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Post-Marketing Safety of Temozolomide: A Pharmacovigilance Study Based on the Food and Drug Administration Adverse Event Reporting System

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Abstract

Introduction: Temozolomide (TMZ) is a widely used chemotherapy agent for the treatment of malignant gliomas and other brain tumors. Despite its established therapeutic benefits, there is an ongoing need to understand better its safety profile, particularly in real-world clinical settings. This study aimed to identify critical adverse drug reactions (ADRs) associated with TMZ by utilizing the FDA Adverse Event Reporting System (FAERS) database, thereby providing valuable safety insights for clinical practice.

Methods: We utilized the reported odds ratio, proportional reporting ratio, Bayesian Confidence Propagation Neural Network, and Empirical Bayes Geometric Mean as primary algorithms for disproportionality analysis. Adverse events (AEs) were classified as ADRs only upon meeting the criteria set by all four algorithms. To ensure the accuracy of our results, we meticulously excluded any AEs deemed unrelated to TMZ.

Results: From October 2003 to September 2023, a total of 10,502,538 case reports and 9,073 cases explicitly attributed to TMZ were retrieved from the FAERS database. After applying our filters, 116 ADRs, each with a corresponding Preferred Term (PT), were identified across 18 System Organ Classes (SOCs). The identified ADRs associated with TMZ primarily involved bone marrow suppression, hepatotoxicity, and various infections, notably Pneumocystis jirovecii pneumonia. Furthermore, our analysis identified valuable ADRs not listed in the drug label, including congenital, familial, and genetic disorders at the SOC level, as well as unexpected ADRs at the PT level, such as seizures, pulmonary embolism, and sepsis.

Conclusion: This real-world pharmacovigilance study has identified significant and previously unreported ADRs associated with TMZ. Further research for validation and resolution is urgently needed to guide the clinical application of TMZ, ensuring the safety and efficacy of its use in treating brain tumors.

Keywords: Adverse drug reactions; Disproportionality Analysis; Food and Drug Administration Adverse Event Reporting System; Pharmacovigilance; Temozolomide.