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Editorial

Plan for Protecting Our Children from Diethylene glycol/Ethylene glycol-associated Acute Kidney Injury

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1. UNEXPECTED ACUTE KIDNEY INJURY (AKI) IN CHILDREN: A BRIEF PROLOGUE

Pediatric acute kidney injury (AKI) is defined as a precipitous decline in renal function that alters the homeostasis of waste products, electrolytes, and fluids. This phenomenon has the potential to substantially changing a patient's course, resulting in serious health consequences (especially in cases of chronic kidney disease) [1].

Recently, uncontrollable diethylene glycol (DEG) and ethylene glycol (EG) remnants were determined to be the source of pediatric AKI in liquid medications. The unfavorable effects of these substances are associated with

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their impact on the development of calcium oxalate monohydrate crystals and oxalic acid in the kidney tubular system, ultimately causing renal failure. This discovery adds to several occurrence of pediatric AKI cases with comparable causes that have been identified and documented since more than 20 years ago [2].

2. SITUATION OF EMERGING AKI IN INDONESIA, GAMBIA AND UZBEKISTAN

The number of AKI cases in children in Indonesia is soaring from August 2022 [3]. As of November 1st, 2022, the overall amount of AKI cases in Indonesia was 325 (mostly toddlers), with 178 deaths. 5 This statistic results in a mortality rate of 54.8%, which is much higher than the previously released data on the pediatric AKI in-hospital mortality rate (15.3%) [4]. The Republic of Indonesia's Ministry of Health established that DEG/EG was the main cause of this condition after conducting a laboratory examination which revealed that 42.2% of medication samples and 60.3% of patient plasma samples were positive for EG/DEG in 28 hospitals and primary care centers [5].

The Gambia is the first nation to disclose this emerging condition as of June 2022. By the time of the report on September 29, 2022, 66 (84.62%) of the 78 clinically suspected pediatric AKI patients had already passed away [6]. The newest country on the list is Uzbekistan, where subpar and tainted pharmaceuticals were discovered and submitted to the World Health Organization. Until the end of December 2022, 18 of 21 (85.71%) children died due to AKI [7]. Within that span, these nations collectively noted more than 250 pediatric deaths linked to AKI. In addition, 52 syrups (47 from Indonesia, 3 from the Gambia, and 2 from Uzbekistan) were determined to be contaminated by DEG/EG and were immediately withdrawn from sale to stop the disease from spreading [5-7].

3. OTHER SOURCE TO BE EXAMINED AND HOW TO PREVENT FUTRE SITUATION?

Concerning the use of EG in water pipelines and water bottles (EG is a monomer of polyethylene terephthalate (PET) and its degradation product), these sources must be thoroughly investigated to trace environmental contaminants. This is because water is deemed a strong solvent with a relatively high likelihood of contamination from the containers. Moreover, the materials and colors of the bottles may affect the degree of contamination. Meanwhile, the pH of the water (beverage) stored in these bottles will be critical for releasing elements from the container walls into the fluid and the frequency of contamination [8]. The Agency for Drug and Food Control of the Republic of Indonesia (*Badan Pengawas Obat dan Makanan Republik Indonesia*/BPOM RI) is also investigating this potential source of EG poisoning.

Considering the source of DEG/EG toxicity has been identified as tainted medications, our efforts to maintain drug quality assurance must be stepped up. It includes evaluation of the target product profile, product and process design, and control strategy (including assessment of parameters for the drug constituent(s), excipient(s), and final drug product as well as monitoring for each phase of production), process capability, and constant improvement [9]. In light of the recent emergence of AKI, the World Health Organization keeps urging nations to improve quality control, regulatory oversight, and vigilance in the production and distribution of pharmaceutical products to prevent similar incidents from happening in the future and safeguard kids from tainted medications.

Based on the present circumstances in Indonesia, several interventions have been made to address the matter. These include the recall and destruction of approximately 47 tainted oral solution products made by six pharmaceutical firms, the introduction of an immediate investigation into the origin of the AKI cases that involved the collection of drug samples, patient plasma samples, and kidney biopsies, and the purchase of fomepizole as the antidote for the specific AKI cases. Furthermore, the issue of shortages in the supply of raw ingredients chain has been identified, and BPOM RI has begun taking the necessary steps to prevent subsequent contamination of medicinal products, with the support of WHO [5]. The interventions were deemed effective because there was no incidence of DEG/EG-associated AKI in the country since early November 2022 until the completion of this editorial on early May 2023.

4. CONFLICT OF INTERESTS

The authors have no conflict of interest to declare. The authors declared that this study has received no financial support.

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