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Nephrotoxicity in rats induced by organophosphate insecticide methidathion and ameliorating effects of vitamins E and C

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Abstract

The effects of organophosphate insecticide methidathion (MD) on kidney tissue and the ameliorating effects of a combination of vitamins E and C against subchronic MD toxicity were evaluated in rats. Experimental groups were: control group (group I), 5 mg/kg body weight MD-treated group (group II), and 5 mg/kg body weight MD plus vitamin E plus vitamin C treated group (group III). The groups II and III were treated orally with MD on five days a week for four weeks. Vitamins E and C were injected at doses of 50 mg/kg body weight, i.m. and 20 mg/kg body weight, i.p., respectively, 30 min after the treatment of MD in the group III. Rats were anaesthesized and venous blood samples were collected by direct right ventricle heart puncture, in addition, the right kidney was removed for histopathological examinations and malondialdehyde (MDA) analyses after four weeks. The serum activity of cholinesterase (ChE) and the kidney level of malondialdehyde, and kidney histopathology were studied in rats. MD caused decreased ChE activity (group I: 2114 ± 63 U/L, group II: 1455 ± 100 U/L) and increased MDA level (group I: 147 ± 20.2 nmol/mg protein, group II: 236 ± 25.6 nmol/mg protein), and kidney damage in rats. Furthermore, a combination of vitamins E and C restored partially (ChE activity: 1670 ± 111 U/L, MDA level: 159 19.4 nmol/mg protein) this changes in MD-treated rats.

Keywords: Methidathion; Histopathology; Kidney; Lipid peroxidation; Vitamin C; Vitamin E

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1. Introduction

Organophosphate insecticides (OPIs) are some of the most useful and diverse classes of insecticides in use for almost five decades. While they continue to be extremely useful in agricultural pest control throughout the world their extensive use has led to numerous poisoning of non-target species [1]. Every year there are million cases of severe poisoning and 220,000 deaths; the majority of these poisoning and 99% of the resulting deaths occur in the Third World [2].

Methidathion (MD) (*S*-[(2,3-dihydro-5-methoxy-2-oxo-1,3,4-thiadiazol-3(2*H*)-yl)methyl] *O*,*O*-dimethyl phosphorodithioate) is one of the most widely used OPIs for agriculture and public health programmes. In general, OPIs are neurotoxic in nature by acting as inhibitors of neuronal cholinesterase (ChE) activity. However, previous studies from the our laboratory focused on in vitro and in vivo effects of OPIs such as chlorpyrifos-ethyl (CE), MD, fenthion, phosalone and diazinon on lipid peroxidation (LPO), and antioxidant enzymes status. The results indicated that these OPIs caused increased LPO in erythrocytes [3–10]. MD and fenthion caused also liver damage, and LPO in these studies has been suggested as one of the molecular mechanisms involved in OPI-induced toxicity [11,12]. Except one study held by our laboratory about effects of CE on kidney histopathology, we could not find any investigations concerning the effects of MD on kidney histopathological changes [13].

Many studies reported that a combination of vitamins E and C can reduce LPO caused by toxic substances [4,5,8,11–14]. We suggested that MD may induce oxidative stress in kidney tissue, and the combination of vitamins E and C may cope with the possible MD toxicity in the kidney of rat. Therefore, in the present study, the rats were administered orally MD to determine its effect on LPO and kidney histopathology. Additionally, a combination of vitamins E and C was administered to rats to evaluate their protective effects on MD-induced kidney toxicity.

2. Materials and methods

2.1. Animals and treatment

Twenty-four adult male Wistar albino rats weighing between 180 and 240 g were divided into three experimental groups as follows: control group (group I), MD-treated group as a dose regimen of 5 mg/kg body weight (group II), and MD plus vitamin E plus vitamin C treated group as a dose regimen of 5 mg/kg body weight (group III). The group I consisted of six rats and the groups II and III consisted of nine rats. The groups II and III were treated orally with MD in corn oil on five days a week for four weeks. Only corn oil was given in the same way to the group I. Vitamin E, as α-tocopherol acetate (Evigen; Aksu Farma, Istanbul, Turkey), and vitamin C, as sodium-L-ascorbate (Redoxon; Roche, Basel, Switzerland) were injected at doses of 50 mg/kg body weight i.m [4,5,8,11,12,14] and 20 mg/kg body weight i.p. [5,8,11,12,14], respectively, 30 min after the treatment of MD in the group III. Equal amounts of physiologic saline instead of vitamins were given to the rats of the groups I and II. The rats were caged individually and fed ad libitum without water restriction. The animals starved overnight for 12 h before the blood was collected. Rats were anaesthesized with ether and venous blood samples were collected by direct right ventricle heart puncture, in addition, after rats were sacrificed, the right kidney were removed for histopathological examinations and malondialdehyde (MDA) analyses after four weeks.

The experiments reported here complied with the current laws and regulations of the Turkish Republic on the care and handling of experimental animals.

2.2. Tissue homogenates

For MDA analyses, the kidneys of rats were washed with physiological saline. They were then homogenized for 3 min (Ultra-Turrax T25, Germany) in the cold phosphate buffer to provide a 10% homogenate. These homogenates were centrifuged at 6000*g* for 10 min to obtain supernatants. The levels of protein and MDA were determined in the supernatants.