

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”

05-08-2024

Saudi Food and Drug Authority (SFDA) – Safety Signal of Gentamicin and the Risk of Clostridium difficile colitis

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

Introduction

Gentamicin is an aminoglycoside antibiotic used in the treatment of several gram-negative infections. It should be indicated based on patient age, symptoms, signs at presentation, and local antimicrobial resistance patterns to enhance the probability of successful treatment in bacterial septicemia, meningitis, urinary tract infections, gastrointestinal tract infections, and soft tissue infections. ^[1] Clostridioides difficile, formerly known as Clostridium difficile, is a gram-positive and spore-forming bacterium. This obligate anaerobic bacillus is recognized for its ability to produce toxins and cause diarrhea, which is often associated with antibiotic usage. ^[2] The aim of this review is to evaluate the risk of Clostridium difficile colitis associated with the use of Gentamicin 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 Clostridium difficile colitis and Gentamicin use. The search conducted on May 2024.

Results

Case Review: Signal detection team at SFDA have searched Saudi national database and WHO database to find individual case safety reports (ICSRs). The WHO database resulted in 77 global case-reports while only one local case found. The authors used signal detection tool (Vigilyze) to retrieve all reported global cases. ^[3] Authors also applied WHO-UMC causality assessment criteria on the extracted ICSR with completeness score 0.81 and above (n=28 cases). ^[4] Among them, 25 cases were probably and possibly linked to Gentamicin, and 1 case assessed as not assessable due to lack of important information, while the remaining 2 case assessed as unlikely.

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 IC result is (2.6) for this drug/ADR combination which reflects strong positive statistical association. ^[4]

Conclusion

The weighted cumulative evidence identified from assessed cases and disproportionality analysis are suggestive for causal association between Gentamicin and Clostridium difficile colitis. Health care professionals and health regulators must be aware of this 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- Chaves BJ, Tadi P. Gentamicin. [Updated 2023 Apr 10]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 Jan-. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK557550/> [Accessed: 29/05/2024].
- 2- Mada PK, Alam MU. Clostridioides difficile Infection. [Updated 2023 Jan 23]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 Jan-. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK431054/> [Accessed: 29/05/2024].
- 3- Vigilyze.who-umc.org. 2024. [online] Available at: <https://vigilyze.who-umc.org/> [Accessed: 30/05/2024].
- 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: 30/05/2024].