



### Levetiracetam davis pdf

#### GABA<sub>A</sub> receptor target of tetramethylenedisulfotetramine

ing Zhao<sup>6,1</sup>, Sung Hee Hwang<sup>b</sup>, Bruce A. Buchholz<sup>6,2</sup>, Timothy S. Carpenter<sup>d</sup>, Felice Light D. Hammock<sup>b,2</sup>, and John E. Casida<sup>6,2</sup>

#### Contributed by John E. Casida, April 24, 2014 (sent for review March 22, 2014).

ise of the highly toxic and easily prepared rodenticide tetrame hydenedisulfotetramine (TETS) was banned after thousands of cidental or intentional human poisonings, but it is of continued by diazepan, bathierates, allog encern as a chemical threat agent. TETS is a noncompetitive dimencation. The programme of the set of the content of the GRA towa A set of the content of the GRA towa A set of the content of the GRA towa A set of the set by diazepam, barbiturates, allopregnanolone, and sodium 2, dimercanto-1, propagesulfonate (NaDMPS) some of which a GABAAR = rectly established for lack of a suitable (Fig. 1). nding with a potency in rat brain GABAAR consistent with

, 32). However, it does not inhibit h t β<sub>2</sub> homopentamer assayed with [<sup>3</sup>H]E are based on the use of [15S]TBPS and [3H]EBOB to assay th action of TETS. Direct observation of the TETS binding site requires the use of TETS as the radioligand. Radioligand binding studies for neu-

to date for TETS. 114 CITETS reported here has a specific a

igent because of its high convulsant toxicity, ease of syn and availability even though it is banned as a rodenticide.

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tetramine) which was then developed

ed more than 80 v ago (1-3). Structure TS is available by accelerator mass spectrom

as reported here. v toxic to mammals with an i.p. LD<sub>30</sub> of 0.11-0.22 , leading to its use as a rodenticide until it in the early 1990s (2, 8, 9). However, it is a and other countries. The estimated lethal dose This paper contains supporting 1075/pnas.14073791115-/DCSup 

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## **CLINICAL PRACTICE AND PROCEDURES**







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Epilepsy Research 1999; 37: 81-87.. Thirteen patients continued on LEV monotherapy for at least 6 months. LEV monotherapy can be effective and well tolerated in this group of patients. Four patients (30.7%) had more than a 50% seizure reduction of seizures. LEV has a favorable pharmacokinetic profile that includes minimal protein binding, lack of hepatic metabolism, and twice a day dosing. 1987; 21: 350View in Article DOI: 03)00070-0 © 2003 BEA Trading Ltd. 1994; 35: 381-390View in Article Scopus (132) PubMed Crossref Google ScholarBrodie, M. A prospective, large, double blind study is needed to confirm this finding. Reflections on the treatment of seizures in the elderly population. Neurology. The remaining six chronic patients had an identifiable cause to their seizures: two secondary to head trauma, two secondary to head trauma, two secondary to strokes, and two secondary to head trauma two secondary to strokes. undertaken in this age group utilising old and new AEDs, 7.Brodie, M. 2000; 41: 1276-1283View in Article Scopus (398) PubMed Crossref Google ScholarDrug use in an ambulatory elderly population: a five-year update.DICP. 1995; 21: 149-157View in Article Scopus (46) PubMed Crossref Google ScholarImpact of valproate and phyentoin on cognitive function in elderly patients: results of a single-blind randomized comparative study. Epilepsia. 1998; 51: S28-S33View in Article PubMed Crossref Google ScholarLevetiracetam for partial seizures: results of a double blind randomized clinical trial. Neurology. 2000; 41: 1179-1186View in Article Scopus (445) PubMed Crossref Google ScholarA systemic review of the safety profiles of Levetiracetam: a new antiepileptic drug. Epilepsy Research. We compared baseline seizure counts at 6 months of follow-up after LEV was started and maintained as therapy. Four patients who began LEV as a first line therapy became seizure free, whereas the remaining four patients who converted to LEV after they failed their previous AEDs became seizure free. Previous AEDs became seizure free. Previous AEDs became seizure free. M.J. Ferrendelli J.A. French J.A. et al.Final results from the K.E.E.P.E.R. trial: a phase 1V community-based clinical trial investigating LEV as add-on therapy in partial onset seizures.. Published by Elsevier Inc. These features and others make it ideal for use as monotherapy in elderly patients. Several factors can influence the pharmacokinetics and pharmacodynamics of AEDs in the elderly. Eight patients were diagnosed with epilepsy after the age of 60. Five patients began LEV as first line therapy. Eight patients were diagnosed with epilepsy after the age of 60. Five patients were converted to LEV monotherapy after they failed their initial trials of AEDs, which included Dilantin, Tegretol, Depakote, and Lamictal (mean 1.6). Of the eight newly diagnosed patients, two had AD and one patient had stroke as a cause of epilepsy. It is estimated that the average number of medications per patient 11. Hale W.E. May F.F. Marks R.G. Stewart R.B. Drug use in an ambulatory elderly population: a five-year update.. A prospective, larger, double blind monotherapy study is needed to confirm this finding elderlymonotherapylevetiracetamAdvanced age patients >60 years of age may have an increased sensitivity to the effects of AEDs, due to age-dependent changes in pharmacokinetics and pharmacodynamics. and the UK Lamotrigine Elderly Study Group. Only one patients had no significant change in seizure frequency after started on LEV. Adverse events (AEs) while on LEV were also noted at each clinic visit. Of particular concern is the lowered serum albumin that frequently occurs in older patients. Two of these patients had liver disease and consequently wished to avoid AEDs that required hepatic metabolism. Falter U. Patients began LEV either as first line therapy (n=5) or were converted to LEV monotherapy (n=9) after failing prior antiepileptic medications (AEDs). The total dosages used to control seizures for all patients were 500-3000 mg/day (mean 1839.2 mg/day). et al. Multicenter double-blind, randomized, placebo-controlled trial of Levetiracetam as add-on therapy in patients with refractory partial seizures. Crossref PubMed Scopus (445) Google Scholar. One patient with newly diagnosed epilepsy (less than 2 years duration) had no significant change in her seizure frequency. Elsevier user license | How you can reuse Permitted For non-commercial purposes: Read, print & download Text & data mine Translate the article in other works Redistribute or republish the final article Sell or re-use for commercial purposes Elsevier's open access license policy Access this article on ScienceDirect These findings support the current belief that most older patients will remain seizure free on AED monotherapy. It is very well tolerated, with minimum reports of minor side effects. All patients were required to have liver function tests, complete blood counts at baseline prior to start LEV, and at 6 months follow-up. Efficacy and tolerability of Levetiracetam 3000 mg in patients with refractory partial seizures: a multicenter, double-blind, responder-selected study evaluating monotherapy. Crossref PubMed Scopus (398) Google Scholar. It has been noted that the elderly have generally increased sensitivity to medications; a factor that may account for the increased incidence of poor tolerability and poor compliance. 2002; 3: 471-474View in Article Scopus (16) PubMed Crossref Google ScholarEfficacy and tolerability of Levetiracetam 3000 mg in patients with refractory partial seizures: a multicenter, double-blind, responder-selected study evaluating monotherapy. Epilepsia. Seizure frequency was determined using a seizure diary completed by each patient or their caregivers, which is standard practice in our clinic. The duration of epilepsy ranged from 1 to 39 years (mean 12.6 years, median 2.5). To our knowledge, this current report is the first one studying the efficacy and tolerability of LEV as monotherapy in this patient population. All patients had their LEV dose titrated up to 3000 mg/day or up to seizure freedom. However, our preliminary data suggests that LEV may be an acceptable choice as monotherapy for the elderly. Of the new AEDs, LEV is believed to be free of drug-drug interactions and minimally protein bound. One patient was lost to follow-up. The remaining three patients chose to start LEV because of its favorable pharmacokinetic and side-effect profile. No blood abnormalities were noted and no other major AEs were reported. This study suggests that LEV monotherapy can be effective in newly diagnosed elderly epilepsy patients >60 years of age who were AED-naive, as well as in elderly patients with chronic epilepsy. Four patients who began LEV as monotherapy became seizure free, whereas the remaining four patients who began LEV as monotherapy became seizure free. Two patients (15%) had more than a 50% but less than 75% seizure reduction and two patients (15%) had more than a 75% but less than 100% reduction of seizures. In that study, more than half of the patients were taking 1000 mg/day. In addition, many of these patients take other medication for various medical conditions that require prolonged treatment. 2000; 35: 236-242View in Article Scopus (517) Crossref Google ScholarMulticenter double-blind, randomized, placebocontrolled trial of Levetiracetam as add-on therapy in patients with refractory partial seizures. Epilepsia. Multi-center, double blind comparison between lamotrigine and carbamazepine in elderly patients with newly diagnosed epilepsy. Inadequate seizure control in this group could suggest poor compliance or progressive disease. Information on efficacy and tolerability of established, as well as new AEDs, is scarce in the elderly population. 2001; 47: 77-90Anticonvulsant therapy in the elderly—a need for placebo-controlled trials. Epilepsy Research. This information was kept in a computerised data system that was maintained up-to-date. We identified 14 patients, ages 62–92 years, mean (66 years) with a history of partial seizures with and without secondarily generalisation. This suggests that LEV may be an ideal choice for this study and the short-term follow-up, along with lack of randomisation may not allow us to make firm

conclusions. Characteristics and demographics of our group of patients are summarised in Table 1.Table 1.Demographics and characteristics of the group.One patient reported being dizzy within days after starting LEV but was able to continue on LEV. We retrospectively identified 14 elderly patients with a history of partial seizures who received level incentified 14 elderly patients are summarised in Table 1.Table 1.Demographics and characteristics of the group.One patient reported being dizzy within days after starting LEV but was able to continue on LEV. We retrospectively identified 14 elderly patients with a history of partial seizures who received level incentified on the patient is an incentified to a lower degree of drug binding to plasma proteins and decreased metabolic and renal drug clearance. Levetiracetam (LEV) has been approved as adjunctive treatment for adults with partial onset seizures, 3. Shorvon S.D. Lowenthal A. Previous work at this center, as well as the work of others have demonstrated that LEV can be effective as monotherapy in newly diagnosed adult patients as well as in patients with difficult to control seizures, 10.Ben-Menachem E. 2002; 43 : 197View in Article Levetiracetam monotherapy for adults with localization-related epilepsy. Epilepsy & Behavior. Of the eight patients with newly diagnosed epilepsy, six patients became seizure free after at least 6 months of follow-up, and one patient was lost to follow-up. Janz D. We wished to evaluate our experience with LEV as monotherapy in this group of patients to examine its efficacy and tolerability. We retrospectively reviewed the charts of all of our elderly patients aged 60 and above with a confirmed diagnosis of epilepsy who had two unprovoked seizures. Of these, 14 patients were tried on LEV either as first line therapy or were converted to LEV monotherapy after failing their prior antiepileptic medications (AEDs). We reviewed demographic data, diagnostic evaluation for epilepsy, seizure types, and seizure frequency prior to and follo

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