Objective

Diethylstilbestrol was a hormone administered for recurrent first trimester miscarriage in the 1970's that was found to cause damaging abnormalities in the female reproductive tract in 1971. Mice were utilized to elucidate the role of DES in cervical abnormalities. In researching diethylstilbestrol, this poster aims to effectively determine what role it has in increased cervical cancer incidents.

Abstract

In the 1970's, diethylstilbestrol (DES), a synthetic form of the hormone estrogen, was prescribed to 2 to 4 million pregnant women for recurrent first trimester miscarriage. In 1973, this medication was found to cause several complications in the reproductive tract, including increased risks of cervical cancer. DES is thought to be able to alter the base structure of DNA, as well as cause epigenetic changes. If this change occurs in the germ line, it could continue onto the next generation. There is also evidence that maternal ingestion of DES not only has effects on the daughters, but can also have effects on the granddaughters. These effects can be studied on a smaller scale, particularly in mice due to their rapid reproduction rates. In a recent study, pregnant mice were treated with daily doses of DES ranging from 0.01 to 100 µg/kg on days 9 to 16 of gestation. In the DES exposed offspring, the cervix was enlarged, a variety of malignant lesions were found, and malformed cervical canals occurred. These findings in DES-exposed mice mirror those found in DES-exposed women. These results show that the developing fetus is particularly sensitive to exogenous estrogens. This data allows us more insight on the effects DES has on a smaller scale, which can then be compared to a larger scale, allowing for more effective cures and a ceasing of usage of detrimental estrogens. Thus, DES studies in mice can provide useful insight on the long-term effects of estrogens on the cervix.

Materials and Methods

In this experiment, twenty CD-1 mice were treated with daily doses of DES ranging from 0.1 to 100 μg/kg on days 9 to 16 of gestation. These doses equal those given to pregnant women. Both female and male offspring were born on day 19 of gestation. Female mice were sacrificed at 12 to 18 months of age to assess the long-term effects of prenatal DES exposure and their reproductive tract tissues were examined for histological alterations.

Discussion

After day 19 of gestation, structural abnormalities were observed in the cervix, which contributed to subfertility. After the sacrifice of female mice at 12 to 18 months of age, the cervix of the DES-exposed offspring was found to be enlarged. A variety of abnormalities such as leiomyoma, papilloma, stromal cell sarcoma, epithelial atypia, and leiomyosarcoma were also found. These findings in mice are relevant to similarly exposed humans, as many abnormalities that occurred in mice also occurred in humans. The extreme sensitivity of the developing fetus is demonstrated here. It is suggested that this sensitivity is due to undeveloped DNA repair mechanisms, an immature immune system, lack of detoxifying enzymes, increased metabolic rate, and more. DES is also thought to possess mutagenic potential, allowing harmful effects to be passed down to the granddaughters of DES-exposed individuals.

Results

This process involves the addition of methyl groups to specific bases in specific parts of genes. It has been shown to regulate gene expression, meaning it underlies cell differentiation. DES causes persistent epigenetic changes to some genes and not others, thus altering the fate of certain tissues and organs. Thus, it can be concluded from evidence from the experiment that fetal exposure to DES causes several abnormalities of the cervix, including cervical cancer due to its mutagenic and epigenetic ability.

References