REVIEW ON TERATOGENICITY EFFECT OF DIFFERENT DRUG AT DIFFERENT STAGES OF PREGNANCY

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ABSTRACT

Teratogenesis is process of induction of malformations or birth defect in foetus or embryo. Around 3% of births suffer from some sort of birth defects. Teratogenesis is caused by teratogen. Many factors causing teratogenesis which are following, Medicinal drugs such as thalidomide, retinoic acid; recreational drug such as alcohol and cocaine; environmental toxins such as heavy metals like cadmium; environmental pollutant include pesticides. Herpes, HIV, Rubella and Zika virus. Hyperthermia. Smoking. Maternal condition pre-eclampsia and gestational diabetes.

To determine how long it takes after a new drug is marketed to establish whether or not its use by pregnant women is likely to pose a substantial teratogenic risk, Analyze environmental factors that affect fetal development, Determine ways to prevent some birth defects, Create an informational advertisement to new parents about common teratogens, Determine pharmacokinetic factors that affect drug transfer during pregnancy: Lipid solubility, Molecular size and pH, Placental Transporters, Protein Binding, and Placental and Fetal Drug Metabolism.

I. INTRODUCTION

Pregnancy is also known as gestation, is the time during which one or more offspring develop inside a woman's womb. Pregnancy is a divided into a three trimester which are following:

First trimester consist of 12 weeks (it is also called embryonic stage).
Second trimester consist of 12 to 24 weeks (it is known as golden period)

Fig 1

Teratogenesis is process of induction of malformations or birth defect in foetus or embryo. Around 3% of births suffer from some sort of birth defects. Teratogenesis is caused by teratogen. Many factors causing teratogenesis which are following,

- Medicinal drugs such as thalidomide, retinoic acid; recreational drug such as alcohol and cocaine; environmental toxins such as heavy metals like cadmium; environmental pollutant include pesticides.
- Herpes, HIV, Rubella and Zika virus.
- Hyperthermia.
- Smoking.
- Maternal condition pre-eclampsia and gestational diabetes.
II. LITERATURE REVIEW

<table>
<thead>
<tr>
<th>Sr. No</th>
<th>Name Of Authors</th>
<th>Title Of Research</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>NEIL Vargesson- (Dec 2017)</td>
<td>Teratogenesis</td>
<td>Studied Teratogenesis Is Process That Cause Birth Defects Or Malformations In An Embryo Or Fetus.</td>
</tr>
<tr>
<td>2</td>
<td>Lucas Rosa Fraga (Dec 2017)</td>
<td>Teratogenesis</td>
<td>Studied Of Teratogens Include Medicinal Drug Such As Thalidomide; Environmental Toxins, For Example Cadmium, Viruses.</td>
</tr>
<tr>
<td>3</td>
<td>Punam Sachdeva*, B. G. Patel And B. K. Patel</td>
<td>Drug Use In Pregnancy</td>
<td>Studied Pregnancy Is A Special Physiological Condition Where Drug Treatment Presents A Special Concern Because: The physiology of pregnancy affects the pharmacokinetics of medications used and certain medications can reach the fetus and cause harm.</td>
</tr>
<tr>
<td>4</td>
<td>Marleen M.H.J. Van Gelder, Nel Roeleveld</td>
<td>Teratogenic Mechanism Medicinal Drug</td>
<td>Studied Teratogenic Mechanisms Of Medical Drugs.</td>
</tr>
</tbody>
</table>

CLASSIFICATION OF ABNORMALITIES

1) Structural abnormalities
It includes affect body parts such as heart lungs kidney etc.

2) Functional abnormalities
It includes blindness and down syndrome

3) Primary abnormalities
It is Caused due to genetic abnormalities.

4) Secondary abnormalities
It is cased due to teratogenic agents.

| Table 1: Examples of teratogens known to cause human birth defects. |
|-----------------------|---------------------------------------------------------------------|
| Agents               | Malformations                                                      |
| Drugs                | Foetal alcohol syndrome, intrauterine growth retardation and intellectual disability |
| Alcohol              | Intrauterine growth retardation, prematurity, urogenital anomalies and brain developmental disorders |
| Cocaine              | Abnormalities of the reproductive tract                            |
| Diethylstilbestrol (DES) | Neural tube defects, craniofacial anomalies, cleft palate and cardiovascular anomalies |
| Retinoic acid        | Teeth anomalies and damage                                         |
| Tetracycline         | Abnormal limb development – typically shortening and loss of proximal bones, facial anomalies, systemic anomalies |
| Thalidomide          |                                                                     |
Drugs/medicine

1) Thalidomide
Thalidomide was released in the late 1950's as a non-addictive.
Thalidomide given to the pregnant women to prevent morning sickness. Thalidomide is most potent teratogenic drug. More than 10,000 children being born with severe birth defects, about 5000 in Germany and death of approximately 2000 children. Widikund Lenz famously determined the time period that thalidomide caused damage in first trimester. Thalidomide affects the tissues of the body including eyes, ears, limbs and internal organs including digestive track and heart. Babies born with malformations such as Amelia, phocomelia, bone hypoplasia and absence of bones.

Table 2: Outward damage caused by thalidomide exposure of human embryos at different times during pregnancy
Single 50 mg tablet of thalidomide during the time sensitive window is sufficient to cause birth defects in up to 50% of pregnancies.

Mechanism of action of thalidomide, it inhibit formation of new blood vessels resulting in cell death and tissue loss or that it induces reactive oxygen species or act through binding to the protein cereblon.

Thalidomide was subsequently withdrawn from UK in Nov 1961 and by 1962 from most of the world. Today, thalidomide is used to successfully treat a wide range of medical condition which includes leprosy, multiple myeloma and cancers as well as crohn’s disease.

2) Alcohol

Foetal Alcohol Syndrome is one of the most serious consequences of drinking alcohol and their products during pregnancy.

Worldwide incidence of Foetal Alcohol Syndrome is 1:2000 live births. Risk of miscarriage almost doubles for women who drink alcohol in any form during pregnancy and birth weight of babies is substantially below normal. Growth and central nervous system problems can occur from alcohol use anytime during pregnancy. Alcohol use in first three months of pregnancy can cause abnormal facial features.

3) Warfarin

Warfarin is known to be teratogenic, producing characteristic abnormalities, namely a hypoplastic nose, stippled epiphyses, and skeletal abnormalities.
Use of warfarin in pregnancy can cause bleeding behind the placenta. This type of bleeding can cause reduced fetal growth, placental abruption, and stillbirth (if severe). The chance of preterm delivery is also higher. Fetal warfarin syndrome is a disorder of the embryo which occurs in a child whose mother took the medication warfarin (brand name: Coumadin, jantoven) during pregnancy. Resulting abnormalities include low birth weight, slower growth, mental retardation, deafness, small head size, and malformed bones, cartilage, and joints. Warfarin is hazardous medication in pregnancy due to take this medication it causes abnormalities of physical and mental development of child.

Teratogenesis is process of induction of malformations or birth defect in foetus or embryo. To development of child as mentally and physically fit and strong.

All parents should know what teratogens are and how to avoid them since they can cause harm throughout pregnancy, starting around the time of conception. For instance, the risk of miscarriage is higher when you smoke or drink alcohol or are exposed to radiation and certain toxic chemicals.

The embryonic period, during which organogenesis takes place, occurs between implantation at around 14 days to around 60 days postconception. This is usually the most sensitive period to teratogenesis when exposure to a teratogenic agent has the greatest likelihood of producing a malformation.

**IV. CONCLUSION**

**V. REFERENCES**


[10] Source PubMed Authors: Marleen M H J van Gelder, Lolkje T W de Jong-van den Ber g Nel Roeleveld Radboud University Medical Centre (Radboudumc).