INTERACTION BETWEEN PARACETAMOL AND LAMOTRIGINE: NEW INSIGHTS FROM THE FDA ADVERSE EVENT REPORTING SYSTEM (FAERS) DATABASE

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Introduction: Lamotrigine is considered a first line treatment for epilepsy and bipolar disorder, because of its favourable tolerability profile. Paracetamol is often co-administered with the anticonvulsant drug for its analgesic and antipyretic proprieties. Only two studies reported that the administration of paracetamol decrease the t½ and increase the clearance of a single dose of lamotrigine, suggesting a possible drug-drug interaction (DDI).

Material and methods: firstly, we performed an analysis of the FDA Adverse Event Reporting System (FAERS) database recovering 128,822ADR reports involving both drugs; to reduce risk of bias we excluded all reports that implied an association of lamotrigine and paracetamol with any other drug. Secondarily we executed the analysis of causality assessment, using the DIPS Algorithm (Drug Interaction Probability Scale).

Results: We identified 45cases in which lamotrigine and acetaminophen were the only suspected and/or concomitant drugs reported; five duplicates were excluded. Of the 40 ADR remaining, 12cases (30%) reported an ADRs related to DDIs between the two drugs (Table 1); these were "seizure" (8), "drug interaction" (5), "generalised tonic-clonic seizure" (3), "drug level decreased" (3) and "tremor" (1). Four reports included the time to onset of the reaction and two of them reported a positive de-challenge: their causality was classified as "possible", using the DIPS Algorithm. All reports were categorised as serious and four patients required hospitalisation. Five reports were of paediatric patients.

Discussion and conclusion: Physicians should take into account this DDI, although rare, in order to administer lamotrigine with caution, especially to fragile populations. Since the metabolic inductive action of paracetamol of the glucuronidation pathways is most likely the cause of the DDI described here, it may have a broader significance also when paracetamol is administered simultaneously to other drugs metabolised through the same enzymatic pathway; this aspect also need to be investigated further. Valuable information might be provided by therapeutic drug monitoring of both drug levels, as it may allow better evaluation of the connection of pharmacokinetic variations with the occurrence of ADR.