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"

21-6-2021

Saudi Food and Drug Authority (SFDA) – Safety Signal of Cefuroxime and the Risk of Kounis Syndrome

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

Introduction

Cefuroxime is cephalosporin antibacterial drug. It has good stability to bacterial β-lactamase, therefore it is active against many ampicillin-resistant or amoxycillin-resistant strains. Cefuroxime is indicated for the treatment of infections caused by sensitive bacteria. The bactericidal activity of cefuroxime results from inhibition of cell wall synthesis by binding to essential target proteins. [1] Kounis syndrome is the occurrence of acute coronary syndromes with hypersensitivity reactions after the exposure to allergenic. It is caused by inflammatory mediators such as neutral proteases including tryptase and chymase, arachidonic acid products, histamine, platelet activating factor and a variety of cytokines and chemokines released during the activation process. [2]

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 Cefuroxime and the risk of Kounis syndrome [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 11 global ICSRs as of April 12th 2021 [3]. The cases reported from six different countries (Germany, Turkey, United States of America, Greece, United Kingdom of Great Britain and Northern Ireland and France). Patient ages varied, and the age group 45–64 accounted for 83.3% of the reported cases. Seven ICSRs concern male patients while four ICSRs concern female patients. Most of ICSRs were classified as

serious cases. The most co-reported adverse reaction was anaphylactic reaction. The reviewers have selected and assessed the causality for all cases (11 ICSRs). Among the reviewed cases, there was one probable case and two possible cases. Eight cases were unassessable due to lack of information and non of the cases assessed as unlikely causality.

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= 2.8) revealed a positive statistical association for the drug/ADR combination, which means "Kounis syndrome" with the use of "Cefuroxime" have been observed more than expected when compared to other medications available in WHO database [3].

Literature: Upon conducting a literature search, six relevant studies were found summarized as below (*see table 1*):

Table 1: Case reports of Kounis Syndrome associated with Cefuroxime administration

Reference	Title	Sex, age	Indication	Time to onset	Type
Andreas Mazarakis.2005[5]	Cefuroxime-induced coronary artery spasm manifesting as Kounis syndrome	F/ 70 Y	Antibiotic prophylaxis	1 minute	Case report
Mitsis. 2018 [6]	Coronary spasm secondary to cefuroxime injection, complicated with cardiogenic shock – a manifestation of Kounis syndrome: case report and literature review	M/ 64 Y	perioperative prophylactic treatment	20 minutes	Case report
Biteker 2008 [7]	Kounis Syndrome Secondary To Cefuroxime-Axetil Use in An Octogenarian	M/ 90 Y	urinary tract infection	10 minutes	Case report
İlhan.2009 [8]	Kounis Syndrome secondary to cefuroxime axetil use in an asthmatic patient	F/ 61 Y	Asthma	10 minutes	Case report
Murat. 2010 [9]	Cefuroxime-axetil induced allergic angina: An insight into classification management of Kounis syndrome	M/ 40 Y	-	5 minutes	Case report
Gao2 2018 [10]	Cefuroxime-associated Kounis syndrome with unique peculiarity in perioperative prophylaxis	F/ 37 Y	perioperative prophylactic treatment	75 minutes	Case report

Conclusion

The weighted cumulative evidences identified from causality assessment of the reported cases, and literature are sufficient to support a causal association between Cefuroxime and the risk of Kounis syndrome. 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:

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