Teratogenic effect of formaldehyde in rabbits

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Abstract

Thirty three pregnant rabbits were exposed to vapour of 10% formaldehyde (12 ppm) throughout the gestation period to know its effect on newborns. The results showed no abortion or foetal mortality but there were some anomalies (23.8%) among the newborns rabbits which includes: meromelia (6.8%), encephalocele (6.1%), Oligodactyly (4.1%), Umbilical hernia (3.4%) and Short tail (3.4%); besides that small for date and decrease in the body weight of the newborns were also noticed. These findings suggest that formaldehyde is a teratogenic agent.

Keyword: Formaldehyde, Teratogenicity, Rabbit.

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Introduction

Formaldehyde is well known as a preservative, a sterilizer and embalming fluids; and approximately 2.1 million workers are exposed to formaldehyde (1,2). Domestic exposures occur mainly from consumer products that include textiles, insulation, paper, cosmetics and wood-products (3).

Formaldehyde exposure has toxic effects on respiratory system, gastrointestinal tract, haemopoitic tissue and nervous system (4-7). Reproductive and developmental effects are believed to be minimal (8-10).

Increased cryptorchidism was investigated in pregnant rats following inhalational exposure to formaldehyde, while formaldehyde inhalation with bipyridyl administration showed cryptorchidism, syndactyly, adhesion of breastbone with tail, and phoceomelia (11). Congenital defects, included cryptorchidism, delay in ossification of hyoid bone, delay in eruption of upper and lower incisors, as well as decrease in body weight were noticed on pregnant rats when exposed to formaldehyde and gasoline (12). Two anencephalic cases of human birth defects were reported in formaldehyde-contaminated homes (13). Also formaldehyde produced incomplete axial rotation and delayed neural tube closure in mice (14). The embryotoxic and teratogenic effect of formaldehyde in chick embryos were noticed to include cranial hematomas, facial abnormalities, eye and beak deformities (15). There were
no related signs of developmental toxicity in pregnant rats when they administrated formaldehyde orally, as well as among pregnant hamsters when treated by topical application of formaldehyde (16,17).

From the above introduction the present study was designed to examine possible teratogenic effect of formaldehyde on newborn rabbits.

**Materials and methods**

Thirty three adult female rabbits were used, their weight ranged between 1085-1622 g and they were kept under the same environmental conditions. The animals were kept in stainless steel mesh cages, the temperature was maintained at 22-27 °C, a dry, absorbent, bedding materials, like wood shaving were provided in all cages. All animals were allowed free access to food and water. An anthelmintic drug (ivermectin 2 mg/kg subcutaneous) was also given as a measure against internal and external parasites. All the animals were observed for 10 days before the beginning of the experiment to exclude any possibility of abnormal behavior and disease.

Female rabbits were mated with males and then randomly assigned irrespective of age and weight into the following groups:

1- Exposed group which included 26 pregnant rabbits.
2- Control group which included 7 pregnant rabbits.

All the females of exposed group (2-3 animals were housed in one separate cage), were exposed to the vapour of 10% formaldehyde during the entire gestation period. The 10% formaldehyde solution was placed in 400- steel containers which is covered by nylon mesh and filled periodically. All the animals were exposed to the same constant surface area of 10% formaldehyde solution.

Analytic procedure (18) was applied several times during the exposed period of this work to determine the concentration of formaldehyde (ppm) in the atmosphere of the exposed cages. From this analytic measurement the concentration of formaldehyde in the exposed cages was (12 ppm).

While the pregnant rabbits of the control group were exposed to a vapor of distilled water, under the same condition of housing, feeding and duration of the exposure (entire gestation period).

**Results**

There was no abortion or fetal mortality among the exposed and control pregnant rabbits along all gestation period.

One hundred forty six and thirty eight newborns were obtained from the exposed and control pregnant rabbits respectively.

Fifty two (35.6 %) of newborns showed small for date (19.85 ± 2.76 g) (Figure 1) when compared with the control newborns (38.62 ± 3.35 g), while the other ninety four (64.4 %) newborns showed significant decrease of body weight (32.57 ± 3.18 g).

The most common anomalies seen were:

1- Meromelia (6.8%) (Figure.2).
2- Encephalocele (6.1%) (Figure.3).
3- Oligodactyly (4.1%) (Figure.4).
4- Umbilical hernia (3.4%) (Figure.5).
5- Short tail (3.4%) (Figure.6).

From this (23.8%) anomalies, (13.6%) were seen among the small for date and (10.2%) from the other newborns.

In some cases there was a combination between two anomalies such as meromelia with short tail (2%) and meromelia with encephalocele (1.3%).

![Figure (1): Showing the small for date (left) and normal (right) newborns.](image1)

![Figure (2): Showing the meromelia (arrow).](image2)
Figure (3): Showing the encephalocele.

Figure (4): Showing the oligodactyly (arrow).

Figure (5): Showing the umbilical hernia (arrow).

Figure (6): Showing the short tail (arrow).

Discussion

Elimination of formaldehyde and its metabolites from fetal tissues is slower than maternal tissues. It has adverse effects on embryos which showed cytological injury and high rate of mortality, and its exposure throughout gestation caused a decreased DNA and RNA concentrations (19).

Formaldehyde is an alkylating agent and treatment with such an agent has caused primordial germ cell mutations which resulted in fetal deaths and malformations (20); it undergoes addition (adducts and alkylation) and condensation (methene bridges) reactions with proteins and amino acids as well as nucleic acids and nucleosides/tides, so it is regarded as a mutagen, crosslinking agent and an immunogen (21).

Formaldehyde is metabolized to formate. Alcohols, particularly methanol and ethanol, are metabolized to formate and lactate via an aldehyde. The toxicity of alcohols and formalin in humans and animals includes metabolic acidosis (22,23). Alcohol toxicity generates free radicals, cause an increase in malondialdehyde, and induce lipid peroxidation resulting in DNA single strand breaks (24,25). Formaldehyde and alcohols probably affect embryos and the fetus via mitochondrial damage. Ethanol and environmental agents trigger apoptotic neurodegeneration in the developing brain (26). Oxygen stress, such as that caused by free radical generation, is associated with apoptotic cell death and fragmentation of mitochondrial genome (27). Moreover, formaldehyde via formaldehyde generators, e.g. alkylating agents, initiates apoptosis (28) and mitochondria are the suicide organelles which control it (29).

In view of the present finding and its interpretation, we can conclude that formaldehyde has a teratogenic effect (23.8%) of newborn of pregnant rabbits at concentration of (12 ppm). This effect is affected with different factors such as the concentration of formaldehyde, time exposure, route of administration, material subject, individual variation (human or animal), order or species of animal.
References

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