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"

21-03-2023

Saudi Food and Drug Authority (SFDA) – Safety Signal of Levofloxacin and the Risk of Dry mouth

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

Introduction

Levofloxacin is a broad-spectrum, third-generation fluoroquinolone antibiotic used to treat bacterial infections. Levofloxacin is a safe and effective medicine on the World Health Organization's essential medicines list. It was patented in 1987 and subsequently received FDA approval in 1996 for medical use in the United States. Levofloxacin is FDA-approved for the treatment of nosocomial pneumonia, community-acquired pneumonia, acute bacterial rhinosinusitis, acute bacterial exacerbation of chronic bronchitis. [1] Xerostomia is the patient's subjective feeling of dry mouth; hyposalivation is the objective and measurable dry mouth. The two concepts do not always coincide. Saliva secretion outside mealtimes is normally 0.3 ml/min. Less than 0.1 ml/min is defined as hyposalivation. Xerostomia occurs when secretion is reduced to about half the normal quantity, but may also be a result of changes in the composition of the saliva. In such cases, the saliva may become viscous, stringy and/or frothy. [2][(3] The aim of this review is to evaluate the risk of dry mouth associated with the use of levofloxacin 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 Dry mouth and Levofloxacin use. The search conducted on March 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 Suadi national database resulted in one reported local case. The WHO database resulted in 857 global case-reports. The authors used signal detection tool (Vigilyze) to retrieve all reported cases. [4] Authors also applied WHO-UMC causality

assessment criteria on ICSRs with completeness score 1.0 (n=30). [5] Among them, 29 cases of Dry mouth were either probably or possibly linked to levofloxacin.

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 IC result is (0.0) for this drug/ADR combination. [4]

Literature: On March 2023, the author searched for eligible publication using terms "levofloxacin" and "Dry mouth".

In a published randomized double-blind controlled trial that included female aged >18 years old with uncomplicated lower urinary tract infection. Patients were randomly assigned to either solifenacin succinate 5 mg (group 1) or placebo (group 2) in addition to empiric levofloxacin 500 mg treatment for 3 days. Group 1 reported a percentage of 22.2% of patients who suffered from dry mouth and on the other hand, in-group 2 a total of 20.0% of participants experienced dry mouth which indicates a plausible association. [6]

Conclusion

The weighted cumulative evidence identified from assessed cases and literature are sufficient to suggest causal association between levofloxacin and Dry mouth. 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- Bush LM, Chaparro-Rojas F, Okeh V, Etienne J. Cumulative clinical experience from over a decade of use of levofloxacin in urinary tract infections: critical appraisal and role in therapy. Infect Drug Resist. 2011;4:177-89.

2- Edgar M, O'Mullane D, Dawes C. Saliva and oral health. 3. utg. London: British Dental Association, 2004.

3- Pedersen AML, Sørensen CE, Proctor GB et al. Salivary secretion in health and disease. J Oral Rehabil 2018; 45: 730–46.

4- Vigilyze.who-umc.org. 2023. [online] Available at: https://vigilyze.who-umc.org/ [Accessed 15/03/2023].

5- 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 15/03/2023].

6- Rahardjo HE, Syahputra FA, Islianti PI, Matondang FA. Efficacy of Additional Solifenacin Succinate Therapy for Storage Symptoms in Females with Uncomplicated Lower Urinary Tract Infection: The SOLUTION Randomized Controlled Trial. Acta Med Indones. 2018 Jul;50(3):200-207. PMID: 30333269