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A REVIEW ARTICLE ON DRUG SAFETY EVALUATION OF PREGNANCY AND LACTATION

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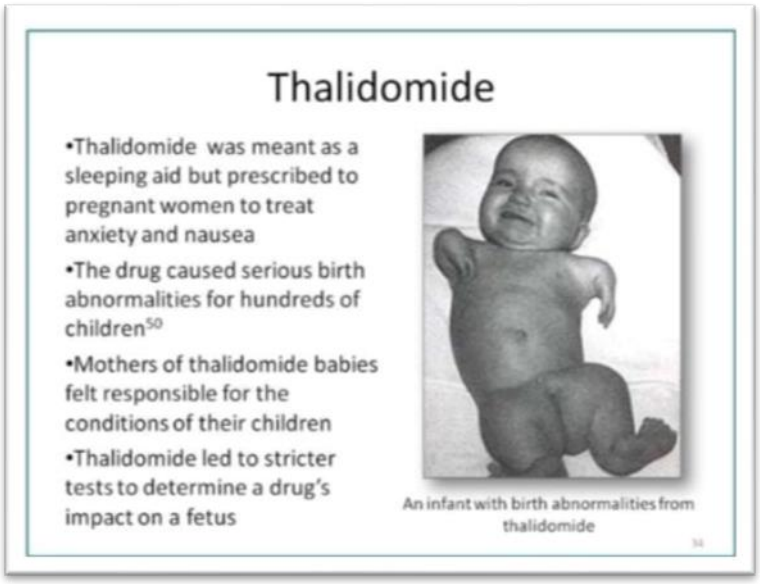
ABSTRACT

Drug safety during pregnancy and lactation is a critical aspect of maternal and child health. Physiological changes in pregnancy and breastfeeding can after drug absorption, distribution, and elimination, increasing the complexity of safety evaluation .Drugs may cross the placenta or pass into breast milk, potentially affecting the fetus or infant. However, limited clinical data and ethical constraints make risk assessment challenging. This review highlights key factors influencing drug safety, including teratogenicity, drug transfer mechanmisms, and infant exposure. It also emphgasizes the importance of a risk-benefit approach, careful drug selection, and monitoring. Improving research, awareness, and regulatory guidelines is essential to ensure safe and effective medication use during pregnancy and lactation.

KEYWORDS: Adverse effects, Birth defects, drug safety, pregnancy, teratogenicity, lactation.

1. INTRODUCTION

In the $1960_{s,}$ more than 10,000 infants worldwide were born with severe congenital abnormalities following maternal use of thalidomide for the treatment of nausea and vomiting during early pregnancy. This catastrophic event remains one of the most significant drug related tragedies in medical history. In November 2023, Australian prime minister Anthony Albanese issued a formal national apology to individuals affected by thalidomide and their families, acknowledging the enduring impact of this disaster.[1]



At the time of this incident, Australia did not have proper rules to check if medicines, were safe before selling them. Because of this tragedy Australia and many other countries made strict laws and safety system to prevent such event in the future. Australia also created an organisation called the Therapeutic Goods Adminstration (TGA).This organisation checks that medicines are safe effective and of god quality before they are used and continuous to monitor them even after they are available in the market.[2]

Estimate the safety of medicines during pregnancy is very difficult. According to the world Health organisation (WHO), about 15% of pregnant women face serious complications, and around 287,000 women die each year due to pregnancy- related problems. [3] Many medicines are not properly tested in pregnant women, so their safety is not well known. Only a small number of drug have been studied for pregnancy-related conditions, mostly for preterm (early) birth. In the last 30 years, only two new drugs have been specially developed for use during pregnancy. Also, about 90% of approved medicines do not have proper studies on how they affect pregnant women. Because of this, there is lack of safety information, which makes drug use during pregnancy risky and challenging.[1]

2. Why drug safety is important?

- Drug can cross the placenta and reach the baby.
- Some drugs can cause birth defects (teratogenic effect).
- Prevents adverse drug reaction(ADR_s)
- Supports regulatory approval of drugs
- Reduce risk of toxicity and overdose.
- Improve patient compliance.[4,5]

3. Teratogenicity (Harmful effects on fetus)

- Teratogenicity refers to the ability of a substance to disturb normal fetal development and cause structural or function abnormalities.

Teratogenicity is the capacity of an external factor tp cause irreversible developmental defect in a fetus.

- Teratogenic drugs cause abnormal development of organ.
- The first trimester (3-8 weeks) is the most sensitive period.
- Thalidomide→limbs defects.
- Valproate→brain development problems.
  Warfarin→birth defects.[6,7,8]

4. Factors affecting drug safety in pregnancy

- **Stage of pregnancy (trimester).**

The first trimester is most sensitive as organs are developing and risk of birth defects highest.

- **Drug dose and duration.**

Higher doses and longer use increase the chances of harmful effect on the fetus.

- **Maternal health condition.**

Diseases like diabetes, hypertension, infectious can influence how drug affect both mother and baby.

- **Placental transfer of the drug.**

Some drugs easily cross the placenta and reach the fetus, which may lead to harmful effects depending on the drugs type.[9,10,11,12]

5. Drug Safety in lactation and Drug transfer into breast milk

Drug safety in lactation focuses on understanding how medicines taken by breastfeeding mother may affect her infant. Breastfeeding provides essential nutrition and immune protection, but exposure to milk through breast milk can raise safety concerns.[13,14,15]

Drug safety into breast milk is a pharmacokinetic process in which medication present in maternal blood pass into milk and may be ingested by the infant. This transfer mainly occurs through passive diffusion, although other mechanisms like active transport may play a role for certain drugs. Therefore, proper evaluation is necessary to ensure safe maternal therapy without interrupting breastfeeding.[,16,17,18]

6. Factors Affecting Drug transfer into Breast milk

A. Drug-related factors

- **Molecular weight:** smaller molecular pass more easily.
- **Lipid solubility:** Higher solubility increases transfer.
- **Protein binding:** Highly bound drugs transfer less.
- **Half –life:** Longer half -life increases accumulation.
- **pka (ionization):**Affects ion trapping in milk.[19,20]

B. Maternal factors

- Dose and frequency of drug use.
- Maternal metabolism and health status.
- Route of drug administration.

C. Infant factors

- Age (newborn are more vulnerable)
- Immature liver and kidney function.
- Feeding pattern n(exclusive or partial breastfeeding)[21,22,23]

7. Evaluation of drug safety in pregnancy

a) Preclinical Studies

- Preclinical studies are the first step to check drug safety before use in pregnancy.
- These studied are done on animals to identify possible risks to the developing baby.
- They assess effects on fertility, growth and development.
- They help detect birth defects or harmful outcomes early.
- The results guide safe use and further clinical testing.[24,25,26]

b) Clinical Studies

- Clinical trails evaluate drugs safety and effectiveness in human.
- Pregnant woman are usually excluded due to ethical concerns.
- These studies monitor both maternal health and prenatal development.
- Doctors observe effects on both mother and unborn baby.[27,28]

c) Post –Marketing Surveillance

- Post –marketing surveillance studies drug safety after it is available in the market.
- It helps detect side effect that were not seen in earlier studies.
- Data is collect from real patient, including pregnant woman.
- Doctors and patients report any adverse drug reactions.
- Its helps identify long – term and are effect of the drug.[29,30,31]

8. CONCLUSION

Drugs safety and its evaluation during pregnancy and lactation remain critical components of maternal and child healthcare. The unique physiological changes that occurs during pregnancy and breastfeeding significantly influences drug pharmacokinetics and pharmacodynamics, making risk assessment more complex.

Current evidence suggests that althrough many drugs can be used safely, there is still a lack of comprehensive clinical data for a large number of medication. Consequently, uncertainly in drug safety profiles continues to be a major challenge for healthcare professionals.

In conclusion, ensuring drug safety during pregnancy and lactation requires careful evaluation, informed clinical judgment, and continuous research effort. Promoting safe medication use while supporting maternal health and infant well-beings should remain the primary goal of health care systems worldwide.

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