Increased risk of childhood cancers in children with epileptic mothers taking high dosage of folic acid during pregnancy

Muhammad Waleed Imran, Sanwal Sardar Nawaz, Muhammad Moaz

Epilepsy is a neurologic condition that is characterized by disrupted electrical activity in the brain leading to seizures. According to WHO's 2010 Global Burden of Disease study, it is the second most common neurological condition in terms of burden associated with disability adjusted life ratio.[1] The prevalence of epilepsy is estimated to be 0.6-0.7% among the general population with women of reproductive age (15-45 years) being at a greater risk for developing the condition as compared to men of the same age group.[2]

The currently preferred mode of treatment to treat epilepsy involves carbamazepine, lamotrigine, levetiracetam, oxcarbazepine, phenobarbital, phenytoin, topiramate, and valproate. However, use of these anti-seizure medicines pose a significant teratogenic risk resulting in congenital malformations.[3] Quite often high dosage of Folic acid supplement is prescribed to pregnant women to reduce the incidence of neural tube and various other birth defects.[4]

A study published in 2022 reported high incidence of cancer among the children born to mothers who took high dosage (> 5mg) Folic acid during pregnancy.[5] This study concluded that increased folic acid supplementation in mothers taking anti-epileptic medication resulted in a paradoxical increase in DNA damage via DNA methylation and oxidative stress in the developing foetus, resulting in an increased risk of childhood cancers. Hence, risks and benefits should be weighed before prescribing optimal doses of folic acid to such patients.

3rd Year MBBS Student, Shifa College of Medicine, Islamabad, Pakistan.
Correspondence: Muhammad Waleed Imran.
Email: waleedimran0022@gmail.com
ORCID ID: 0009-0008-2667-4923

Submission complete: 06-07-2024 **First Revision received:** 30-08-2024
Acceptance: 07-12-2024 **Last Revision received:** 06-12-2024

DOI: https://doi.org/10.47391/JPMA.21399

Disclaimer: None.

Conflict of Interest: None.

Source of Funding: None.

References

1. Bastos F, Cross JH. Epilepsy. Handb Clin Neurol 2020;174:137-58. doi: 10.1016/B978-0-444-64148-9.00011-9
2. Christensen J, Dreier JW, Sun Y, Linehan C, Tomson T, Marson A, et al. Estimates of epilepsy prevalence, psychiatric co-morbidity and cost. Seizure 2023;107:162-71. doi: 10.1016/j.seizure.2022.06.010
3. Battino D, Tomson T, Bonizzoni E, Craig J, Perucca E, Sabers A, et al. Risk of Major Congenital Malformations and Exposure to Antiseizure Medication Monotherapy. JAMA Neurol 2024;81:481-9. doi: 10.1001/jamaneurol.2024.0258
4. Wilson RD, O'Connor DL. Guideline No. 427: Folic Acid and Multivitamin Supplementation for Prevention of Folic Acid-Sensitive Congenital Anomalies. J Obstet Gynaecol Can 2022;44:707-19.e1. doi: 10.1016/j.jogc.2022.04.004.
5. Vegrim HM, Dreier JW, Alvestad S, Gilhus NE, Gissler M, Igland J, et al. Cancer Risk in Children of Mothers With Epilepsy and High-Dose Folic Acid Use During Pregnancy. JAMA Neurol 2022;79:1130-8. doi: 10.1001/jamaneurol.2022.2977

AUTHORS' CONTRIBUTIONS:
MWI: Proposal, data collection, drafting and final approval and agreement to be accountable for all aspects of the work.
SSN & MM: Review, drafting, revision and final approval and agreement to be accountable for all aspects of the work.