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 Ibuprofen and the Risk of Renal tubular acidosis

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

Introduction

Ibuprofen is indicated for its analgesic and anti-inflammatory effects in the treatment of rheumatoid arthritis, ankylosing spondylitis, osteoarthritis and other non-rheumatoid (seronegative) arthropathies. In the treatment of non-articular rheumatic conditions, Ibuprofen can also be used in soft tissue injuries such as sprains and strains. Ibuprofen is also indicated for its analgesic effect in the relief of mild to moderate pain such as dysmenorrhea, dental and post-operative pain and for symptomatic relief of headache, Including migraine headache.[1] Renal tubular acidosis (RTA) occurs when the kidneys do not remove acids from the blood into the urine as they should. The acid level in the blood then becomes too high, a condition called acidosis. Some acid in the blood is normal, but too much acid can disturb many body functions.[2] The aim of this review is to evaluate the risk of Pruritus associated with the use of Lactulose 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 Renal tubular acidosis and Ibuprofen use. The search conducted on February 2022.

Results

Case Review: Signal detection team at SFDA have searched Saudi national database and WHO database to find individual case safety reports (ICSRs). The Saudi national database resulted in zero reported local case. The WHO database resulted in 116 global case-reports. The authors used signal detection tool (Vigilyze) to retrieve all reported cases. [3] Authors also applied WHO-UMC causality assessment criteria on ICSRs with completeness score (0.5) and above (n=10). [4] Among them, two cases were probable, one possible and seven cases were not assessable.

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 results of (IC= 4.2) revealed a positive statistical association for the drug/ADR combination. [3]

Literature: On February 2022, the author searched for eligible publication using terms "Ibuprofen" and "Renal tubular acidosis".

A study that described four patients who presented with profound hypokalaemia and muscle weakness due to renal tubular acidosis associated with excessive ibuprofen ingestion.[5] Literature also showed a case report of 72-year-old woman was admitted because of severe acute tetraparesi. She was taking Ibuprofen daily for six months. The biochemical findings suggest renal tubular acidosis. [6]

Conclusion

The weighted cumulative evidence identified from assessed cases, literature and data mining are sufficient to suggest causal association between Ibuprofen and Renal tubular acidosis. 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- Tabuk Pharmaceutical Manufacturing Company (2014). Saudi Summary of Product Characteristics (SPC) of Ibuprofen (Prof) ® (retrieved from: EURS). [Accessed 28/02/2023]
2- Acidosis, R. and Health, N., 2022. Renal Tubular Acidosis | NIDDK. [online] National Institute of Diabetes and Digestive and Kidney Diseases. Available at: <https://www.niddk.nih.gov/health-information/kidney-disease/renal-tubular-acidosis#:~:text=Renal%20Tubular%20Acidosis-,What%20is%20renal%20tubular%20acidosis%3F,can%20disturb%20many%20bodily%20functions.> [Accessed 28/02/2023].
3- Vigilyze.who-umc.org. 2023. [online] Available at: https://vigilyze.who-umc.org/ [Accessed 28/02/2023].
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 [Accessed 28/02/2023].
5- . Ng, J., Morgan, D., Loh, N., Gan, S., Coleman, P., Ong, G. and Prentice, D., 2011. Life-threatening hypokalaemia associated with ibuprofen-induced renal tubular acidosis. Medical Journal of Australia, 194(6), pp.313-316.
6- Gaul C, Heckmann JG, Druschky A, et al. [Renal tubular acidosis with severe hypokalemic tetraparesis after ibuprofen intake]. Deutsche Medizinische Wochenschrift (1946). 1999 Apr;124(16):483-486. DOI: 10.1055/s-2007-1024347. PMID: 10341751.