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Research Article

Developmental Toxicity of Dicofol Containing Formulation Colonel-S in Swiss Albino Mice

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ABSTRACT

The teratogenicity of a commercial formulation of the insecticide Colonel- S containing Dicofol 18.5% EC (Emulsifiable Concentrate) as an active ingredient was evaluated in the developing foetus of mice. Colonel– S is a commercial insecticide used in agriculture and horticulture to control spider mites and soft bodied mites in apples, pears, soft fruits, cucumber, tomatoes, vines, lettuce and ornamentals. The insecticide was orally administered with the doses of 4 and 16 mg /kg body weight to pregnant female during the entire organogenetic period of gestation (Day 5-14). Dams were sacrificed on 18th day of gestation and uteri were examined for teratological changes. The results revealed that Colonel – S treatment produced maternal toxicity among the dams as evidenced by reduced maternal weight gain during gestation as compared to control. In the experimental groups a dose related decline in litter size and rise in percentage of resorbed fetus was observed. Percentage of alive fetus was greatly reduced at higher dose level. The study indicates that the insecticide formulation is toxic to the developing mice foetus and suggests that it may be potentially harmful to fetal development in humans.

KEY WORDS: Foetus, organochlorine insecticide, dicofol, resorption.

INTRODUCTION

Pesticides are widely used to control agricultural pests and insects causing public health hazards. They are indented to be toxic to living organisms. In addition to their toxic effect on target pests,

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they also harm non target organisms like beneficial insects, earthworms, soil fungi and bacteria, fish, domestic animals, and humans. Problems or outbreak occur among animals and human from insecticide toxicity, which usually occur either from direct exposure or indirectly from contaminated feeds or water by such chemicals. Acute toxicities of pesticides are well documented but little attention has been given to the chronic low dose effects of pesticides, especially as environmental pollutants. Animals exposed to pesticides have a greater risk of adverse reproductive outcomes, including embryonic and fetal death [1].

A large number of chemicals occurring in our environment have the potential to interfere with the endocrine system of animals [2]. Many of these chemicals can disrupt development of the endocrine system and of the organs that respond to endocrine signals in organisms indirectly exposed during prenatal and/or early postnatal life; effects of exposure of such chemicals during development are permanent and irreversible [3]. Several pesticides have been reported to produce gonadal toxicity, among these are persistent and bioaccumulative organochlorine pesticides (O`Ch). Increasing interest has been observed among environmental and health institutions regarding the potential reproductive effects due to exposure to occupational and environmental chemicals. Over the past decade, there has been an increasing focus on the effects of synthetic chemicals on human endocrine system-specially on effects related to androgen and estrogen homeostasis [4]. An understanding of the developmental consequences of endocrine disruption in wildlife can lead to new indicators of exposure to endocrine disrupting contaminants. Organochlorine substances that contain chemically combined carbon and chlorine are endocrine disrupting chemicals. They resist the degradation by normal biochemical and physical processes. Hence, they have a long half life and accumulate in environment as persistent organic pollutants [5-7]. Organochlorine occurs naturally in the environment at very low concentration. According to Fischer [6] and Hall [8], humans and wild life have not evolved mechanical or biochemical pathways to detoxify and get stored and accumulated in the lipids and fatty tissue.

Dicofol [2,-2,-2-trichloro-1,-1-bis (4-cholorophenyl-) ethanol] an organochlorine pesticide is a miticide which is very effective against red spider mite. It is used for the control of mites in agricultural situations, and is also applied to a variety of fruit, vegetable, nut, and fiber (cotton) crops. It is used in nurseries and also applied to ornamental flowers, shrubs, trees, and lawns [9]. It is approved for use on cotton, apples and citrus cultivates and sold under a number of trade names including acarin, benzenemethanol, carbax, cekudifol, kelthane, hilfol, colonel and acarin. Dicofol

is one of the world's last organochlorines still in widespread use. It has perhaps survived because its environmental persistence is low relative to DDT. The United States, Environmental protection Agency (EPA) has classified dicofol as toxicity class II - moderately toxic, and toxicity class III - slightly toxic [10].

Dicofol is fairly toxic to mammals but isn´t carcinogenic. It is reported to be repro-toxic in wildlife, and it may reduce eggshell quality as well. Dicofol is very toxic for aquatic organisms with lethal/effective concentration, L(E)C50 values of 15-120 µg/l obtained by acute toxicity tests and, no observed effect concentration, NOEC values of 4.4-125 µg/l for chronic effects [11].

MATERIALS AND METHODS

Toxicant: Colonel-S, a formulated product containing Dicofol (18.5 %) emulsifiable concentrate (EC) was used for the study.

Doses: The test concentrations was calculated from the percentage of the active ingredient of the commercial formulation of dicofol

Two doses of the toxicant used in the study are

1. Low dose – 4 mg/Kg body weight
2. High dose -16 mg/Kg body weight

Mode of administration of dose: Oral route of administration of the test compound has been chosen since the human exposure to the pesticide is most likely to occur this way.

Experimental Animals and Groups: Female Swiss albino mice of 8-10 weeks old weighing 31± 2 gm were selected. The animals were kept under hygienic conditions and maintained at a temperature of 25 ± 2and photo period of 12 h dark/light .The water was given *ad libitum* during the entire experimental period. Animals were allowed to be acclimatized for a minimum of 2 weeks prior to the experiment.

Animals were classified randomly into three groups

1.Group I (Control received distilled water only)

2.Group II (Low dose)

3.Group III (High dose)

Experimental Design: Fifteen inseminated females were selected and divided into three groups; two experimental and one control. Each group contained 5 females. The day vaginal plug was seen was considered as 0 day of gestation. Pregnant females were orally administered low and high

doses of the formulation and distilled water to the control group once daily from day 5 to day 14 of gestation. Females of all the groups were weighed on every alternate day throughout pregnancy. The pregnant females were sacrificed on 18th gestation day by cervical dislocation and the dams were examined for teratological changes. The uteri were examined for routine teratological changes. The live fetuses and placental discs were removed and their wet weights recorded. All the fetuses were sexed and inspected for external abnormalities.

RESULTS

The maternal average weight gain in control animals during periods of pregnancy was normal, being 52±0.61. All foetus implantated were born and no mortality was observed in the foetus. No resorptions were seen. The average no of implants per dam was 10.4±0.28 and average body weight of the litter was1.04±0.02. No external abnormalities were examined. The sex ratio of male and female pups was 54and 46 respectively (Table 1).

Table 1. Effect of COLONEL-S on maternal weight, number of implants, resorbed fetal percentage

Groups	Maternal weight (gm)	Number of implant fetuses (Mean ±SE)	Number of alive fetuses	Living Fetuses			Fetal Body Weight (Mean ±SE)	No of resorbed fetuses (%)
				Avg body wt (gm)	Sex ratio (%)			
					M	F		
Control	52.00±0.61	10.4±0.28	10.4±0.28	1.04±0.02	53.85	46.15	1.04± 0.02	0
Low dose	41.90±0.65	8.40±0.17	4.00±0.22	1.01±0.06	50	50	1.01 ± 0.06	52.38
High dose	39.00±0.53	5.40±0.42	2.40±0.48	0.80± 0.14	33.33	66.66	0.80 ± 0.14	40.74

Low dose treated animals show lowered litter size and increased no of resorbed fetuses. Mortality rate was increased as compared to control. The average weight gain during periods of pregnancy was 41.9±0.65 which was low as compared to control. The average no of implants per dam was 8.4±0.17 and mean size of a litter was 1.01±0.006. The resorption percentage in this group was 30. External abnormalities were not observed. The sex ratio of male and female pups was 50 and

50respectively.The high dose treatment caused a greater number of resorption of foetus in the uterus of pregnant females. In some cases complete resorptions of foetus was observed. Fetal observations shows reduced litter size Mortality rate was increased as compared to control and low dose .The reduction in average weight gain during periods of pregnancy was 39±0.53. The average no of implants per dam was 5.4±0.42 and mean size of a litter was 0.80±0.14 low as compared to control counterparts. The resorption percentage increased to 70%. External abnormalities like dysplasia and micromelia were examined in fetuses. The sex ratio of male and female pups was 33 and 66 respectively.

DISCUSSION

The exposure of pregnant women to xenobiotics is of major concern as they cause potential harm on the fetuses. In the present study exposure of commercial formulation Colonel-S, containing dicofol exerted toxic effects on the growth, maternal weight gain, survival percentage and dose dependent decrease in the number of implants and high resorption of foetus was observed. Similar results were obtained in a three-generation study of rats where feeding of cyfluthrin caused pups to have decreased viability and decreased weight [12]. This decrease in maternal weight gain may be due to the lower litter size which seems to involve both implantation failure and resorptions. Our results are in concomitant with results of Purkerson-Parker et al. [13] and Farag et al. [14] who observed a similar dose related reduction in maternal weight gain on administration of heptachlor and chlorpyrifos during pregnancy respectively. Similar results were also obtained by Farag et al. [15] and Tian et al.[16] who witnessed depressed maternal body weights accompanied by reduced fetal weights and increased number of resorptions in rats treated with other pesticides like dimethoate and chlorpyrifos. Shanthalatha et al. [17] also reported that when mice are treated with higher doses (2.5 or 5 mg kg-1 b.w.) of methomyl (40%) showed more pronounced loss in body weight than 1 mg treated mice.

Similar results were observed by Farag et al. [18] when mice were exposed to acephate. Maternal exposure to acephate during organogenesis significantly affected the number of implantations, number of live fetuses, number of early resorptions, mean fetal weight, and the incidence of external and skeletal malformations in the 28 mg/kg/day dose group. Bhaskar and Shahani [19] also observed increased mortality in dicofol treated chick embryos as compared to control.

Ambali et al. [20] observed the post-implantation losses exposed to chlorpyrifos. They stated that loss in groups were due to fetal death and resorption and were dose dependent. The chlorpyrifos - induced post-implantation losses recorded in mice may have been due to *in utero* exposure of the pups to the chemical. It may have also resulted in alteration of the maternal hormonal levels either from the effect of chlorpyrifos on the central nervous system, suppressing the brain release of gonadotropins, apparently due to AChE activity [21]. This alteration may result in changes of the uterine biochemical content, hence alteration in intrauterine environment, leading to fetal death and resorption.

Decreased birth weight and length of newborns have been associated with high levels of chlorpyrifos in plasma samples of urban minority women [22]. Our results are similar with the results of Syed et al. [23] also observed a dose related decrease in the weight gained by the females during the gestation period when the pregnant mice was exposed to 16 mg/kg and 32 mg/kg body weight of cyfluthrin (Baygon and Solfac). The higher dose affected the litter size, number of live fetuses, resorptions and the average fetal weight significantly.

From the present investigation it can be concluded that the higher dose of the pesticide caused significant reduction in the litter size and an increase in the number of resorbed fetuses. However, the animals that received the lower dose did not exhibit significant alterations. Therefore, it can be inferred that the pesticide formulation produced embryotoxic and teratogenic effects in a dose dependent manner.

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