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IFCC Professional Scientific Exchange Programme Report - LINK BETWEEN PARAOXONASE GENOTYPE AND PROGNOSIS IN SUICIDES WITH ORGANOPHOSPHORUS PESTICIDES

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Dr. Sozmen worked at the Lipid Research Laboratory in the Department of Medicine at Manchester Royal Infirmary as a fellow funded by FEBS-short term fellowship and IFCC-Professional Scientific Exchange programme. During this fellowship, she worked with Dr. Bharti Mackness under the guidance of Dr. Michael Mackness and learned the methods to determine several enzymes and PON genotyping as follows:

- CETP (cholesterol ester transfer protein)
- LCAT (lecithine cholesterol acyl transferase)
- PON 1 activity
- PON mass
- PON genotyping (bath 55 and 192 polymorhisms)

Introduction

Organophosphorus (OP) pesticides are the most prevalent agents used (either by oral or inhalation means) in suicide attempts in Turkey especially in the Aegean region where cultivation is one of the main means of subsistence. The potential effect of organo- phosphates depends upon the amount and form ingested, the toxicity of the agent, the time lapse involved and a variety of host factors. However, it has been observed that patients have different clinical signs independent of the environmental factors listed above. Serum paraoxonase (PON1) is an enzyme located on HDL and it hydrolyses various substrates including the organophosphate pesticides and lipid peroxides on LDL. The amino acid polymorphism at position-192 (glutamine and arginine) results in two allozymes (R and Q), which differ in their hydrolytic activity towards paraoxon. Another polymorphism at amino acid 55, which is a leucine (L) to methionine (M) substitution, modulates PON1 activity independently of the 192 polymorphism. The difference in individual clinical findings is clearly the most important risk factor for susceptibility against OP's. These differences seem to be closely related to PON1 activity and ON1 polymorphism since it has been shown that R-allele is more efficient than the Q-allele in hydrolysing paraoxon in vitro. The effect of PON1 polymorphism on the level of toxicity of the patients exposed to OP is still obscure. The aim of the project was to determine the link between possible individual risk factors (age, PON1 activity, PON1 genotypes, serum PON1

Concentration, butyrylcholine esterase activity) and prognosis in suicides with organosphosphorus pesticides.

Materials and Methods

During the period of October 1999-July 2000, 28 patients (men and women) were admitted to the Emergency Service at Ataturk Research and Educational Hospital in Izmir/Turkey due to OP poisoning. 26 of them drank a different amount of a variety of OP's to attempt suicide, one used injection and one other was exposed to OP's by inhalation. They were treated and monitored in the hospital by a team led by Dr. B. Sozmen and Dr. L.Aslan. Their blood samples were from them upon arrival. As a control group, 66 healthy persons (men and women) matched for age and sex, volunteered to participate in this study. Sera and buffy coats with EDTA of both groups were kept in -80°C until sending them to Manchester Royal Infirmary. Butyrylcholine esterase activities were determined using butyrylthiocholin as substrate according to the method of Ellman et al, at the Dept. of Biochemistry in Ege University. PON1 activities were measured by the method proposed by Dr. Mackness et al using paraoxon as a substrate. PON mass was also determined with an ELISA method, at Lipid Research Laboratory in Dept. of Medicine of Manchester Royal Infirmary. PON genotypes (for both polymorphism 55 and 192) were demonstrated in the same laboratory.

Results

Allele frequencies of patients and controls are detailed in table 1.

We observed an inhibition in PON1 activity as well as BuChE activity due to exposure to OP pesticides, which was independent of the type and dose of them. After the patients will be evaluated for PON1 and BuchE activities again, we will discuss our data.

Genotype	Controls N = 66	Patients N = 28
LL	0.67	0.68
MM	0.33	0.32
QQ	0.78	0.91
RR	0.22	0.09

Table 1