

Medicines – allergic reactions to antiepileptic drugs

Around 1% of the global human population – ca. 65 million - suffer from epilepsy – a chronic neurological disease with one of the most prominent symptoms being so called epileptic seizures. With a range of antiepileptic drugs (AEDs) available, it is possible to mitigate the seizures and the majority of patients (70%) display a good control over epilepsy. However, there are patients in whom AEDs cause unwanted, and often dangerous, adverse side-effects. These include, among other things, dizziness, gastric problems, depression, impaired cognition and allergic skin reactions, which will be discussed in more detail here.

Adverse skin reaction are the direct consequence of hypersensitivity to AEDs. They can range from mild skin rashes and changes in skin pigmentation to extremely severe and potentially lethal conditions (such as Stevens-Johnson syndrome, DRESS – drug rash with eosinophilia and systemic symptoms or TEN – toxic epidermal necrolysis). The morbidity rate in patients who develop these severe symptoms is estimated to be about 10%.

The reasons for allergic reaction have not yet been determined unequivocally. Currently, there are several hypotheses about the source of hypersensitivity of epileptic patients. According to some studies, due to a varied mechanism of action, certain AEDs are more likely to induce severe allergic reactions (e.g. SJS/TEN) than others. Another identified cause can be related to genetics –it has been discovered that the presence of the antigen (HLA)-B*1502 in various Asian populations (particularly South-Eastern Asian, e.g. Han Chinese) is linked with hypersensitivity. Similar associations have also been found between the severe skin reactions and the occurrence of the antigen (HLA) –A*31:01 in Japanese and European populations. Other theories assumed that certain disorders (SJS/ TEN) could be reactions of the immunological system. Among other factors that may trigger negative allergic reactions are patients' gender, hormones, drug dosage schedule and administering two or more types of drugs simultaneously (co-medication). There have been reports that a negative reaction to one AED may trigger hypersensitivity to a different one, previously tolerated. Age can be yet another risk factor for allergic reactions, due to age-related differences in drug metabolism – certain forms of hypersensitivity are more likely to affect children than adults. Also, drug dosage schedule and starting dose can play a role here– it has been found that higher starting doses of some AEDs are more likely to increase the risk of adverse skin reactions.

As mentioned earlier, the allergic reactions can vary in intensity, from quite benign and harmless, like rashes or pigmentation change, to potentially deadly, with failure of internal organs and severe skin damage. Such hypersensitivity reactions are difficult to diagnose as they induce a broad range of clinical manifestations. In addition, different AEDs cause different reactions.

The first step to take when such allergic symptoms occur is the immediate cessation of therapy that employs the specific AED. It is recommended that patients with hypersensitivity to one type of AEDs (e.g. aromatic) switch to the drugs with a different mechanism of action. If no alternative to

the drug is available, then it is suggested to perform desensitization using antihistamines or steroids. However, it must be stressed that desensitization is usually efficient in benign cases. When serious allergic conditions are developed, clinicians recommend to treat such patients in hospital burn units to ensure proper care.

Modern AEDs provide a good control over epileptic seizures and enable normal functioning of patients. However, certain percentage of them may experience a broad range of negative reactions that can seriously impact their health condition and quality of life.

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