



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”

19/12/2016

Saudi Food and Drug Authority (SFDA): Reports of Potential Safety Signal Concerning Fixed Drug Eruptions Caused by Doxycycline

The Saudi Food & Drug Authority (SFDA) would like to highlight a safety signal concerning fixed drug eruptions associated with the use of doxycycline

Doxycycline is a tetracycline broad-spectrum antibiotic with a bacteriostatic characteristics. It is used as treatment or prophylaxis against wide range of Gram-negative and Gram-positive organisms.

Fixed drug eruption (FDE) is a rare type of cutaneous adverse drug reactions (ADRs), which, basically, recurs at the same site on skin/mucosa each time the offending drug is administered.

The SFDA has initiated a signal validation report based on a published case report of potential association between doxycycline and risk of FDE. Data mining of the World Health Organization (WHO) global ADRs database along with literature screening have been carried out to retrieve all related information for the sake of investigating causality of drug-event combination. Three hundred and sixty-four international ADR reports were identified, of them, 356 cases were not sufficiently documented for proper medical assessment. Besides, they were not merely classified the ADR of interest as serious ADR. The rest of the cases (i.e. eight cases), were reported with a

positive de-challenge*. Of those eight cases, one case was reported with unknown re-challenge[‡] outcome.

A published study evaluating the Cross-Reactivity of FDE with tetracyclines, showed that 16 patients were clinically confirmed to have FDE as a result of tetracycline use. The patients challenged to doxycycline and minocycline at least 6 weeks after the last episode of FDE. Among these 16 patients, ten cases developed FDEs to doxycycline within 6 hours of intake.¹

Another recent case study found that there is a probable association between doxycycline and fixed drug eruptions. A 37-year-old female presented to the hospital with a history of fluid filled lesions all over her body. History information (medical, pharmacological and social) were taken and revealed that the patient had taken one dose of doxycycline prescribed by a local practitioner day following history of accidental fall and sustained injury over her right lower limb. A previous medical record shows, also, a history of rashes over the trunk due to former doxycycline intake.²

Podder et.al. reported a case of a 30-year-old male who was presented to an ER with a 4-day-history of multiple itchy and painful erythematous patches with vesicles and bullae of varied sizes scattered all over the body along with oral and genital ulcerations. The patient reported that these lesions developed suddenly three hours following the ingestion of single dose of doxycycline (100 mg). A diagnosis of generalized bullous FDE was absolute based on clinical and histopathological evidence. Doxycycline was stopped, and the patient was managed conservatively along with a short course of oral corticosteroid for 10 days. As a result the lesion were resolved with some hyperpigmentation residuals. Furthermore, the patient stated that similar lesions with less severity were appeared two years ago after the same drug intake.³

* Dechallenge: This refers to the stopping of the drug, usually after an adverse event (AE) or at the end of a planned treatment.

‡ Rechallenge: his refers to the restarting of the same drug after having stopped it, usually for an AE.

The SFDA investigation concluded that the current available evidence may support probable relationship between doxycycline and fixed drug eruption. Therefore, the summary of product characteristics (SPC) and patient information leaflet (PIL) will be updated accordingly. The SFDA will continue its through investigations for close monitoring such a drug-event combination and will update all concerned healthcare providers upon availability of new safety data.

Report Adverse Drug Events (ADEs) to the SFDA

The SFDA urges both healthcare professionals and patients to continue reporting adverse drug events (ADEs) originated from using any medications to the SFDA either online, by regular mail or by fax, using the following contact information:

National Pharmacovigilance and Drug Safety Center (NPC)

Saudi Food and Drug Authority - Drug sector

3292 Northern Ring Road

Al Nafal District

Riyadh 13312 – 6288

Kingdom of Saudi Arabia

Toll free number: 8002490000

Tel: 011 2038222 ext. 2317, 2356, 2340,

Fax: 011 2057662

Email: NPC.Drug@sFDA.gov.sa

References:

1. Tham, S. N., Y. K. Kwok, and H. L. Chan. "Cross-reactivity in fixed drug eruptions to tetracyclines." *Archives of dermatology* 132.9 (1996): 1134-1135.
2. Nitya, Selvaraj et al. "Doxycycline Induced Generalized Bullous Fixed Drug Eruption – A Case Report." *Journal of Young Pharmacists : JYP* 5.4 (2013): 195–196. PMC. Web. 13 June 2016.
3. Podder, Indrashis et al. "Doxycycline Induced Generalized Bullous Fixed Drug Eruption." *Indian Journal of Dermatology* 61.1 (2016): 128. PMC. Web. 13 June 2016.