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The effect of organophosphate insecticide poisoning on the brain cells and neurotransmitters in humans

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بسم الله الرحمن الرحيم

" وَوَصَّيْنَا الْإِنسَانَ بِوَالِدَيْهِ حَمَلَتْهُ أُمُّهُ وَهْنًا عَلَىٰ وَهْنٍ وَفِصَالُهُ فِي عَامَيْنِ أَنِ اشْكُرْ لِي وَلِوَالِدَيْكَ إِلَيَّ الْمَصِيرُ "

صدق الله العظيم

سورة لقمان الآية (١٤)

I declare that this thesis has been composed by myself and the work there in has not been submitted for a degree at this or any other university

Mohamed Abdel-Azeem Abdel-Aziz

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لو لم يأمرنى ربى بشكرك لإستحييت من شكرك

فقد أعطيتنى عمرك و برعايتك أصبح لى من كل

أخ أب و من كل أخت أم ورزقنى الله بعد أمى

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أدعو الله الكريم أن يشكر لك

وليس جزاءاً لشكر الله إلا المغفرة والجنة

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و جزاك الله عنا خيراً

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Abstract

Organophosphates (OPs) are lipophilic; they penetrate the blood brain barrier, resulting in severe brain damage. The toxic effects of organophosphate poisoning (OPP) on the central nervous system (CNS) include nonspecific symptoms as irritability, restlessness, disorientation and confusion. The objective of this study was to prospectively evaluate early levels of serum S100B protein, neuron specific enolase (NSE) and myelin basic protein (MBP) to assess their potential as diagnostic and/or prognostic tools that may aid in the management of organophosphates-poisoned patients and chronically exposed subjects. Also the correlation between serum levels of S100B, NSE, and MBP with other biochemical parameters such as acetylcholine (ACh) (as a neurotransmitter), pseudo cholinesterase (PChE), lactate dehydrogenase (LDH), creatine phosphokinase (CPK), aspartate transaminase (AST), alanine transaminase (ALT), urea, creatinine, sodium (Na^+) and potassium (K^+) were studied. This study was conducted on 40 adult patients of both sexes admitted with acute OPP to the Poison Control Center of Ain Shams University (PCC-ASU). In addition to 20 chronically exposed subjects and 30 healthy volunteers serving as control. The study revealed that there were marked significant differences between the markers of nerve cells degeneration (S100B, NSE, MBP, ACh and PChE) in patients groups when compared with the control group. Therefore serum S100B, NSE and MBP can be used as early markers in brain cells degeneration in OPP. Also the chronic exposure to OPs affected the CNS cells where neuro-degenerative markers (S100B and NSE) showed significant increase in chronic group.

Key words: Organophosphate, S100B protein, neuron specific enolase, myelin basic protein, acetylcholine and pseudocholinesterase.

List of abbreviations

ACh	Acetylcholine
AChE	Acetylcholine esterase
ADP	Adenosine diphosphate
ALT	Alanine aminotransferase
AMP	Adenosine monophosphate
AST	Aspartate aminotransferase
ATP	Adenosine triphosphate
AZ	Active zone
BBB	Blood brain barrier
BSA	Bovine serum albumin
BTC	Butyrylthiocholine
BuChE	Butyrylcholinesterase
C-F	Carbon fluoride bond
CNS	Central nervous system
CPK	Creatine phosphokinase
CSF	Cerebrospinal fluid
CYP	Cytochrome-P450
DTNB	5,5-dithiobis-2-nitrobenzoic acid
EAPCCT	European association of poisons centers and clinical toxicologists
EC	European community
EF-hand	Helix-loop-helix structural domain or motif found in a large family of calcium-binding proteins
ELISA	Enzyme-linked immunosorbent assay
G6P	Glucose-6-phosphate
G6PDH	Glucose-6-phosphate dehydrogenase
GABA	Gama-aminobutyric-acid
GOS	Glasgow outcome scale
HK	Hexokinase
HRP	Horseradish peroxidase
ICU	Intensive care unit
IMS	Intermediate syndrome
IPCS	International program on chemical safety

KDa	Kilodalton
LDH	Lactate dehydrogenase
mAChRs	Muscarinic acetylcholine receptors
MAPK	Mitogen-activated protein kinase
MBP	Myelin basic protein
MDH	Malate dehydrogenase
MS	Multiple sclerosis
NAC	N-acetyl-L-cysteine
nAChRs	Nicotinic acetylcholine receptors
NAD	Nicotinamide adenine dinucleotide
NADP	Nicotinamide adenine dinucleotide phosphate
N-P	Nitrogen phosphorus bond
NSE	Neuron-specific enolase
O.D.	Optical density
OP	Organophosphate
OPICN	Organophosphate-induced chronic neurotoxicity
OPIDN	Organophosphate-induced delayed neurotoxicity
OPP	Organophosphates poisoning
PCC-ASUH	Poison Control Center of Ain Shams University Hospitals
PChE	Pseudocholinesterase
P-CN	Phosphorus cyanide bond
P-F	Phosphorus fluoride bond
PNS	Peripheral nervous system
r	Spearman correlation coefficient
RAGE	Receptor for advanced glycation end products
Rpm	Revolution per minute
SEM	Standard error of the mean
TBI	Traumatic brain injury
TM	Trans-membrane
TMB	Tetramethylbenzidine
WHO	World Health Organization

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Aim of work

To our knowledge, there have been no studies focused on the diagnostic and prognostic value of serum S100B protein, neuron specific enolase (NSE) and myelin basic protein (MBP) in human patients with organophosphate compounds toxicity. The objective of this study is to:

- Evaluate the level of serum S100B protein, neuron specific enolase (NSE) and myelin basic protein (MBP) in chronic exposed subjects to organophosphate compounds and acute poisoning patients.
- Detection of their usefulness as early prognostic and diagnostic markers in brain cells degeneration in organophosphate compounds poisoning.
- Study the correlation between serum level of (S100B protein, NSE, MBP) and serum level of other biochemical parameters such as acetylcholine (as a neurotransmitter), pseudocholinesterase, lactate dehydrogenase (LDH), creatine phosphokinase (CPK), aspartate aminotransferase (AST), alanine aminotransferase (ALT), urea, creatinine, sodium and potassium.