Editorial
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Why should we monitor for hematologic adverse drug reactions to oxcarbazepine?

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Adverse drug reaction (ADRs) are unwanted effects of drug administration regardless of etiology and pathogenic mechanism. ADRs occur in about 10%–20% of all hospitalized patients and involve various mechanisms. Delayed type ADRs may appear after several months. Thus, periodic follow-up examinations are necessary.[1)]

According to the report of Korea Institute of Drug Safety & Risk Management (KIDS) in 2015, antiepileptic drugs (AEDs) account for 2.2% of total drugs causing ADRs ranging from nausea to skin rash to death. Leukopenia caused 2,562 of 112,418 cases (0.9%), while neutropenia caused 2,303 cases (0.8%). Among ADRs in AEDs, hematologic disorders range from thrombocytopenia or neutropenia to bone marrow failure.[2,3)]

Several hypotheses have been proposed to explain the mechanisms of ADRs, including direct toxicity, immune complexes, hapten formation, inhibition of colony forming units in bone marrow, complement-mediated mechanisms, and association with human leukocyte antigen (HLA). HLA-B*15:02 is significantly associated with oxcarbazepine (OXC)-induced Stevens-Johnson syndrome in Asian populations (Chinese and Thai). In Korean patients, OXC-induced maculopapular eruptions are significantly associated with HLA-B*40:02 and HLA-DQB1*04:03, whereas HLA-B*15:01 is a protective allele. The mechanisms of drug-induced neutropenia are not yet fully understood. Prolonged exposure to drugs affects the microenvironment of the bone marrow or the myeloid precursors. The metabolic pathways that metabolize drugs and chemicals are regulated by genetic factors.[3-5)]

The neutropenic patient (absolute neutrophil count [ANC], 1,500 cells/mm^3) is highly susceptible to bacterial, fungal, and viral infections, with the risk of infection associated with neutropenia grade and duration, while patients with grade IV neutropenia (ANC, 500 cells/mm^3) are at a greater risk of infection regardless of the duration. Previous studies reported hematological side effects of carbamazepine (CBZ) at a frequency of 1:38,000–1:10,800, whereas ADRs of OXC are reportedly rare. OXC is used to treat partial and secondarily generalized tonic-clonic seizures, and its active metabolite, monohydroxy derivative, exerts its effects on sodium channels and possibly potassium and calcium channels with a mechanism of action similar to that of CBZ and comparable efficacy but superior safety.[6-9)]

According to the KIDS report, there were 212 cases of OXC-induced ADRs in patients under 18 years of age between 2011 and 2015, including 3 cases (1.4%) of hematologic side effect, 1 case of leukopenia, 1 case of neutropenia, and 1 case of thrombocytopenia. However, cases of OXC-induced side effects are possibly underestimated.[2,3)]

In the current issue of the *Korean Journal of Pediatrics*, Jung and Yoo[10)] evaluated the hematologic profile of 184 patients treated with OXC. Hematologic side effects developed in 10 of the 184 patients (5.4%) who were prescribed OXC between 2001 and 2018. Although the study was limited by its a single-center design, retrospective nature, and small number of cases, the 5.4% frequency of hematologic side effects of OXC indicates that they are not rare; in fact, this rate is actually higher than previous data suggested. These data provide the basis for the need for careful follow-up of patients treated with OXC.

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Conflicts of interest

No potential conflicts of interest relevant to this article was reported.

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