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The Effect of Organophosphate Pesticides on the Blood Glucose Levels in the Mouse

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Abstract: The aim of the present study was to study the effect of two selected agents of this group on blood glucose levels in an animal model. Forty-two adult male mice were divided into 7 groups of 6 each. Animals were exposed by their entire tail for 10 sec once a day for 7 successive days to either 0, 0.1, 1, or 10% azynphos methyl (AZP) malathion (MLT). On days 1, 4 and 8, a small drop of blood was taken from tail of the animals that had been kept fasted overnight. Blood glucose levels were measure using a glucometer. The animals then were fed and after 1 h the blood glucose measurement was performed again. Results of this study indicated that the administration of organophosphate agents significantly prevented from the rise of blood glucose after feeding in comparison to the control animals. This reached the level of statistical significance on day 1 with MLT 1% ($p<0.001$). It is concluded that exposure with organophosphate pesticides may suppress excessive blood glucose levels with no effect on the basal blood glucose in the fasting animals.

Key words: Organophosphates, malathion, azinphos methyl, mouse, blood glucose

INTRODUCTION

Organophosphates are widely used as agricultural pesticides after organochlorine pesticides were forbidden. Many toxic organophosphates persist in the environment and tend to accumulate in the body fat of animals occupying a higher trophic level (Wang *et al*., 2005). The potential risks to humans resulting from the usage of a pesticide must be carefully assessed before the product is registered. One of the components in the risk assessment is the determination of the amount of pesticide to which the applicator is exposed. Traditional methods estimated dermal exposure by measuring the amount of pesticide deposited on absorbent patches worn on the applicator's body (Franklin, 1984). A detailed laboratory toxicity study on laboratory mice was conducted as part of a comprehensive laboratory and field study to field validate laboratory-based risk assessment of pesticides (Meyers and Wolff, 1994).

Globally, the prevalence of chronic, non-communicable diseases is increasing at an alarming rate. About 18 million people die every year from cardiovascular disease, for which diabetes and hypertension are major predisposing factors (Hossain *et al*., 2007). There are several opposing data on the effect of organophosphate pesticides on blood glucose levels. For instance, blood glucose increased in rats treated with a single ip dose of 650 mg kg^{-1} of malathion (Rodrigues *et al*., 1986).

Based on the observations on increased agricultural applications of these chemicals in one hand and the increased metabolic disease in the globe in another, a detailed set of experimental studies are suggested to find a possible correlation between them.

This study was designed to investigate the effect of two selected organophosphate insecticides, malathion (MLT) and azynphos methyl (AZP), on blood glucose levels in fasting and postprandial conditions in the mouse as an experimental animal model.

MATERIALS AND METHODS

This study was performed in the year 2007 in Urmia University, Faculty of Veterinary Medicine, Urmia, Iran.

Animals: Forty-two adult, male mice (20-25 g b.wt.) were used in this study. They were fed with commercial chow and tap water *ad lib* and kept at room temperature with 12 h artificial light in 24 h.

Experimental protocol: Animals were divided into 7 groups of 6 each. Once daily for 7 successive days, they were exposed by their entire tail for 10 sec to either of the following solutions: Water (control), AZP 0.1%, AZP 1%, AZP 10%, MLT 0.1%, MLT 1%, or MLT 10%. Animals were kept fasting on the nights on days 0, 3 and 7. Blood glucose was measured on days 1, 4 and 8 once before feeding the animals and once again 60 min after pesticide

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exposure and feeding the animals (no exposure to chemicals on day 8 was done). For this, a light general anesthesia was induced by inhalation of diethyl ether. Thereafter, the end point of the tail was incised and a drop of blood was obtained. Blood was transferred onto the strips of a hand glucometer (Bionime Rightest™ GM 300, Bionime GmbH, Switzerland). The level of glucose was determined with a sensitivity of 1 mg dL^{-1}.

Chemicals: Chemicals used were malathion (Ghazal Company, Tehran, Iran), azynphos methyl (Bayer AG, Leverkeusen, Germany) and Diethyle ether (Merck, Darmstadt, Germany).

Statistics: Data are presented as means±SEM. Differences between groups were analyzed using one-way ANOVA and when $p<0.05$, data were compared group by group with Bonferroni's t-test (a post-ANOVA test). A p-value smaller than 0.05 was considered to reflect a statistically significant difference.

RESULTS AND DISCUSSION

There was no significant difference in the weight gain during the study between control and treated animals, eliminating a considerable effect on general health of the animals after exposure to the chemicals. However, all animals treated with AZP 10% died within 24 h after the first treatment whereas all other groups survived during the experimental work. For this reason, the results of 10% concentration of the chemicals were omitted in this study.

In control animals, the fasting blood glucose levels were 68.17±5.57, 115±6.54 and 95±4.87 mg dL^{-1} on days 1, 4 and 8, respectively. After feeding the animals, those values increased to 168.33±5.57, 170.67±9.12 and 156.33±14.55 mg dL^{-1}. The increase reached to the level of statistical significance in all cases ($p<0.05$).

Neither AZP (Fig. 1A) nor MLT (Fig. 1C) affected the fasting blood glucose in the animals at the concentrations that were used. AZP-treated animals showed some decreased postprandial glucose levels, which did not reach the level of significance (Fig. 1B). On day 1, MLT 1% prevented the increased postprandial glucose levels ($p<0.001$). In the control animals it was 168.33±5.57 and in the treated animals it was declined to 113.17±11.94. This effect persisted on day 4, however, it was not significant. The effect was almost abolished on day 8 (Fig. 1D).

Present findings showed that AZP and MLT did not affect the fasting, basal glucose levels in the mouse. However, there was a tendency to a lower glucose levels after feeding the animals that were treated with these substances.

In the literature, there is a limited number of reports on the effect of organophosphate compounds on glucose levels. For instance, blood glucose was reported to increase in rats treated with a single ip dose of 650 mg kg^{-1} of MLT (Rodrigues *et al*., 1986). The effect of a single oral dose of MLT (1 g kg^{-1} b.wt.) on the

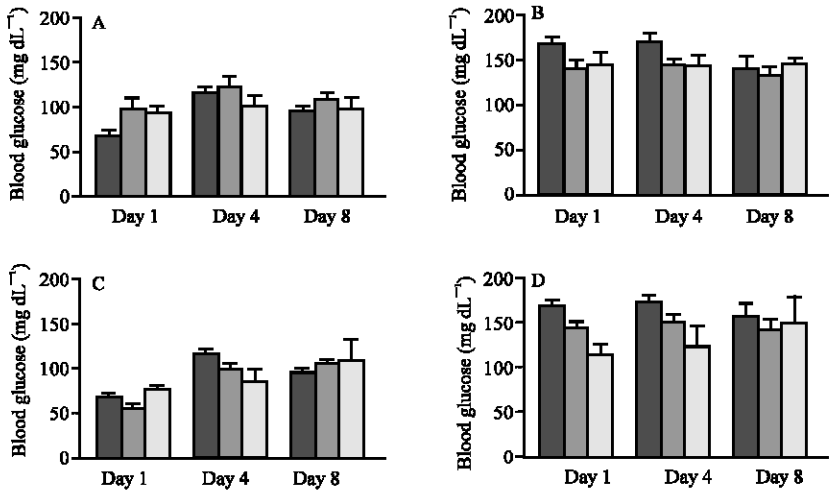

Fig. 1: Fasting (A and C) and postprandial (B and D) blood glucose levels in the mouse after exposure to AZP (A and B) or MLT (C and D) at concentrations of 0% (■), 0.1% (■), or 1% (■). In all cases (except AZP 0.01% and MLT 1%), the postprandial glucose levels were significantly higher than the fasting levels ($p<0.05$)

digestive and absorptive functions of the intestinal epithelium has been investigated in rats. The absorption of glucose was considerably reduced (35%) in pesticide fed animals (Chowdhury *et al*., 1980). In addition, an early study suggested that intraventricular injection of MLT may cause hyperglycemia, the mechanism of which was stipulated to be the accumulation of Acetylcholine (Ramu and Korner, 1975). MLT was administered orally for 4 weeks in the rat. Administration of malathion at doses of 100, 200 and 400 ppm increased plasma glucose concentrations by 25, 17 and 14% of control, respectively (Abdollahi *et al*., 2004).

Although dermal LD 50 values for various organophosphate insecticides have been determined in mice by application of solutions to hind feet (Skinner and Kilgore, 1982) no study has been accomplished on the effect of these substances on blood glucose levels using dermal application. In fact, while people are exposed to organophosphate agents mostly through dermal route, this kind of studies are neglected by most researchers all over the world.

One of the reasons that could explain the difference between our findings and those of the others is the chronic form of the exposure in this study. Indeed, MLT had no effect on blood glucose levels when administered intragastrically by stomach tube daily for 32 days (Rezg *et al*., 2006).

In conclusion, the current research work is the first one on the effect of organophosphate pesticides on blood glucose after dermal application. This route resembles what happens to people involved in the agricultural and occupational exposure to pesticides in practice. The novel findings is that these chemicals may prevent the postprandial blood glucose increase which may be a positive impact in diabetics whereas it could be considered a negative impact in healthy subjects.

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