Annals of Clinical Psychiatry, 18[4]:273–274, 2006

ISSN: 1040-1237 print / 1547-3325 online
DOI: 10.1080/10401230600948548

informa
healthcare

Letter to the Editor

Efficacy and Tolerability of Divalproex Extended Release in Psychiatric Patients

RICHARD S. JACKSON, MD
Assistant Clinical Professor, University of Michigan, Ann Arbor, MI, USA
Wayne State University School of Medicine, Detroit, MI, USA

SANJEEV VENKATARAMAN, MD
Bloomfield Hills, MI, USA

RICHARD B. ATKINS, MD
Commerce, MI, USA

MARK OWENS, DO
Brooklyn, NY, USA

TO THE EDITOR:

Non-compliance with pharmacological treatment is a common problem in bipolar patients and a major risk factor for recurrence of acute bipolar symptoms, which can necessitate acute psychiatric hospitalization (1,2). Simplification of medication regimens with drugs requiring only once-a-day administration may lead to improved patient compliance and better overall treatment outcomes.

We conducted an open-label, prospective investigation of 52 psychiatric patients with bipolar disorder or bipolar type schizoaffective disorder, who were previously stabilized on divalproex delayed release (DR; requires administration on a two-to-three times a day basis) and then switched at study entry to an identical daily dose of divalproex extended release (ER) administered once daily for up to 24 weeks. The average age of the study population was 47.2 years (S.D. = 10.2 years, range = 20 to 66 years). The mean divalproex daily dosage was 1191 mg (range = 500–2000 mg) at baseline and study endpoint (after up to 24 weeks of divalproex ER therapy).

As compared to baseline (just before discontinuation of divalproex DR), mean HAM-D 21 ($P = 0.0025$, Wilcox signed-rank test) and mean YMRS ($P = 0.0385$, Wilcox signed-rank test) were lower at study endpoint. Repeated measures analysis confirmed a general decreasing trend over time in HAM-D 21 ($F = 12.09$, degrees of freedom = 1,212, $P = 0.0006$) and YMRS ($F = 4.54$, degrees of freedom = 1,212, $P = 0.0006$).

There were no statistically significant changes from baseline to study endpoint in any of laboratory indices. Mean serum valproate level at baseline was 66 µg/ml and ranged from 56 to 82 µg/ml throughout the study, with no statistically significant change from baseline to study endpoint.

Divalproex ER was well tolerated, with patients experiencing a decrease in overall adverse events as compared to when they were previously taking divalproex DR. Adverse events noted during therapy with divalproex resolved in 7

The data summarized in this paper were presented during a poster session at the 2004 Annual Meeting of the American Psychiatric Association, May 2004, New York, NY.

Address correspondence to: Richard S. Jackson, M.D., Assistant Clinical Professor, University of Michigan, Wayne State University, E 4111 Andiver Rd., Suite 220, Bloomfield Hills, MI 48302, USA. E-mail: richardjackson2000@yahoo.com

patients after the switch was made to the ER formulation. Only one patient reported an adverse event (dyspepsia) while taking the ER formulation that was not present while taking the DR formulation. No patients dropped out due to adverse events. Although our sample size was small, the improvement in adverse events with divalproex ER may be explained by its improved pharmacokinetic profile as compared to the DR formulation. With the ER formulation, the peak serum concentration is lower, which likely leads to an improved adverse event profile, and the trough serum concentration is higher with less fluctuation in peak-to-trough levels, which may explain the improved mood stability (3). Our safety and tolerability results are consistent with those in other studies of divalproex ER (4,5).

In summary, psychiatric patients previously treated with multiple daily doses of divalproex DR maintained clinical stability and experienced fewer adverse events after an immediate switch to once daily dosing of divalproex ER.

REFERENCES

1. Keck PE Jr., McElroy SL, Strakowski SM, Stanton SP, Kizer DL, Balistreri TM, Bennett JA, Tugrul KC, West SA: Factors associated with pharmacologic noncompliance in patients with mania. *J Clin Psychiatry* 1996; 57:292–297
2. Colom F, Vieta E, Martinez-Aran A, Reinares M, Benabarre A, Gasto C: Clinical factors associated with treatment noncompliance in euthymic bipolar patients. *J Clin Psychiatry* 2000; 61:549–555
3. Depakote ER Product Information. Abbott Laboratories, North Chicago, IL, c. 2000.
4. Horne RL, Cunanan C: Safety and efficacy of switching psychiatric patients from a delayed-release to an extended-release formulation of divalproex sodium. *J Clin Psychopharmacol* 2003; 23:176–181
5. Thibault M, Blume WT, Saint-Hilaire JM, Zakhari R, Sommerville KW: Divalproex extended-release versus the original divalproex tablet: Results of a randomized, crossover study of well-controlled epileptic patients with primary generalized seizures. *Epilepsy Res* 2002; 50:243–249