

SFDA SAFETY SIGNAL

“A signal is defined by the SFDA as reported information on a possible causal relationship between an adverse event and a drug, the relationship being unknown or incompletely documented previously. Usually more than a single report is required to generate a signal, depending upon the seriousness of the event and the quality of the information. A signal is a hypothesis together with data and arguments and it is important to note that a signal is not only uncertain but also preliminary in nature”

01-03-2023

Saudi Food and Drug Authority (SFDA) – Safety Signal of Folic acid and the Risk of Constipation

*The Saudi Food and Drug Authority (SFDA) recommends all health care professionals to be aware of the safety signal of **Constipation** associated with the use of **Folic acid**. The signal has been originated as a result of routine pharmacovigilance monitoring activities.*

Introduction

Folic acid or Folate (vitamin B-9) is important in red blood cell formation and for healthy cell growth and function. The nutrient is crucial during early pregnancy to reduce the risk of birth defects of the brain and spine. Folate is found mainly in dark green leafy vegetables, beans, peas and nuts. Fruits rich in folate include oranges, lemons, bananas, melons and strawberries. The synthetic form of folate is . It's in an essential component of prenatal vitamins and is in many fortified foods such as cereals and pastas. ^[1] Constipation is generally described as having fewer than three bowel movements a week. Though occasional constipation is very common, some people experience chronic constipation that can interfere with their ability to go about their daily tasks. Chronic constipation may also cause people to strain excessively in order to have a bowel movement. ^[2] The aim of this review is to evaluate the risk of Constipation associated with the use of Folic acid and to suggest regulatory recommendations if required.

Methodology

Signal Detection team at SFDA performed a signal review using National Pharmacovigilance Center (NPC) database, and World Health Organization (WHO) database, VigiBase, with literature screening to retrieve all related information to assess the causality between Constipation and Folic acid use. The search conducted on February 2023.

Results

Case Review: Signal detection team at SFDA have searched Saudi national database and WHO database to find individual case safety reports (ICSRs). The Saudi national database resulted in one reported local case. The WHO database resulted in 157 global case-reports. The author selected top 30 cases with completeness score of 1.0 for further analysis. ^[3] Authors also applied WHO-UMC causality assessment criteria on the 30 ICSR, which resulted in most of them possibly linked to Folic acid (21 possible + 9 unlikely = 30 ICSR). ^[4]

Datamining: The disproportionality of the observed and the expected reporting rate for drug/adverse drug reaction pair is estimated using information component (IC), a tool developed by WHO-UMC to measure the reporting ratio. Positive IC reflects higher statistical association while negative values indicates less statistical association, considering the null value equal to zero. The results of (IC= 1.1) revealed a positive statistical association for the drug/ADR combination. ^[3]

Conclusion

The weighted cumulative evidence identified from assessed cases and data mining are sufficient to suggest causal association between Folic acid and Constipation. Health care professionals and health regulators must be aware of the potential risk in drug recipients.

Report Adverse Drug Events (ADRs) to the SFDA

The SFDA urges both healthcare professionals and patients to continue reporting adverse drug reactions (ADRs) resulted from using any medications to the SFDA either online, by regular mail or by fax, using the following contact information:

National Pharmacovigilance Center (NPC)
Saudi Food and Drug Authority-Drug sector
4904 northern ring branch rd
Hittin District
Riyadh 13513 – 7148
Kingdom of Saudi Arabia
Toll free number: 19999
Email: NPC.Drug@sfd.gov.sa

References:

- 1- Mayo Clinic (2021). Folate (folic acid) page. Available at: <https://www.mayoclinic.org/drugs-supplements-folate/art-20364625> [Accessed 27/02/2023]
- 2- Mayo Clinic (2021). Constipation page. Available online at: <https://www.mayoclinic.org/diseases-conditions/constipation/symptoms-causes/syc-20354253#:~:text=Constipation%20is%20generally%20described%20as,go%20about%20the%20daily%20tasks.> [Accessed 27/02/2023]
- 3- Vigilyze.who-umc.org. 2023. [online] Available at: <https://vigilyze.who-umc.org/> [Accessed 28/02/2023].
- 4- World Health Organization WHO (2013). WHO-UMC system for standardised case causality assessment. Available at <https://www.who.int/publications/m/item/WHO-causality-assessment> [Accessed 28/02/2023].