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 m ore 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"

05-02-2025

Saudi Food and Drug Authority (SFDA) – Safety Signal of Ceftriaxone and the Risk of Cholelithiasis

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

Introduction

Ceftriaxone is a third generation' semisynthetic cephalosporin with a long half-life. It has a broad spectrum of activity against Gram-positive and Gram-negative aerobic, and some anaerobic, bacteria. [1] Cholelithiasis or gallstones are hardened deposits of digestive fluid that can form in the gallbladder. [2] The aim of this review is to evaluate the risk of Cholelithiasis associated with the use of Ceftriaxone 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 Cholelithiasis and Ceftriaxone use. The search conducted on December 2024.

Results

Case Review: Signal detection team at SFDA have searched Saudi national database and WHO database to find individual case safety reports (ICSRs). The WHO database resulted in 914 global case-reports while only one local case found. The authors used signal detection tool (Vigilyze) to retrieve global cases. [3] Authors also applied WHO-UMC causality assessment criteria on the extracted ICSRs with completeness score 1.0 (30 cases). [4] Among them, 23 cases were probably and possibly linked to Ceftriaxone, while the remaining seven cases assessed as unlikely.

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. The IC result is (2.4) for this drug/ADR combination which reflects positive statistical association. [4]

Literature: The signal team searched the literature to find related publications linking this ADR to Ceftriaxone. The search showed a published case-report of cholelithiasis following the use of Ceftriaxone. [5]

Conclusion

The weighted cumulative evidence identified from assessed cases, disproportionality analysis and literature are suggestive for causal association between Ceftriaxone and Cholelithiasis. 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@sfda.gov.sa

References:

1- Richards, D. M., Heel, R. C., Brogden, R. N., Speight, T. M., & Avery, G. S. (1984). Ceftriaxone. A review of its antibacterial activity, pharmacological properties and therapeutic use. Drugs, 27(6), 469–527. https://doi.org/10.2165/00003495-198427060-00001

2- Tanaja J, Lopez RA, Meer JM. Cholelithiasis. [Updated 2023 Aug 7]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK470440/

3- Vigilyze.who-umc.org. 2024. [online] Available at: https://vigilyze.who-umc.org/ .

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 .

5- Abdelaziz, H., Cormier, N., Levesque, T., St-Yves, J., Habash, M. A., Diaz, O., Haberer, M. P., Calugaroiu, D., & Nashed, M. (2022). Rapid Onset of Ceftriaxone-Induced Cholelithiasis in an Adult Patient. Journal of global infectious diseases, 14(1), 31–34. https://doi.org/10.4103/jgid.jgid_11_21