Assessment of the prognostic value of nerve damage biomarkers in acute and chronic organophosphate toxicity

Study protocol

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INTRODUCTION

Organophosphates are among the most easily accessible toxic compounds worldwide. The global occurrence of poisoning due to organophosphates is estimated to be 300,000 to 2 million cases per year, varying between accidental exposure and suicidal attempts [1,2]. Owing to the high incidence of exposure, research focused on the detection of the possible mechanisms of toxicity, as well as evaluation of various antidote efficacy and biomarkers that can be used as mortality predictors. The main mechanism of pesticides toxicity is via inhibition of acetylcholinesterase enzyme responsible for the degradation of the neurotransmitter acetylcholine. This abrupt increase in acetylcholine levels leads to a cholinergic surge with continuous stimulation of receptors leading to the manifestation of signs and symptoms that vary according to the route of exposure to organophosphates [3,4]. Another suggested mechanism was the oxidative stress induced by the pesticides [2].

However, only few studies focused on biomarkers and their quantitation. Results emphasized the importance of detecting the levels of serum cholineesterase as a prognostic indicator for acute toxicity [5,6]. Nevertheless, it has been shown that the reliability on serum cholinesterase levels is controversial [2,7,8]. Oxidative stress biomarkers (malondialdehyde (MDA) and total antioxidant capacity (TAC)), activity of the apoptotic biomarkers (caspase 3 and caspase 9) and pseudocholinesterase (p.ChE) were further investigated as mortality predictors [2]. Significantly, there is paucity of evidence regarding the value of biomarkers addressing the involvement of nerve damage resulting from organophosphate poisoning in acute and chronic toxicities despite the accumulating evidence of their chronic neurological impact associated with their action on neurotoxic esterase [5,8]

AIM OF THE STUDY

To assess the possible prognostic value of markers of neuroinflammation and damage by a full proteomic and glycomic profile of acute and chronic organophosphate exposure patients. The profiling will be generated together with an assessment of their genotoxic effect. This will be conducted in parallel to the assessment of traditional markers of inflammation and oxidative stress.

PLAN OF THE STUDY

Study setting:

- Acute exposure patients will be recruited from the Poison Center and Emergency Department of Alexandria Main University Hospital.
- Chronic exposure patients will be recruited from farm field workers with a confirmed history of repeated occupational exposure to organophosphate pesticides.
- Control subjects will be recruited from city dwellers without any medical conditions (healthy subjects) with comparable age and gender.

Study design:

Type of the trial: cross-sectional trial

Inclusion criteria:

Chronic Patients: Adult males with age above 18.

Acute Patients: Adult males and females with age above 18 .

Controls: Adult males and females with age above 18 without previous exposure to organophosphate pesticides.

No restrictions on comorbidities in the three groups except those mentioned under Exclusion Criteria.

Exclusion criteria:

Pediatric patients, patients with neurological diseases (Parkinsonism, epilepsy, Alzheimer's disease , etc.) and any patient who does not meet the inclusion criteria.

Target population:

Patients with acute and chronic exposure to organophosphates.

Sample size: Total number between 60 to 90 patients, divided into three groups:

1- Controls without previous exposure to organophosphates ($n \geq 15$).

2- Patients with chronic exposure to pesticides ($n \geq 30$).

Patients with acute exposure to organophosphates ($n \geq 30$).

Outcome assessment:

Identification of a neuroinflammatory biomarker that correlates with neve injury**.**

Type of sample and method of selection:

Convenience sample through nonprobability sampling methods

Data collection methods and tools:

1-Patient demographics and data regarding chronic patients including: 1) history of organophosphates exposure 2) compliance to safety instructions during handling of pesticides 3) medical history 4) general health status 5) cholinergic symptoms if any will be recruited through a questionnaire answered by the patients on the day of recruitment.

2-Blood sample collection with required preparations for serum extraction.

3- Laboratory analysis for some biomarkers.

4-Proteomic and glycomic analysis to identify the biomarker that correlates with nerve injury[(9)].

Ethical consideration:

1. The researcher will seek the approval of the Ethics Committee of Faculty of Pharmacy & Alexandria University for conducting the research.
2. The researcher will comply with the International Guidelines for Research Ethics for medical research involving human subjects for the declaration of Helsinki [(10)].
3. The researcher declares that there is no conflict of interest.
4. All participants will sign an informed consent before being included in the study.

Statistical analysis:

The collected data will be subjected to statistical analysis by the use of suitable techniques to achieve the objectives of the study.

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