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"

2-5-2021

Saudi Food and Drug Authority (SFDA) – Safety Signal of Azithromycin and the Risk of Mitral valve incompetence

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

Introduction

Azithromycin is antibiotic that indicated to treat community-acquired pneumonia and pelvic inflammatory disease caused by susceptible organisms, including Legionella pneumophila, in patients indicated for IV therapy [1]. Mitral insufficiency, is an improper closing of the mitral valve causes the blood to flow backwards into the heart [2]. The aim of this review is to evaluate the risk of Mitral valve incompetence associated with the use of Azithromycin and to suggest regulatory recommendations if required.

Methodology

Signal Detection team at the National Pharmacovigilance Center (NPC) of Saudi Food and Drug Authority (SFDA) performed a comprehensive signal review using its national database as well as the World Health Organization (WHO) database (VigiBase), to retrieve related information for assessing the causality between Azithromycin and the Risk of Mitral valve incompetence [3]. We used the WHO-Uppsala Monitoring Centre (UMC) criteria as standard for assessing the causality of the reported cases [4]

Results

Case Review: The number of resulted cases for the combined drug/adverse drug reaction are 6 global ICSRs as of February 1st 2021 [3]. The reviewers have selected and assessed the causality for All ICSRs (6 ICSRs). Among the reviewed cases, more than half of them provides supportive association (4 possible cases).

Data Mining: 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= -2.1) revealed a negative statistical association for the drug/ADR combination, which means "Mitral valve incompetence" with the use of "azithromycin" have been observed less than expected when compared to other medications available in WHO database [3].

Literature Upon conducting a literature search, two relevant studies were found:

A 47-year-old female, had sudden cardiac arrest outside of the hospital after treatment with azithromycin. The patient was previously healthy. The ECG showed a little prolongation of the QT of 495 ms and myxomatous mitral valve disease with flail posterior leaflet resulting in severe eccentric mitral regurgitation. She underwent slightly invasive mitral valve repair 3 months after the initial event [5].

Another study aimed to detect signals of cardiac disorders associated with azithromycin from Health Canada database. The authors found that, Mitral valve disease was reported in 2% of pediatrics and 1% of the adult population among of all cardiac related ADRs [6].

Conclusion

The weighted cumulative evidences identified from causality assessment of the reported cases, and literature are sufficient to support a causal association between Azithromycin and the risk of Mitral valve incompetence. Health regulators and health care professionals must be aware of this potential risk and it is advisable to monitor any signs or symptoms in treated patients.

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. Pharmacia Upjohn Company LLC. Saudi Summary of Product Characteristics (SPC) of Azithromycin (ZITHROMAX) ®; (retrieved from EURS). [Accessed 2/4/2021]
2. Mitral Insufficiency: Causes, Symptoms & Treatment. Available at: https://www.ssmhealth.com/heart-vascular-health/valvular-disease/mitral-insufficiency [Accessed on: 2/8/2021].
3. Uppsala Monitoring Center (UMC) (2020), Vigilyze database; Available at: https://vigilyze.who-umc.org [Accessed 1/31/2021].
4. Uppsala Monitoring Center (UMC) (2020), The use of the WHO-UMC system for standardized case causality assessment; Available at https://www.who.int/medicines/areas/quality_safety/safety_efficacy/WHOcausality_assessment.pdf?ua=1 [Accessed 1/31/2021].
5. American Journal of Medicine, Available at: https://www.amjmed.com/article/S0002-9343(15)00514-8/pdf [Accessed 2/8/2021].
6. International Journal of Pharmacy and Pharmaceutical Sciences. Available at: https://www.researchgate.net/publication/317366190_SAFETY_SIGNAL_DETECTION_OF_CARDIAC_DISOR

DERS_ADVERSE_DRUG_EVENTS_FOR_AZITHROMYCIN_IN_PEDIATRIC_POPULATION_USING_HEALTH_CANADA_ADVERSE_EVENT_REPORTING_SYSTEM_DATABASE [Accessed 2/8/2021].