

Teratogens

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Abstract

Teratogen is a substance or process that can harm or cause defect in fetus during pregnancy time. There are various types of teratogens that causes defects in fetus during pregnancy. They can be different type of chemicals, physical agents, metabolic conditions or different infections. They can cause problems like preterm labors, spontaneous abortions, or miscarriages. There are different factors which influence the working of teratogens. These factors include timing, genetic variation and type of exposure. Various studies have been made to study the effects and working of teratogens, but till date the exact mechanism of action of most teratogens are unknown.

Key Words: Metabolic conditions, Preterm Labors, Spontaneous abortions, Genetic variability

Introduction

Teratogen is a substance, organism or process that can harm a fetus during pregnancy. Teratogens can be an infectious agent, medicines or drugs or types of environmental exposures [1]. Teratogens may produce physical or functional defects in the human fetus after the pregnant woman is exposed to the substance [2]. The word teratogen originates from, “teratos” which is the Greek word for monster. They may cause a birth defect in the child or they may terminate the pregnancy outright. The types of teratogens include radiation, maternal infections, chemicals, and different drugs [1]. Nearly 4 to 5 percent of birth defects are caused by exposure to a teratogen during pregnancy. Teratogens may also influence pregnancies and cause problems like preterm labors, or miscarriages. Teratogens are classified into four different types: physical agents, metabolic conditions, infections, and finally, types of different drugs and chemicals [2].

The teratogenic effects of different agents (chemical, physical and environmental) are mostly related to their capacity to damage DNA [1,2]. A teratogen is basically something in the environment that the mother may be vulnerable to during her pregnancy. It could be a prescribed medicine, drug, use of alcohol, or a disease present in the mother itself which could increase the probability that the baby can be born with birth complications. About 4 to 5 percent of birth problems in baby are caused by exposure to a teratogen [1]. Sometimes a prescribed medicines or medicines necessary for health is also a teratogen: Antibiotics tetracycline (Achromycin), thyroid medicines, blood thinners, and Acne medication isotretinoin are just a few examples. In these cases, pregnant patients should co-operate carefully with their doctors to ensure if an alternative treatment is possible before and during pregnancy [2].

Most of the teratogens act via an unknown mechanism on developing cells and tissues to start a cascade of altered developmental events. Effects of teratogens depend on the nature of the teratogen, including

chemical properties of the chemical, way of exposure, fetal bio-activation, placental transport, etc. [2]. Teratogens affect the fetus in a different ways, causing physical abnormalities, behavioral problems or development in emotional behavior of the child, and decreased intellectual quotient (IQ) level of child. Besides, teratogens also affect pregnancies and cause problems such as preterm labors, or miscarriages [2]. Teratogens are known to have the capacity of effecting the fetus about 10 to 14 days after fertilization [1]. These physical, anatomical or structural defects are present at birth although they may not be detected until later in life. They may be visible on the body surface or inside to the viscera. The congenital abnormalities hold responsibility for nearly 20% of deaths in the period immediately before and after birth. Teratogens affect morphogenesis, development and differentiation through death of cells, unsuccessful cell interactions or alterations in the movement of cells. As these affect the normal processes of cells, not only may a teratogen have a basic effect on different tissues, but several teratogens may produce common effects [2].

Types of teratogens

Teratogens are classified into different four types: physical agents, metabolic conditions, diseases, and, drugs or chemicals [1, 2]. Physical agents are the energy sources that may cause injury or disease. It includes ionizing radiation or other agents that are reason of hyperthermia, or increased body temperature. Ionizing radiation such as X-rays, or gamma rays that carry enough energy to free an electron from an atom or molecule, resulting in electrically charged ions in matter. Second category of teratogens are metabolic conditions which affects pregnant females such as malnutrition, Gaucher disease, Hunter syndrome, diabetes, and thyroid disorders. Third kind are infections such as those caused by rubella virus, herpes simplex virus, and syphilis. Drugs and chemicals such as Lithium, alcohol, cocaine, thalidomide, Agent Orange, and vitamin A and retinoid (derivatives of vitamin A) are the fourth kind of teratogens [2].

Teratogens and their effects

Alcohol is a common teratogenic agent effecting pregnant women. Babies born to alcoholic mothers show prenatal and postnatal growth problems and deficiency, mental issues, and other deformations. There are fine but classical facial deformations associated with fetal alcohol syndrome including short palpebral fissures, maxillary hypoplasia, congenital heart disease and a smooth philtrum. Many factors influence the effect of alcohol such as the quantity of alcohol taken by pregnant woman, the time period over for the alcohol was consumed, the mother's genetical build-up and her ability to digest alcohol, if she is eating well or has any deficiencies [1]. Retinoic acid is extremely teratogenic for humans. Even at very less doses, oral medicines such as isotretinoin, which is used in the treatment of acne, are capable teratogens. The exposure period that may cause teratogenic effect is from the 2nd to the 5th week of incubation. The most common problems include craniofacial dimorphism, and defects in neural tube thymic aplasia [2]. Chemotherapeutic agents are potent teratogenic as these agents stops rapidly dividing cells. These

medicines should be avoided if possible but are occasionally used in the third trimester if urgently needed.

Nicotine does not cause congenital deformations, but nicotine does have an effect on embryo development. Parental smoking is a known cause of intrauterine growth inhibition. Chain smokers were also more likely to have a premature delivery. Nicotine restricts uterine blood vessels and causes less uterine blood flow thereby decreasing the supply of oxygen and nutrients available to the fetus. Obesity as overweight women have twice the risk of the normal population of having a child with a neural tube defect (NTD), such as anencephaly or spina bifida. Obese women also have increased risk for having a baby with a cardio defect or cleft palate. The risk to the baby increases as the body mass index (BMI) of woman increases above normal limits [1]. Thalidomide which was used to treat symptoms (such as morning sickness) in pregnant women in the 1950s and early 1960s. It was found to cause different harmful birth defects, the most visible of which were harsh defects to baby's arms and legs. Thalidomide was used commonly in Europe in 1959, after which nearly 7000 infants were born with the meromelia. The basic features of this syndrome include limb malformations that span from absence of the limbs to abnormally short limbs [1, 2]. Congenital rubella includes triad of cataracts, cardiac malformation, and deafness. The earlier embryo in the pregnancy is exposed to maternal rubella, the greater the likelihood that it will be affected. Most infants are exposed during the first few i.e. 4 to 5 weeks after fertilization will have effects of this exposure. Exposure to rubella during the second and third trimester results in a much lower frequency of malformation but continues to increase a risk of mental deformity and hearing loss [2]. Ionizing radiation can injure the developing fetus due to cell death or chromosome defects. The harshness of damage to the embryo depends on the dose absorbed and the time of development at which the exposure occurred. Study of Japanese atomic bombing survivors demonstrated that exposure at 10 to 18 weeks of pregnancy is a period of greatest sensitivity for the CNS and developing brain [1]. X-ray pose a minimal risk to the embryo. The common abnormalities were small head circumference, or microcephaly, and small eyes [2]. Thyroid disorders include disorders in which the thyroid gland malfunctions, hence producing abnormal amounts of the thyroid hormones, thyroxine and triiodothyronine, which controls metabolism. Thyroid disorders can cause a number of teratogenic effects to a developing fetus, as well as negative effects on pregnancy such as miscarriage, placental abruption, preterm labor, and lower IQ scores in the children [2]. Diabetic mother's babies have increased cases of congenital heart disease, gastrointestinal deformations, renal and central nervous system malformations such as NTD (neural tube defects). Tight glycemic control during the third to sixth week post-conception is important [1]. Phenylketonuria mothers who are not well controlled and have high levels of phenylalanine, their infants have a significant risk of mental retardation, low birth weight, and congenital heart disease [1]. Oligohydramnios are with congenital dislocation of the hip and clubfoot. Tetracycline can cross the placental membrane and is deposited in the embryo in bones and teeth. Tetracycline exposure can result in yellow staining of the primary or deciduous teeth and less growth of the long bones. Tetracycline exposure after birth has same effects [2].

Both epidemiological and animal studies indicate that low-frequency magnetic fields do not exert strong effects on embryo development. No gross malformations have been found in animal studies, and epidemiological studies have not shown evidence of an excess of birth defects. The results of the multigeneration animal studies do not suggest any major effects of magnetic field on male reproduction [2].

Conclusions

Pregnant women exposed to various teratogens showed clear evidence of congenital defects, malformations and abnormalities. Different type of teratogens can have different types of defects in fetus or infants. Teratogens can be either different types of chemicals, drugs, physical radiations or even infections. Effects of teratogens depends on series of factors such as time of exposure, genetic make-up of infant or their parents. Alcohol, Nicotine and some medicines during pregnancy are potent teratogens. Even today some potent teratogens are unknown, and efforts have been made to identify them. The pregnant mothers need to be careful about the food or medicines they are consuming.

References

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