ عَلَيْكُولُ اللّهُ عَلَيْكُ اللّهُ عَلَيْكُولُ اللّهُ عَلَيْكُولُولُ اللّهُ عَلَيْكُ عَلَيْكُولُ اللّهُ عَلَيْكُولُ اللّهُ عَلَيْكُ اللّهُ عَلَيْكُ عَلَيْكُ عَلَيْكُ



صدق الله العظيم [سورة: التوبة - الآية: ١٠٠]

Acknowledgments

First and foremost, I feel always indebted to **Allah** the Most Beneficent and Merciful.

I wish to express my deepest thanks, gratitude and appreciation to **Prof. Dr. Manal Ali Abd Al-Kareem**, Professor of Clinical Toxicology, Faculty of Medicine, Ain Shams University, for her meticulous supervision, kind guidance, valuable instructions and generous help.

Special thanks are due to **Dr. Aya Shawky Khater**, Assistant Professor of Clinical Toxicology,
Faculty of Medicine, Ain Shams University, for her
sincere efforts, fruitful encouragement.

I would like to express my hearty thanks to all my family for their support till this work was accomplished.

Last but not least my sincere thanks and appreciation to all my colleagues for their support and to all the patients who participated in this work.

Manar Yehia Ali El-Khashab

List of Contents

Title	Page No.
List of Tables	1
List of Figures	6
List of Abbreviations	10
Introduction	1
Aim of the Work	17
Review of Literature	18
Subjects and methods	67
Results	81
Discussion	127
Summary	155
Conclusion	160
Recommendations	162
References	163
Arabic Summary	

Tist of Tables

Table No.	. Title Page	No.
7	Tables of Review and Methodology	
Table (1):	Structures of main groups of OP pesticides	22
Table (2):	WHO classification of OP pesticides accordi	ing
	to their hazardousness	24

Table (3):	Summary of clinical features of acute cholinergic crisis	34
Table (4):	Chart reflects blood pressure categories	70
Table (5):	Peradeniya Organophosphorus Poisoning (POP) Scale	72
Table (6):	Data sheet for the patients included	79
	Tables of Results	
Table (1):	Distribution of the patients according severity by POP score and the outcome included in the present study.	82
Table (2):	Frequency of sociodemographic distribution as regards sex, age, residence and occupation of patients in the present study	84
Table (3):	Frequency and percentage of manner of poisoning, place, route of intake, preconsultation treatment and delay time (hour) among the patients in the present study	86
Table (4):	Independent t- test statistical analysis of delay time among deaths and discharged patients in the present study	88
Table (5):	Frequency and percentage of vital data of the patients in the present study	89
	Tist of Tables cont	
Table No.	Title Page No	
Table (6):	Chi-Square statistical analysis for comparing vital data among mild, moderate and severe patients included in the present study	90
Table (7):	Frequency and percentage of cutaneous and pupillary manifestations among the patients in the present study	

Table (8):	Chi-Square statistical analysis for comparing cutaneous and pupillary manifestations among mild, moderate and severe patients included in the present study
Table (9):	Frequency and percentage of GIT, respiratory and neurological manifestations among the patients included in the present study
Table (10):	Chi-Square statistical analysis for comparing GIT, respiratory and neurological manifestations among mild, moderate and severe patients in the present study
Table (11):	Frequency and percentage of serum Na, serum K and arterial blood gases (ABGs) interpretation of the patients included in the present study
Table (12):	Chi-Square statistical analysis of arterial blood gases (ABGs), serum Na and serum K among mild, moderate and severe groups of patients in the present study
Table (13):	Chi-Square statistical analysis for comparing arterial blood gases (ABGs), serum Na and serum K among deaths and discharged patients in the present study

Tist of Tables cont...

Table No.	Title	Page No.
Table (14):	One-way ANOVA and statistical analysis of serum Pseudocholinestrase (PChE Copeptin among mild, mode groups of patients included study	K levels, serum E) and serum erate and severe I in the present
Table (15):	Independent t- test statist serum Na, serum K Pseudocholinestrase (PChE Copeptin among deaths patients included in the prese	levels, serum E) and serum and discharged
Table (16):	Multivariate logistic regress the predictors of the outc patients included in the prese	ome among the
Table (17):	Sensitivity and specificity of as early predictor of morta patients included in the prese	ality among the
Table (18):	Pearson correlation between hospital stay duration (days among the patients in the pre) and POP score
Table (19):	Pearson correlation between and total atropine dose (amp the patients in the present st	serum Copeptin poules) needed of
Table (20):	Frequency and percentage received in emergency roo patients included in the prese	m (ER) by the
Table (21):	Chi-Square statistical analysis management received in the (ER) among mild, moderate a of the patients in the present s	sis for comparing emergency room and severe groups

Tist of Tables cont...

Table No.	Title	Page No.
Table (22):	Frequency and percentage of disposition and hospital stay durat of the patients included in the presentation.	ion (days)
Table (23):	Chi-Square statistical analysis for chospital disposition, complication outcome among mild, moderate a patients in the present study	comparing and the nd severe
Table (24):	One-way ANOVA and TUKE statistical analysis of hospital stay (days), initial and total atropine (received among mild, moderate at the patients in the present study	Y'S Test duration ampoules) nd severe
Table (25):		nalysis of and total lischarged
Table (26):	Chi-Square statistical analysis for a hospital disposition, complications a outcome of the patients in the present	comparing among the

List of Figures

Figure No.	Title	Page No.
Figu	res of Review and Methodology	
Figure (1):	General chemical structure Organophosphate compounds	
Figure (2):	Process of thiophosphates toxic act and biodegradation of oxophosphate	
Figure (3):	Acetylcholine (Ach) and AChE synaptic cleft	
Figure (4):	Reaction of inhibition of esterases Reactivation (3) and aging (4)	v
Figure (5):	Synthesis and release of Copept AVP.	
Figure (6):	Cleavage of pro-AVP and it products	_
Figure (7):	Standard curve of Copeptin	76
	Figures of Results	
Figure (1):	Pie chart of classification of pati the study according to POP score	
Figure (2):	Pie chart of the outcome of patients study	
Figure (3):	Pie chart of occupation distribution patients in the present study	
Figure (4):	Pie chart of residence distribution patients in the present study	
Figure (5):	Pie chart of manner of poisoning the patients in the present study	•
Figure (6):	Pie chart of route of poisoning amorpatients in the present study	0

Tist of Figures cont...

Figure No.	Title	Page No.
Figure (7):	Multiple bar chart of heart rat groups of severity of the patients in the present study.	included
Figure (8):	Multiple bar chart of blood among groups of severity of the the present study	patients
Figure (9):	Multiple bar chart of respirat among groups of severity of the included in the present study	patients
Figure (10):	Bar chart of cutaneous manifamong the patients in the present	
Figure (11):	Pie chart of pupillary size an patients in the present study	
Figure (12):	Multiple bar chart of c manifestations among groups of of the patients included in the study	severity present
Figure (13):	Multiple bar chart of pupillary size groups of severity in the present s	ze among
Figure (14):	Bar chart of GIT (gastroin manifestations among the included in the present study	patients
Figure (15):	Bar chart of respiratory manifamong the patients included present study	in the
Figure (16):	Pie chart of conscious level assess POP score among the patients income the present study	cluded in
Figure (17):	Pie chart of fasciculation perce classified by POP score am patients included in the present s	ong the

Tist of Figures cont...

Figure No.	Title	Page No.
Figure (18):	Bar chart of serum Copeptin le groups of severity of the patient in the present study.	s included
Figure (19):	Bar chart of serum Na level voutcome of the patients in the study	ne present
Figure (20):	Bar chart of serum K level voutcome of the patients in the study	ne present
Figure (21):	Bar chart of serum (Pseudocholinestrase) level voutcome of the patients in the study	ersus the ne present
Figure (22):	Bar chart of serum Copeptin le the outcome of the patients in the study	he present
Figure (23):	The receiver operating characteristics (ROC) curve of serum Copepting predictor of the outcome	n as early
Figure (24):	Pearson correlation test betwee Copeptin and POP score	
Figure (25):	Pearson correlation test betwee stay duration (days) and POP so	-
Figure (26):	Pearson correlation test betwee Copeptin and total atrop (ampoules)	ine dose
Figure (27):	Pie chart of hospital disposition the patients in the present study	
Figure (28):	Multiple bar chart of hospital of among groups of severity of the in the present study.	e patients

Tist of Figures cont...

Figure No.	Title P	age No.
Figure (29):	Multiple bar chart of the complicat among groups of severity of the pati in the present study.	ents
Figure (30):	Multiple bar chart of the outcome an groups of severity of the patients in present study.	the
Figure (31):	Multiple bar chart of the complicate among the outcome of the patients in present study.	the

Tist of Abbreviations

Abb.	Full term
ARC	Airway Preathing Circulation
	Airway-Breathing-Circulation Arterial blood gases
	Arterial blood gases Acetylcholine receptors
Ach	
	· · · · · · · · · · · · · · · · · · ·
	Acetylcholine esterase Adrenocorticotropic hormone
	American Heart Association
	Alanine transaminase
	Acute myocardial infarction
	• •
Amp	One-way analysis of variance
	Autonomic nervous system
	Acute organophosphorus poisoning
	Acute Organophosphorus poisoningAcute Physiology and Chronic Health Evaluation
AI ACHE II	II
<i>APE</i>	Acute pulmonary embolism
	Aspartate transaminase
	Ain shams university hospitals
	Area under Curve
<i>AVP</i>	Arginine vasopressin
	Blood brain barrier
<i>BPM</i>	Beats per minute
<i>BuChE</i>	Butyryl cholinesterase
<i>BZD</i>	Benzodiazepines
	Catecholamine
CI	Confidence interval
<i>CNS</i>	Central nervous system
<i>CRH</i>	Corticotropic-releasing hormone
	C-reactive protein
	Computerized tomography angiography
	Cardiovascular system
	Chemical warfare agents
	5, 5'-Dithiobis-2-nitrobenzoic acid
ECG	Electrocardiogram
ELISA	Enzyme-linked immune-sorbent assay

Tist of Abbreviations cont...

Abb.	Full term
<i>ER</i>	Emergency room
	Endotracheal tube
<i>FFP</i>	Fresh-frozen plasma
<i>GABA</i>	Gamma-aminobutyric acid
<i>GCS</i>	Glasgow Coma Score
<i>GGT</i>	γ-glutamyl transpeptidase
<i>GIT</i>	Gastrointestinal tract
<i>GL</i>	Gastric lavage
<i>GSH</i>	Glutathione
<i>HPA</i>	Hypothalamic-pituitary-adrenal
<i>Hr</i>	Hour
<i>HRP</i>	Horseradish peroxidase
<i>ICU</i>	Intensive care unit
	Intermediate syndrome
IPCS/EC/EAPCCT	International Program on Chemical Safety, the
	Commission of the European Union, and the
	European Association of Poison Centers and
	Clinical Toxicologists.
<i>IV</i>	
<i>K</i>	
<i>LD</i>	
	Lactate dehydrogenase
	Mean arterial pressure
	Myocardial infarction
	Mechanical ventilation
<i>Na</i>	
<i>NAs</i>	
<i>NG</i>	8
	Neuromuscular junctions
	Negative Predictive Value
	Neuropathy target esterase
O.D	•
	Octomethyl pyrophosphotetramide
	Organophosphorus
<i>OPICN</i>	Organophosphorus ester-induced chronic
	neurotoxicity

Tist of Abbreviations cont...

OPIDPOrganophosphate-induced delayed polyneuropathy
ΙΟΟΙ ΥΠΕΜΙ ΟΙΣΜΙΙΙ Υ
OTCOver the counter
PAMPralidoxime
Pcc
PChEPseudocholinestrase
PNSPeripheral nervous system
PONParaoxonase
POPPeradeniya organophosphorus poisoning
POXPhosphonyl pyridine oxime intermediate
PPVPositive Predictive Value
PSSPoison Severity Score
rCorrelation coefficient
RCTRandomized control trail
ROCReceiver operating characteristic
ROSReactive oxygen species
S. CPPSerum Copeptin
SAPS IISimplified Acute Physiology Score II
SBPSystolic blood pressure
SDStandard deviation
SOFASequential Organ Failure Assessment
TIndependent t test
TEPPTetraethyl pyrophosphate
T(hs-TnT) high-sensitive troponin
TMBTetramethylbenzidine
TTTTreatment
WHOWorld health organization
X_2