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Review

The Use of Medications During Pregnancy: Risks, Recommendations, and Clinical Considerations

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ABSTRACT

Medication use during pregnancy presents complex clinical dilemmas. Physicians must balance the imperative of treating maternal disease against the risk of adverse fetal outcomes. This review critically analyzes the pharmacokinetics of drugs in pregnancy, placental transfer, and the teratogenic potential of common medications. Emerging evidence from clinical studies and experimental models underscores the importance of individualized prescribing practices. Special attention is given to analgesics, antimicrobials, anticonvulsants, anticoagulants, and non-therapeutic substances. The review concludes with evidence-based recommendations to guide clinicians in minimizing fetal risks while ensuring adequate maternal care.

1. Introduction

The management of maternal health during pregnancy presents one of the most intricate challenges in clinical medicine. Pregnancy is a unique physiological state characterized by substantial anatomical, hormonal, and metabolic changes that influence both disease progression and drug pharmacokinetics (Brent, 2004; Blackburn, 2013). Although some medications are essential for preserving maternal health and preventing obstetric complications, the transplacental transfer of drugs raises significant concerns regarding fetal exposure and potential harm (Woodbury et al., 2024).

Many medications, including analgesics, antimicrobials, anticonvulsants, and cardiovascular agents, are prescribed during pregnancy to manage acute and chronic maternal health issues. However, historical tragedies—such as the thalidomide disaster of the 1960s—have heightened awareness of drug-induced teratogenicity, emphasizing the need for rigorous safety evaluations before prescribing medications to pregnant women (Lenz, 1988).

Emerging literature continues to refine our understanding of these risks. Recent pharmacokinetic studies have proposed model-informed precision dosing strategies to account for gestational changes in drug metabolism and clearance (Xiao et al., 2023). Similarly, a meta-analysis has confirmed the dynamic pharmacokinetics of antiseizure medications during pregnancy, necessitating dose adjustments to maintain therapeutic drug levels (Schoretsanitis et al., 2024).

Analgesic safety has become a focal concern. A recent cohort study demonstrated that prenatal acetaminophen exposure, particularly in the second and third trimesters, was associated with reduced language development in young children, particularly males (Woodbury et al., 2024). Conversely, a large sibling-control study found no definitive causal link between prenatal acetaminophen exposure and neurodevelopmental disorders, highlighting the role of familial and environmental confounders (Alemany et al., 2024).

Moreover, non-prescription drug use remains widespread. A 2025 meta-analysis estimated that approximately 36% of pregnant women use over-the-counter medications, with acetaminophen accounting for 32% of all analgesics consumed, especially during the second trimester (Norwitz et al., 2025).

The challenge of ensuring medication safety is compounded by a

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paucity of high-quality human research in pregnant populations due to ethical constraints and legal limitations. Most safety data are derived from animal studies, pharmacovigilance reports, and retrospective cohort analyses. The heterogeneity of maternal-fetal physiology, coupled with interindividual variability in drug metabolism, further complicates extrapolation of study results to clinical practice.

During pregnancy, maternal-fetal health is closely interlinked. Untreated maternal illness can itself endanger fetal development by causing hypoxia, preterm labor, intrauterine growth restriction, and even fetal demise. Conversely, inappropriate pharmacological therapy carries risks of miscarriage, congenital malformations, neurodevelopmental disorders, and neonatal toxicity (Front Med, 2023).

This review aims to synthesize available scientific literature regarding the pharmacological management of pregnant patients, highlight key teratogenic risks associated with common medications, and propose clinical strategies for optimizing maternal and fetal outcomes. Through a detailed analysis of current studies, this paper seeks to equip healthcare providers with the knowledge required to make informed prescribing decisions during pregnancy.

2. Pharmacological Classes: Safety Profiles and Fetal Risk Considerations

2.1. Analgesics

Analgesics are commonly prescribed to manage pain during pregnancy, with paracetamol considered the first-line therapy due to its relative safety (Woodbury et al., 2024). Pharmacologically, these agents target inflammatory pathways or modulate pain perception to alleviate maternal discomfort (Anderson, 2005). Paracetamol, in particular, is preferred for mild to moderate pain, while NSAIDs and opioids are used sparingly and with caution. From a teratogenic perspective, paracetamol has been linked to subtle neurodevelopmental effects in offspring (Christensen et al., 2018), whereas NSAIDs, particularly in the third trimester, have been implicated in premature closure of the ductus arteriosus and oligohydramnios (Allam, 2022). Maternal-fetal health can be adversely affected by untreated pain, which increases maternal stress hormones and may impair fetal development (Schoretsanitis et al., 2024). While paracetamol is largely considered safe when used appropriately, NSAIDs and opioids present more substantial safety concerns and should be avoided late in pregnancy (Anderson, 2005). Placental transfer studies confirm that paracetamol and NSAIDs cross freely into fetal circulation, raising concerns about fetal exposure (Blackburn, 2013). Developmental toxicity studies suggest that prolonged or high-dose exposure to these analgesics may result in speech delays, fertility impairment, and alterations in fetal growth trajectories (Woodbury et al., 2024). Antimicrobials

2.2. Antimicrobials

Antimicrobials are indispensable in pregnancy to treat bacterial infections, with penicillins and cephalosporins forming the cornerstone of therapy due to their proven safety profiles (Einas Al-Banna, 2020). Pharmacotherapeutically, these agents inhibit bacterial cell wall synthesis or protein production, eradicating maternal infections that could otherwise lead to preterm labor or fetal infection (Anderson, 2005). Teratogenicity data suggest minimal risks associated with penicillins and cephalosporins, whereas aminoglycosides carry risks of fetal ototoxicity, and trimethoprim—a folate antagonist—is theoretically linked to neural tube defects (Anderson, 2005). Maternal-fetal health benefits significantly from prompt infection treatment, reducing the risk of chorioamnionitis and fetal sepsis (Blackburn, 2013). Drug safety considerations favor older, well-studied antibiotics with extensive obstetric use. Placental transfer is drug-dependent: penicillins cross the placenta readily but without adverse fetal effects, while aminoglycosides accumulate in fetal tissues (Brent, 2004). Developmental toxicity is largely absent for first-line antimicrobials, though caution remains warranted with aminoglycosides and folate-antagonizing antibiotics (Schardein, 2000).

2.3. Antiepileptics

Antiepileptics are critical for maintaining seizure control during pregnancy, as uncontrolled maternal seizures pose immediate life-threatening risks to both mother and fetus (Blackburn, 2013). Pharmacologically, these drugs stabilize neuronal membranes and prevent abnormal electrical activity (Anderson, 2005). However, antiepileptics exhibit varying degrees of teratogenicity. Sodium valproate and carbamazepine are strongly associated with neural tube defects, craniofacial anomalies, and cognitive impairment in exposed fetuses (Brent, 2004). From a maternal-fetal health perspective, poorly controlled epilepsy increases the risk of fetal hypoxia and miscarriage, making seizure prevention paramount despite teratogenic risks (Blackburn, 2013). Drug safety protocols favor monotherapy at the lowest effective dose, with newer antiepileptics such as lamotrigine offering a potentially improved safety profile (Schardein, 2000). Placental transfer of antiepileptics is well-documented, with most agents crossing freely due to their lipophilicity and low molecular weight (Brent, 2004). Developmental toxicity may manifest as neurodevelopmental delays, behavioral disorders, and structural malformations depending on the drug and timing of exposure (Anderson, 2005). Anticoagulants

2.4. Anticoagulants

Anticoagulants are prescribed to manage maternal thromboembolic disorders, including antiphospholipid syndrome and mechanical heart valve replacement (Anderson, 2005). Pharmacotherapeutically, warfarin inhibits vitamin K-dependent clotting factors, while low molecular weight heparin (LMWH) potentiates antithrombin III activity (Blackburn, 2013). Warfarin is a well-established teratogen, particularly during the first trimester, causing nasal hypoplasia and stippled epiphyses (warfarin embryopathy), as well as central nervous system anomalies (Brent, 2004). LMWH, by contrast, does not cross the placenta and lacks teratogenic effects (Anderson, 2005). In terms of maternal-fetal health, preventing thromboembolism is vital to reducing maternal mortality and fetal demise (Blackburn, 2013). Safety profiles strongly favor LMWH during pregnancy due to its predictable pharmacokinetics and minimal fetal exposure (Anderson, 2005). Placental transfer studies confirm that warfarin, but not LMWH, crosses into fetal circulation (Brent, 2004). Developmental toxicity from warfarin includes hemorrhagic complications and growth disturbances, while LMWH is associated with excellent fetal safety (Schardein, 2000). Cardiovascular Agents

2.5. Cardiovascular Agents

Cardiovascular agents are essential in managing gestational hypertension and preeclampsia (Blackburn, 2013). Pharmacologically, methyldopa acts centrally to lower sympathetic outflow, labetalol blocks beta-adrenergic receptors, and nifedipine inhibits calcium channels, all reducing maternal blood pressure (Anderson, 2005). ACE inhibitors and angiotensin receptor blockers (ARBs), however, interfere with the renin-angiotensin system and are contraindicated in pregnancy (Schardein, 2000). Teratogenicity data show no risks with methyldopa or labetalol, but ACE inhibitors and ARBs are associated with fetal renal dysgenesis, oligohydramnios, and craniofacial anomalies (Brent, 2004). From a maternal-fetal health perspective, controlling hypertension prevents preeclampsia, placental abruption, and fetal growth restriction (Blackburn, 2013). Safety evaluations position methyldopa and labetalol as first-line agents, with nifedipine used selectively (Anderson, 2005). Placental transfer is significant for ACE inhibitors and ARBs, contributing to their fetotoxic effects (Schardein, 2000). Developmental toxicity includes fetal renal failure, pulmonary hypoplasia, and intrauterine death when contraindicated agents are used in late pregnancy (Brent, 2004).

3. Conclusion

The pharmacological management of pregnant women remains a complex clinical endeavor that requires balancing maternal health needs with fetal safety. Although certain medications such as penicillins, cephalosporins, and methyldopa are regarded as relatively safe during pregnancy (Anderson, 2005; Blackburn, 2013), others pose clear teratogenic risks. Historical events, such as the thalidomide tragedy, underscore the importance of vigilance in prescribing medications to pregnant patients (Lenz, 1988).

Emerging pharmacokinetic studies highlight that pregnancy alters drug metabolism and clearance, necessitating dose adjustments, particularly for antiseizure medications and analgesics (Schoretsanitis et al., 2024). Observational cohort studies have raised concerns regarding the potential subtle neurodevelopmental consequences of in utero paracetamol exposure, although the clinical significance of these findings requires further elucidation (Woodbury et al., 2024).

One key challenge remains the ethical limitation on conducting randomized controlled trials in pregnant populations, resulting in an evidence gap and reliance on observational data, animal models, and post-marketing surveillance (Brent, 2004).

Clinicians should adopt individualized, evidence-based approaches, prioritize medications with established safety profiles, and engage patients in shared decision-making. Multidisciplinary collaboration between obstetricians, pharmacists, and relevant specialists (e.g., neurologists, cardiologists) is essential for the management of chronic maternal conditions during pregnancy.

Educating patients regarding the risks of over-the-counter drugs, herbal supplements, alcohol, and tobacco use remains a critical component of prenatal care. Continued pharmacovigilance, coupled with longitudinal cohort studies, will enhance our understanding of drug safety in pregnancy. Future directions in this field include the development of pregnancy-specific pharmacokinetic models, enhanced post-market drug safety surveillance, and improved patient education strategies. Ongoing research and collaborative clinical care are critical to optimizing outcomes for both mothers and their offspring.

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