Risk factor of Lamotrigine related severe cutaneous adverse reaction in Taiwan

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Background

Lamotrigine has been associated with severe cutaneous adverse reactions (SCARs). Around 90 cases with SCARs which included 84 cases of SJS/TEN were reported between 2000~2014 in Taiwan. Most of them happened within 30 days from initial dose. Recent data indicated that rapid dosage titration or the concomitant use of enzyme inhibitors, especially valproic acid, are predisposing risk factors. These serious events have been continuously reported to the Taiwan National Adverse Drug Reaction (ADR) Reporting System.

Objectives

To evaluate the prescription pattern of lamotrigine and its association between SCARs in Taiwan.

Methods

All Lamotrigine prescriptions were retrieved from a longitudinal cohort dataset with 1,000,000 individuals randomly sampled from the National Health Insurance Research Database (NHIRD) between January 1, 2003 and December 31, 2011 to describe usage patterns.

Logistic regression model was used to identify risk factors of SCAR. Interruption period of two prescriptions >14days would be recruited again as a new treatment episode. SCAR cases were defined as inpatient claims using ICD-9-CM diagnostic code 695.1, 695.11-15, 695.19 or 693.0.

Results

119,540 prescriptions were identified and only 11% of them were new treatment episodes which would be analyzed. There was an increasing trend of lamotrigine usage during the observational period and 80% of them were prescribed in medical centers and metropolitan hospitals.

The does of 50% first prescriptions was three times higher than recommended which based on their concurrent medication such as valproic acid. Although the guideline recommended dose titration within two weeks of initial prescription, we found 70% of new treatment episodes were with prescription days more than 14 days(mode: 28-30 days).

In our regression analysis, concurrent use of enzyme inhibitors (i.e. valproic acid) was associated with higher risk of SCAR (OR: 2.86, 95%CI: 1.304-6.282). Shorter prescription period and experienced lamotrigine user were associated with lower risk (OR:0.961, 95%CI: 0.922-1.002 and OR: 0.397, 95%CI: 0.202-0.780, respectively).

Conclusion

Most of first prescription written were exceed the recommend dosage documented and concomitant administer of lamotrigine with enzyme inhibitor was significantly associated with SCAR.

Reference

1. Choi, H. and M.J. Morrell, Review of lamotrigine and its clinical applications in epilepsy. Expert Opin Pharmacother, 2003. 4(2): p. 243-51.
2. Guberman, A.H., et al., Lamotrigine-associated rash: risk/benefit considerations in adults and children. Epilepsia, 1999. 40(7): p. 985-91.
3. National health insurance research database (Taiwan). http://nhird.nhri.org.tw/en/Data_Subsets.html