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 Prednisone and the Risk of Osteonecrosis

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

Introduction

Prednisone is a synthetic, anti-inflammatory glucocorticoid that derives from cortisone. It is biologically inert and converted to prednisolone in the liver. delayed-release corticosteroid indicated as an anti-inflammatory or immunosuppressive agent to treat a broad range of diseases, including immunosuppressive/endocrine, rheumatic, collagen, dermatologic, allergic states, ophthalmic, respiratory, hematologic, neoplastic, edematous, gastrointestinal (GI, acute exacerbations of multiple sclerosis, and as an anti-inflammatory and an antineoplastic agent. Prednisone is a corticosteroid (cortisone-like medicine or steroid). It works on the immune system to help relieve swelling, redness, itching, and allergic reactions.[1] Osteonecrosis, which is also called avascular necrosis (AVN) or aseptic necrosis, is the death of bone cells due to decreased blood flow. It can lead to pain and collapse of areas of bone. This collapse of bone, in turn, can lead to degenerative arthritis (also called osteoarthritis) of nearby joints, most often the hips and knees. Less often affected spots are the shoulders, hands and feet. Rarely, osteonecrosis can occur in the jaw. This can result in ulcers (sores) of gum tissue, exposed jawbone and pain.[2] The aim of this review is to evaluate the risk of Osteonecrosis associated with the use of Prednisone 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 Osteonecrosis and Prednisone 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 1037 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 of 1.0 (n=30). [4] Among them, (1 probable+19 possible + 8 unlikely + 2 not assessable = 30 ICSRs).

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= 4.0) revealed a strong positive statistical association for the drug/ADR combination. [4]

Literature: On March 2023, the author searched for eligible publication using terms "Prednisone" and "Osteonecrosis".

Osteonecrosis (avascular necrosis) of the femoral head (ONF) has been related to prolonged high-dose cortico- steroid therapy. There is some evidence to suggest it also occurs with increased frequency at doses used in organ transplantation. In the study discussed a comparison between 589 kidney transplant recipients not receiving maintenance prednisolone and 465 historical controls, osteonecrosis was significantly more frequent in patients receiving corticosteroids. Another study was done retrospectively, comparing 374 kidney transplant recipients prescribed an average daily dose of prednisone 12.5 mg in the first year post-transplant with 276 patients prescribed an average daily dose of 6.5 mg, the incidence of ONF was 11 and 5.1 % in the two groups, respectively (p \ 0.005). [5]

Conclusion

The weighted cumulative evidence identified from assessed cases, literature and data mining are sufficient to suggest causal association between Prednisone and Osteonecrosis. 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- Puckett, Y., Gabbar, A., & Bokhari, A. A. (2018). Prednisone.
2- American College of Rheumatology (2023). Osteonecrosis page. Available at: https://rheumatology.org/patients/osteonecrosis [Accessed 01/03/2023]
3- Vigilyze.who-umc.org. 2023. [online] Available at: https://vigilyze.who-umc.org/ [Accessed 01/03/2023].
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 02/03/2023].
5- Bergmann, T.K., Barraclough, K.A., Lee, K.J. et al. Clinical Pharmacokinetics and Pharmacodynamics of Prednisolone and Prednisone in Solid Organ Transplantation. Clin Pharmacokinet 51, 711–741 (2012). https://doi.org/10.1007/s40262-012-0007-8