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"

7-9-2020

Saudi Food and Drug Authority (SFDA) – Safety Signal of Hypokalemia Associated with the Use of Ceftriaxone products

The Saudi Food and Drug Authority (SFDA) recommends all health care professionals to be aware of the safety signal of ***Hypokalemia*** *associated with the use of* ***Ceftriaxone****. The signal has been originated from local case that has been reported to the National Pharmacovigilance Center (NPC).*

Background: Ceftriaxone is a broad-spectrum cephalosporin antibiotic Indicated for the treatment of the infections works by inhibiting the mucopeptide synthesis in the bacterial cell wall leading to cell death. [1] Hypokalemia refers to a lower than normal potassium level in bloodstream which can be life threatening and requires urgent medical attention [2]

Methodology: on November 13, 2019, the Signal Detection team at Saudi Food and Drug Authority (SFDA) performed a safety review using NPC database, and World Health Organization (VigiBase), along with literature screening to retrieve all related information which would be beneficial to assess the causality between Hypokalaemia and Ceftriaxone use.

Results:

Local Cases: The Saudi NPC database has only one case of Ceftriaxone associated with Hypokalaemia, it reported with reasonable time to onset and positive dechallenge. This case has probable association according to WHO-UMC causality assessment.

Global Cases: The WHO database (VigiBase) searched for all individual case safety reports (ICSRs) reported with "Hypokalaemia" and "Ceftriaxone" yielded to 91 ICSRs. Initial review

revealed that 67 cases were not documented sufficiently for proper medical assessment. However the rest cases (24) have been furthered evaluated resulted in nine cases with positive dechallenge and one with negative rechallenge and after applying the WHO causality assessment criteria, resulted in six cases with probable association, nine with possible association, eight with unlikely association and one case was un-assessable due to lack on information. [3]

Literature: During literature search, only one article support the association founded, it was aiming to explore the possible association of antimicrobial agents use and the development of hypokalaemia as an adverse drug reaction. Retrospective analysis of ICSRs received from January 2015 to September 2017, for any case of hypokalemia following the use of antimicrobial agents. Fifty-three ICSRs reported with hypokalemia and the suspected reason was antimicrobial agent and the most reported antimicrobial agent was Ceftriaxone (n=14) [4]

Datamining: The disproportionality between observed and expected reporting rate of drug-adverse drug reaction combination calculated using Information Component (IC). Higher IC value means a strong statistical association between certain medications with the event in comparison to other medications. The combination of Ceftriaxone and Hypokalaemia has observed less than expected (IC -1.8) when compared with other medications. [3]

Conclusion

The weighted cumulative evidences identified from global cases, data mining and published literature are sufficient to support a causal association between Hypokalaemia and Ceftriaxone. Therefore, health care professionals should be aware of this safety concern and may consider monitoring any signs or symptoms of Hypokalaemia in patients treated with Ceftriaxone.

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- Drug bank. (2019) Ceftriaxone. Retrieved from: https://www.drugbank.ca/drugs/DB01212 [Accessed 11/14/2019]

2- Mayo clinic. (2019). Low potassium (hypokalemia). Retrieved from: https://www.mayoclinic.org/symptoms/low-potassium/basics/definition/sym-20050632 [Accessed 11/13/2019]

3- Uppsala Monitoring Center (UMC) (2019), Vigilyze database; Available at: https://vigilyze.who-umc.org/#/ [Accessed 11/13/2019]

4- Singh Rehan, H., & Hotha, P. (2019). Antimicrobial Agents-induced Hypokalemia: A Possible Causality Association. Indian journal of critical care medicine : peer-reviewed, official publication of Indian Society of Critical Care Medicine, 23(4), 175–177. doi:10.5005/jp-journals-10071-23148