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THERAPEUTIC DRUG MONITORING IN PREGNANCY: PHARMACOKINETIC CHANGES, CLINICAL IMPLIACTAIONS WITH A FOCUS ON LAMOTRIGINE

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ABSTRACT:

Significant physiological changes brought on by pregnancy affect drug pharmacokinetics, including absorption, distribution, metabolism, and elimination. These alterations are crucial for the treatment of women with epilepsy because they can result in lower plasma concentrations of various medications, including antiepileptic drugs. Lamotrigine, a frequently used AED during pregnancy, is extensively metabolized by glucuronidation, and its clearance increases noticeably during gestation. If doses are not changed, this frequently leads to subtherapeutic levels and an increase in the frequency of seizures. The physiological underpinnings of pharmacokinetic changes during pregnancy are outlined in this study, along with particular modifications seen with lamotrigine and the clinical importance of therapeutic drug monitoring (TDM) to improve outcomes for both the mother and the fetus. For pregnant women with epilepsy to get safe and effective treatment, a thorough understanding of these changes and customized dose management are crucial.

KEYWORDS: Pregnancy, TDM, Pharmacokinetic, ADE.

INTRODUCTION:

Therapeutic drug monitoring (TDM) is a particular clinical pharmacology technique that uses drug serum concentration measurements, interpretation, and close collaboration with doctors to track therapy. Pregnant women are almost always exposed to some kind of medicine. Teratogenic effects were found to be significantly correlated with maternal or

umbilical cord concentrations of some medications, but not dose. To estimate and potentially eliminate the teratogenic risk of these medications on the fetus, TDM in the mother during pregnancy is therefore more helpful than the prescribed dosage. A significant interindividual variation in the impact of pregnancy on the kinetics of several medications was also noted, along with a decrease in plasma concentrations throughout pregnancy. In order to maximize treatment for women using these medications throughout the time of unstable kinetics, frequent TDM during pregnancy and after delivery is required.

Pregnancy is a special physiological state that affects medication pharmacokinetics (absorption, distribution, metabolism, and elimination) due to significant changes in organ function, body composition, and endocrine activity. These changes may have a substantial impact on therapeutic medication levels, thereby jeopardizing safety or effectiveness. To avoid seizures that could endanger the mother and the fetus, women with epilepsy must receive ongoing antiepileptic medication (AED) therapy during pregnancy. Women who are pregnant or of reproductive age are often prescribed lamotrigine, a second-generation AED with broad effectiveness and a somewhat benign teratogenic risk. However, lamotrigine concentrations may be lowered by fetal physiological changes, requiring close observation and dose modifications.

Pregnancy-Related Physiological Changes Impacting Pharmacokinetics:

Increased plasma volume and cardiac output, altered gastrointestinal motility and pH, changes in plasma protein concentrations, induction or inhibition of drug-metabolizing enzymes, and increased renal blood flow and glomerular filtration rate are just a few of the changes in maternal physiology that are pertinent to drug disposition during pregnancy. All of these changes can change the free fraction of drugs in circulation and lower drug exposure. For instance, while enzyme induction might speed up metabolism and lower effective drug levels, decreased plasma protein concentrations may increase the unbound percentage of medications that are typically bound to albumin.

Pharmacokinetics of Lamotrigine During Pregnancy:

The primary enzyme responsible for the metabolism of lamotrigine is UDP-glucuronosyltransferase (UGT1A4). Lamotrigine clearance is significantly boosted during pregnancy, especially in the second and third trimesters, due to increases in UGT activity and improved renal excretion. Lamotrigine plasma concentrations can drop by as much as 60–80% from pre-pregnancy levels, with significant interindividual variability, according to

clinical research. If dosages are not changed, this decrease frequently occurs before clinical seizure deterioration.

Improved seizure control and better clinical outcomes have been linked to baseline plasma levels set before to pregnancy and regular therapeutic drug monitoring (TDM) during gestation. Through monitoring, doctors can increase dosages as clearance changes throughout pregnancy and lower doses after delivery when clearance returns to baseline to prevent toxicity.

Modified Lamotrigine Disposition's Clinical Consequences:

Correlations between decreasing plasma concentrations and an increase in seizure frequency highlight the therapeutic significance of lamotrigine's modified pharmacokinetics during pregnancy. Breakthrough seizures brought on by subtherapeutic levels carry dangers, including trauma, hypoxia, and unfavourable foetal outcomes. Frequent TDM directs postpartum dose decreases to avoid toxicity and facilitates dose titration to maintain therapeutic levels, usually aiming to match pre-pregnancy amounts.

Strategies for Therapeutic Drug Monitoring and Dose Adjustment:

An essential component of treating AED medication during pregnancy is therapeutic drug monitoring. Prior to pregnancy, establishing baseline lamotrigine levels serves as a guide for further monitoring. Drug concentrations should be checked routinely during pregnancy, usually every trimester or every month, in order to identify patterns and direct suitable dose increases. Drug clearance quickly returns to normal after delivery, necessitating a dose revaluation to prevent side effects.

Restrictions and Prospects:

The lack of large-scale prospective research, interindividual variability, and small sample sizes limit the available information. Furthermore, nothing is known about how pregnancy affects other more recent AEDs and their metabolites. Standardized dosage procedures, extended pharmacokinetic profiling in a variety of groups, and the incorporation of pharmacogenetic techniques to improve tailored treatment plans should be the main areas of future study.

CONCLUSION:

Drug pharmacokinetics are greatly impacted by pregnancy-related physiological changes, which might also lessen the effectiveness of AEDs like lamotrigine. Maintaining seizure

control and guaranteeing the safety of both the mother and the fetus requires an understanding of these dynamics and the use of routine therapeutic medication monitoring. The foundation of the best therapeutic therapy for pregnant women with epilepsy is individualized dosage modifications based on shifting pharmacokinetics and close observation.

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