Switching the pharmaceutical dosage form of extended-release valproate is associated with therapeutic modification of antiepileptic therapy

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Katrin Schuessel, PhD[1], Stephanie von Klot, PhD[2], Martin Schulz, PhD[1,3].

[1]DAPI - German Institute for Drug Use Evaluation, 65760 Eschborn, Germany
[2]Helmholtz Zentrum München, Institute of Epidemiology II, 85764 Neuherberg, Germany
[3]Drug Commission of German Pharmacists (AMK), 10117 Berlin, Germany.

Background:

Product switching of extended release (ER) antiepileptic drugs (AED) is discussed controversially since evidence from bioequivalence studies may not translate into clinical practice.

Objectives:

To explore whether two different aspects of product switching - a change of pharmaceutical manufacturer or a change of the pharmaceutical dosage form - in patients treated with ER valproic acid/valproate (VPA) is associated with therapeutic modification of AED therapy, i.e. prescribing of an additional AED as a proxy for treatment failure.

Methods:

A cohort study was performed utilizing the DAPI database of ambulatory drug claims from more than 80% of German community pharmacies. Patients initiating VPA therapy with ER dosage forms between 2003 and 2006 and filling a second prescription (index) within 180 days were included. Time periods between subsequent VPA prescriptions were classified as product switch if a different ER VPA product was dispensed, considering information on a different manufacturer as well as the type of pharmaceutical dosage form (monolithic vs multi-unit). Patients were followed from the index date until the occurrence of the event (prescription of additional AED) or censoring (due to interruption or discontinuation of ER VPA treatment, or 12/31/2009, the latest). Hazard ratios (HR) for the event were estimated using proportional hazards regression modelling with time-varying exposure.

Results:

78,427 medication profiles were identified of which 15,065 (19.2 %) experienced the event. Switching the type of the dosage form was associated with an increased hazard for the event compared to no switch (switch from monolithic to multi-unit dosage forms: HR = 1.43 [99% CI 1.16-1.77]; switch from multi-unit to monolithic: HR = 1.36 [1.10-1.67]), whereas switching between different pharmaceutical manufacturers was not (HR = 1.01 [0.92-1.12]).

Conclusions:

Switching of ER VPA products is associated with an increased risk of AED regimen modification, and the type of pharmaceutical dosage form is probably more influential than differences between pharmaceutical manufacturers.

Disclosure:

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