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Literature search results

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Search details

Effect on cognitive and neuropsychological functioning on adult patients with epilepsy, using the drug topiramate. Comparison with either no anti epileptic drugs(AEDs), pre AEDs and/or compared to any other AEDs eg. Valproate, gabapentin, lamotrigine.

Resources searched

NHS Evidence; TRIP Database; Cochrane Library; AMED; BNI; CINAHL; EMBASE; HMIC; Health Business Elite; MEDLINE; PsychINFO; Google Scholar; Google Advanced Search

Database search terms:

Evidence search string(s):

Google search string(s): Epilepsy AND Topiramate AND effect on cognitive and neuropsychological functioning

Summary

There is a lot of information about the drug, Topiramate in relation to epilepsy and cognitive functioning. When looking for comparisons with other named drugs – it’s a difficult task to isolate the most appropriate/useful papers.

I have included the first page of Google searches – just to show what is available from there. There are many more articles listed within the first 50 items which look as though they might be useful.
Evidence-based reviews

Jette N, Hemming K, Hutton JL, Marson AG
Topiramate add-on for drug-resistant partial epilepsy
Cochrane Review, 2009
This is really worth a look at – plenty of references, some of which are included in this document.

Published research – Databases

1. Use of generic medicines in the treatment of epilepsy using topiramate as an example.
Citation: Neuroscience and Behavioral Physiology, July 2012, vol./is. 42/6(550-555), 0097-0549;1573-899X (Jul 2012)
Author(s): Rudakova, I. G; Kotov, A. S; Belova, Yu. A
Abstract: Quantitative analysis of the causes of termination of pharmaceutical remission lasting more than one year was undertaken in 220 adult patients with epilepsy. The most frequent cause of loss of seizure control was switching from an original proprietary medicine to a generic analog (60.4%); a total of 28.2% of patients had been switched to generic topiramate. Comparative analysis of the results of switching of 160 patients form the original form of topiramate (Topamax) to its generics was performed. The control group consisted of 52 patients continuing the original formulation. Switching led to loss of remission in 75.6% of patients, with status epilepticus in 3.75% and emergency care or hospitalization were required in 51.9% of patients. Switching back to the original formulation was performed in 86.2% of patients, after which the initial doses of Topamax were increased in 58.0%, 60.0% of patients transferred from monotherapy to polytherapy, and baseline levels of seizure control were achieved in only 32.9% of patients.
(PsycINFO Database Record (c) 2012 APA, all rights reserved) (journal abstract)
Publication Type: Journal; Peer Reviewed Journal
Source: PsycINFO
Full Text: Available from ProQuest in Neuroscience and Behavioral Physiology;

Citation: Epilepsy & Behavior, January 2012, vol./is. 23/1(36-40), 1525-5050 (Jan 2012)
Author(s): Yu, Pei-min; Zhu, Guo-xing; Ding, Ding; Xu, Lan; Zhao, Ting; Tang, Xing-hua; Shi, Yun-bo; Hong, Zhen
Abstract: Objective: The goal of this study was to survey a group of epileptologists in China regarding the treatment of adult epilepsy. Methods: A questionnaire on treatment of adult epilepsy was sent to a group of opinion leaders in the field of epilepsy. Results: For initial monotherapy for idiopathic generalized epilepsy (IGE), valproate was rated as the treatment of choice. In symptomatic localization-related epilepsy (SLRE)/simple partial seizures and SLRE/complex partial seizures, carbamazepine and oxcarbazepine were the respective treatments of choice, whereas in SLRE/secondarily generalized tonic-clonic seizures, carbamazepine, lamotrigine, and oxcarbazepine were treatments of choice. For women who were pregnant or trying to conceive, lamotrigine was the treatment of choice for both IGE and SLRE. In people with epilepsy who were HBsAg positive, whether liver function was normal or not, topiramate and levetiracetam were treatments of choice for IGE. Valproate and levetiracetam were treatments of choice for seizures in the emergency department. Conclusion: A high level of consensus was reached on most treatments of choice and first-line treatments for patients with epilepsy, which were in accordance with published US expert opinion. (PsycINFO Database Record (c) 2012 APA, all rights reserved) (journal abstract)
Publication Type: Journal; Peer Reviewed Journal
Source: PsycINFO

3. Patient-reported cognitive side effects of antiepileptic drugs: Predictors and comparison of all commonly used antiepileptic drugs.
Citation: Epilepsy & Behavior, January 2009, vol./is. 14/1(202-209), 1525-5050 (Jan 2009)
Author(s): Arif, Hiba; Buchsbaum, Richard; Weintraub, David; Pierro, Joanna; Resor,
Abstract: Subjective cognitive side effects (CSEs) are common in patients taking antiepileptic drugs (AEDs). The objective of this study was to predict which patients are at risk for CSEs, and compare the CSE profiles of all commonly used AEDs. In this nonrandomized retrospective study, medical records of 1694 adult outpatients with epilepsy seen at our center over a 5-year period who had taken one or more AEDs were examined. Non-AED predictors of CSEs were investigated, and rates of AED-related CSEs were compared in 1189 patients (546 on monotherapy) newly started on an AED at our center. The average rate of AED-related intolerable CSEs (leading to dosage change or discontinuation) was 12.8%. On multivariate analysis, no significant non-AED predictors of CSEs were found. Significantly more intolerable CSEs were attributed to topiramate (21.5% of 130 patients) than to most other AEDs, including carbamazepine (9.9%), gabapentin (7.3%), levetiracetam (10.4%), lamotrigine (8.9%), oxcarbazepine (11.6%), and valproate (8.3%). CSE rates with zonisamide (14.9%) were significantly higher than those for gabapentin and lamotrigine. After exclusion of CSEs during the first 8 weeks of therapy, rates of CSEs were lower, but relative differences remained unchanged. In monotherapy, significantly more intolerable CSEs occurred with topiramate (11.1% of 18 patients) than with carbamazepine or valproate, and both phenytoin and zonisamide were associated with more CSEs than valproate. From this study, it can be concluded that intolerable patient-reported CSEs are most common with topiramate, followed by zonisamide, phenytoin, and oxcarbazepine. They are least likely to be reported with gabapentin, valproate, lamotrigine, carbamazepine, and levetiracetam. (PsycINFO Database Record (c) 2012 APA, all rights reserved) (journal abstract)

Publication Type: Journal; Peer Reviewed Journal
Source: PsycINFO

Citation: Epilepsy & Behavior, November 2010, vol./is. 19/3(332-342), 1525-5050 (Nov 2010)
Author(s): Villanueva, V; Sanchez-Alvarez, J. C; Pena, P; Salas-Puig, J; Caballero-Martinez, F; Gil-Nagel, A
Abstract: Objective: The goals of this study were to explore the diverse criteria surrounding indications for antiepileptic therapy and to establish a consensus on drug selection for initial monotherapy in adult patients with epilepsy. Methods: The study was performed using the modified Delphi method, which aims to achieve professional consensus by means of a series of questionnaires. Three different groups of items were evaluated: the beginning of antiepileptic treatment, the drug selected for initial monotherapy with respect to the type of epilepsy, and the drug selected for initial monotherapy with respect to comorbidity. Results: Sixty experts completed two rounds of a questionnaire. In the first round, consensus was reached on 135 of the 194 questions analyzed. After the second round, consensus was reached on 148 items. The main findings of the survey revealed a consensus on beginning treatment after the first seizure when the EEG showed abnormalities such as generalized spike-wave discharges, when MRI demonstrated an epileptogenic brain lesion, and in elderly patients. Regarding to the antiepileptic drug selected for initial monotherapy with respect to type of epilepsy, levetiracetam and lamotrigine were recommended for generalized tonic-clonic seizures regardless of sex or age; levetiracetam was recommended for myoclonic epilepsy regardless of sex; valproic acid, ethosuximide, levetiracetam, and lamotrigine were chosen for absence epilepsy; and carbamazepine, levetiracetam, lamotrigine, and oxcarbazepine were recommended for partial epilepsy regardless of age or sex. Finally, in the evaluation of drug selection with respect to comorbidity, first-generation drugs were less recommended than second-generation drugs, which were clearly preferable. The drugs on which there was a greater consensus were levetiracetam, lamotrigine, valproic acid, and topiramate. Conclusions: There is a tendency to begin treatment after the first seizure, depending on the results of additional testing. In general, first-generation drugs are less recommended for different types of epilepsy, especially in the presence of a comorbid condition. However, the authors are conveying perceptions and opinions, the effect of which on treatment outcomes has not been evaluated. (PsycINFO Database Record (c) 2012 APA, all rights reserved) (journal abstract)
Publication Type: Journal; Peer Reviewed Journal
Source: PsycINFO

5. Effects of lamotrigine and topiramate on hippocampal neurogenesis in experimental temporal-lobe epilepsy.
Abstract: Lamotrigine (LTG) and topiramate (TPM), two of the most commonly used new-generation antiepileptic drugs (AEDs), have been shown to produce no adverse and impaired cognitive effects in patients with epilepsy, respectively. As seizure-induced neurogenesis might contribute to cognitive deficits that are associated with status epilepticus (SE), we examined whether these two drugs produce differential effects on seizure-induced neurogenesis in the hippocampus of adult rats. Lithium pilocarpine model was used to mimic human temporal-lobe epilepsy. Five hours after SE, LTG and TPM were administered intragastrically twice daily throughout the entire length of the experiment with total daily dose of 20 and 80 mg/kg, respectively. The hippocampal neurogenesis was examined using 5-bromodeoxyuridine and doublecortin immunohistochemistry. Both LTG and TPM treatments significantly inhibited seizure-induced proliferation of neural progenitors in the hippocampus, but did not affect the neuronal differentiation of newborn cells. Long-term treatment with both AEDs decreased the number of spontaneous recurrent seizures after SE and alleviated chronic seizure-induced neuronal injury in the dentate hilus. Eventually, TPM significantly increased the number of newborn neurons in the dentate granular cell layer after seizures likely by promoting the survival of newborn neurons. In contrast, LTG treatment significantly reduced the number of ectopic hilar newborn neurons after seizures. Neither of them prevented the formation of hilar basal dendrites of newborn neurons in the epileptic hippocampus. These results indicate that TPM but not LTG promotes aberrant neuron regeneration in the hippocampus after SE, which might be partially related to their differential effects on cognitive function. (PsycINFO Database Record (c) 2012 APA, all rights reserved) (journal abstract)
preferred treatment strategy. Valproate was first choice in idiopathic generalized epilepsy. Carbamazepine and oxcarbazepine were first choice in focal epilepsy with partial seizures. Valproate was also first choice in focal epilepsy with secondarily generalized seizures. New antiepileptic drugs were recommended in second line. However, in special treatment situations, they were considered first-line, e.g. lamotrigine in case of women in childbearing age. In comparison with 2003, there was a trend of using earlier the new antiepileptic drugs. Conclusions: In end 2006, carbamazepine, valproate and oxcarbazepine were considered to be first choice drugs, whereas other newer drugs, like lamotrigine, levetiracetam and topiramate were predominantly prescribed in second line. (PsycINFO Database Record (c) 2012 APA, all rights reserved) (journal abstract)

Publication Type: Journal; Peer Reviewed Journal
Source: PsycINFO
Full Text: Available from EBSCOhost in Acta Neurologica Scandinavica

8. Spotlight on topiramate in epilepsy.
Citation: CNS Drugs, February 2008, vol./is. 22/2(171-174), 1172-7047;1179-1934 (Feb 2008)
Author(s): Lyseng-Williamson, Katherine A; Yang, Lily P. H
Abstract: Topiramate (Topamax) is a structurally novel broad-spectrum antiepileptic drug (AED) with established efficacy as monotherapy or adjunctive therapy in the treatment of adult and paediatric patients with generalized tonic-clonic seizures, partial seizures with or without generalized seizures, and seizures associated with Lennox-Gastaut syndrome. The incidence and severity of many adverse events, including CNS-related events, may be reduced through the use of slow titration to effective and well tolerated dosages. It is associated with few clinically significant interactions with other drugs, is effective when used with other AEDs, is not associated with drug-induced weight gain and, at lower dosages, does not interfere with the effectiveness of oral contraceptives. Therefore, topiramate is a valuable option as monotherapy or adjunctive therapy in the treatment of epilepsy in adult and paediatric patients. (PsycINFO Database Record (c) 2012 APA, all rights reserved) (journal abstract)
Publication Type: Journal; Peer Reviewed Journal
Source: PsycINFO
Full Text: Available from EBSCOhost in CNS Drugs

9. Efficacy of topiramate (Topamax) in epileptic patients of different ages.
Citation: Neuroscience and Behavioral Physiology, July 2007, vol./is. 37/6(547-551), 0097-0549;1573-899X (Jul 2007)
Author(s): Voronkova, K. V; Pylaeva, O. A; Petrukhin, A. S
Abstract: The aim of the present work was to assess the efficacy and tolerance of topiramate (Topamax) in patients of different ages with different types of epilepsy. This agent was used as monotherapy and combined therapy in 114 patients (53 male, 61 female) of the following age groups: early childhood (16), preschool and school age (20), pubertal (16), young (23), adult (38), and elderly (1). Treatment produced complete clinical remission in 48% of patients and decreases in fit frequency by more than 50% in 44% of patients. In terms of remission, Topamax was more effective in adolescents, youths and adults than in younger children, and this pattern was also seen in the treatment of symptomatic epilepsy. Tolerance was good in patients of all groups, and cases of side effects (weight loss, irritability, allergic skin reactions, paresthesia) were occasional. (PsycINFO Database Record (c) 2012 APA, all rights reserved) (journal abstract)
Publication Type: Journal; Peer Reviewed Journal
Source: PsycINFO
Full Text: Available from ProQuest in Neuroscience and Behavioral Physiology;

10. Daytime Sleepiness in Epilepsy Patients Receiving Topiramate Monotherapy.
Citation: Epilepsia, April 2004, vol./is. 45/4(333-337), 0013-9580;1528-1167 (Apr 2004)
Author(s): Bonanni, Enrica; Galli, Renato; Maestri, Michelangelo; Pizzanelli, Chiara; Fabbrini, Monica; Manca, Maria Laura; Iudice, Alfonso; Murri, Luigi
Abstract: Purpose: Limited research has focused to date on objective neurophysiological evaluation of daytime sleepiness in patients treated with newer antiepileptic drugs (AEDs), especially when used as monotherapy. This study was aimed at assessing occurrence of daytime sleepiness in newly diagnosed, drug-naive patients with partial epilepsy receiving...
initial topiramate (TPM) monotherapy. Methods: Daytime vigilance was assessed in 14 consecutive, newly diagnosed and never medicated adult patients with focal epilepsy, receiving monotherapy with TPM. At baseline and 2 months after slowly titrated therapy with TPM, 200 mg/day, patients underwent the Multiple Sleep Latency Test (MSLT), visual simple and choice reaction times (VRT), and self-rated their own degree of sleepiness with the Epworth Sleepiness Scale. A group of 14 age- and gender-matched healthy volunteers served as controls. Results: At baseline, mean daytime sleep latencies on the MSLT were comparable in patients and in controls. Two months after TPM monotherapy, MSLT scores did not significantly change in patients as compared with pretreatment values. Accordingly, subjective daytime sleepiness and VRTs, which were comparable in controls and in untreated patients at baseline, did not change in patients after TPM monotherapy. Conclusions: Study results suggest that an initial short-course monotherapy with TPM, 200 mg/day, does not impair daytime vigilance in newly diagnosed adult patients with partial seizures. (PsycINFO Database Record (c) 2013 APA, all rights reserved) (journal abstract)

**Publication Type:** Journal; Peer Reviewed Journal  
**Source:** PsycINFO  
**Full Text:** Available from EBSCOhost in Epilepsia (Series 4)

11. Hemichorea-Hemiballismus May Respond to Topiramate.  
**Citation:** Clinical Neuropharmacology, May 2005, vol./is. 28/3(142-144), 0362-5664;1537-162X (May-Jun 2005)  
**Author(s):** Driver-Dunckley, Erika; Evidente, Virgilio Gerald H  
**Abstract:** Topiramate is a broad-spectrum anticonvulsant that is now widely used for adult and pediatric epilepsy. In a singular case, topiramate was recently reported to benefit vascular hemichorea-hemiballismus. The authors describe three cases of hemichorea-hemiballismus, one of vascular etiology and two of metabolic etiology, effectively treated with topiramate. (PsycINFO Database Record (c) 2012 APA, all rights reserved) (journal abstract)

**Publication Type:** Journal; Peer Reviewed Journal  
**Source:** PsycINFO

12. Topiramate-Induced Lithium Toxicity.  
**Citation:** Primary Psychiatry, November 2004, vol./is. 11/11(24-25), 1082-6319 (Nov 2004)  
**Author(s):** Ginsberg, David L  
**Abstract:** Topiramate is a sulfamate-substituted monosaccharide indicated for adjunctive treatment of adult partial-onset epilepsy. This article presents an overview of a report of topiramate-induced lithium toxicity. A 26-year-old woman with a 10-year history of bipolar disorder was transferred to the mood disorders service from a general hospital unit for further stabilization. Upon admission to the general hospital 1 week prior, she had been taking lithium 900 mg/day (serum lithium level of 0.82 mmol/L), valproate 2,000 mg/day (serum level not reported), and clonazepam as needed. Subsequently, topiramate 75 mg/day was added to her regimen. The following week, in a mixed state with a predominance of manic symptoms, she was transferred to the mood disorders service. The patient demonstrated symptoms and signs of lithium toxicity including worsened concentration, confusion, and lethargy. The increase in lithium levels following the introduction of topiramate, and the subsequent rise in lithium levels with increasing topiramate doses, suggests that topiramate may have reduced lithium elimination by the kidneys. Clinicians who prescribe topiramate in patients taking lithium should be aware of the potential of precipitating lithium toxicity via topiramate-induced reductions in lithium excretion. (PsycINFO Database Record (c) 2012 APA, all rights reserved)

**Publication Type:** Journal; Peer Reviewed Journal  
**Source:** PsycINFO

13. Topiramate-Induced Palmar Erythema.  
**Citation:** Primary Psychiatry, October 2004, vol./is. 11/10(26-27), 1082-6319 (Oct 2004)  
**Author(s):** Ginsberg, David L  
**Abstract:** Topiramate is a sulfamate-substituted monosaccharide indicated for adjunctive treatment of adult partialonset epilepsy. It blocks voltage-gated sodium channels, enhances y-aminobutyric acid (GABA) via its actions on the GABAA receptor, antagonizes the kainate a-amino-3-hydroxy-5-methylisoxazole- 4-propionic acid (AMPA) subtype of the glutamate receptor, and inhibits carbonic anhydrase. Due to its ability to suppress appetite and cause weight loss, it has increasingly gained widespread use among clinicians as a treatment for psychotropic-induced weight gain, binge-eating disorder, and even bulimia...
nervosa. Other research suggests that topiramate may also be effective for the treatment of posttraumatic stress disorder, obstructive sleep apnea, opiate withdrawal, kleptomania, alcohol dependence, and psoriasis. A recent report suggests that topiramate may also be an effective agent to promote healing of scars. (PsycINFO Database Record (c) 2012 APA, all rights reserved)

**Publication Type:** Journal; Peer Reviewed Journal  
**Source:** PsycINFO

14. A past psychiatric history may be a risk factor for topiramate-related psychiatric and cognitive adverse events.  
**Citation:** Epilepsy & Behavior, October 2003, vol./is. 4/5(548-552), 1525-5050 (Oct 2003)  
**Author(s):** Kanner, Andres M; Wuu, Joanne; Faught, Edward; Tatum, William O IV; Fix, Aaron; French, Jacqueline A; The PADS Investigators  
**Abstract:** Topiramate (TPM) is a new antiepileptic drug (AED) that has been found to be associated with a high prevalence of cognitive adverse events (CAEs). The prevalence of psychiatric adverse events (PAEs) has yet to be established. The purpose of this study was to determine the prevalence of PAEs related to TPM when used in polytherapy regimens in a large cohort of adult patients with epilepsy, to identify any association between the occurrences of CAEs and PAEs and to identify predictors of PAEs and CAEs. Investigators from 16 epilepsy centers (PADS group) prospectively obtained postmarketing safety and efficacy data on 596 patients aged 16 years and older. All data were recorded on standardized data retrieval forms, completed at the initial visit, while follow-up data were obtained every 6 months or at the time of discontinuation. PAEs were identified in 75 (12.6%) patients: 30 (5%) experienced symptoms of depression and 34 (5.7%) of aggressive behavior and irritability, while 9 patients experienced symptoms of psychosis (1.5%). CAEs were reported by 247 (41.5%) patients. There was a significant association between the occurrences of CAEs and PAEs. A past psychiatric history was a predictor of CAEs, while older age and past psychiatric history were predictors of PAEs. (PsycINFO Database Record (c) 2012 APA, all rights reserved)

**Publication Type:** Journal; Peer Reviewed Journal  
**Source:** PsycINFO

15. Analysis of efficiency and safety of topiramate depending on patient's age and forms of epilepsy  
**Citation:** Epilepsia, June 2013, vol./is. 54/(177), 0013-9580 (June 2013)  
**Author(s):** Kholin A.; Il'ina E.; Zavadenko N.  
**Abstract:** Purpose: The aim of the study was analysis of efficiency and safety of topiramate at children and adult epileptic population depending on patient's age and forms of epilepsy. Method: Seven hundred and twenty-two epileptic patients receiving topiramate (male = 374, female = 348) of the age from 3 month till 57 years are observed in dynamics with video-EEG control at the period 2002-2012 in the Department of Neurology, Neurosurgery and Medical Genetic of Russian National Research Medical University and Psycho- Neurological Department N2 of Russian Children Clinical Hospital. Results: Topiramate was effective at 64.4% of patients (n = 465), and among the patient at monotherapy effectiveness (72.2%, at 127 from 176 patients) was higher than in combined therapy (61.9% at 338 of 546 patients). Low efficiency was seen at 27.4% (n = 198) patients. The aggravation effect has been noted at 8.2% (n = 59) of patients. Drug compliance (for >1 year) was 60.7% (n = 438). High efficiency in group <1 year (n = 58) was 55.2% (n = 32), low 34.5% (n = 20), aggravation 10.3% (n = 6); in group 1-3 years (n = 201) high efficiency 54.8% (n = 110), low 31.8% (n = 64), aggravation 13.4% (n = 27); in pediatric population >3 years (n = 385) high efficiency 67.3% (n = 259), low effect in 26.2% (n = 101), and 6.5% aggravation (n = 25), in adult population >18 years (n = 78) the efficiency was 82.1% (n = 64), low effect 16.6% (n = 13) and aggravation in 1.3% (n = 1). Conclusion: Topiramate is highly effective drug in therapy of idiopathic generalized epilepsies without absences and in symptomatic/cryptogenic focal forms of epilepsy. Topiramate also could be useful additional drug in therapy of epileptic encephalopathies. With increasing of patients age the efficiency of topiramate raises, while aggravation risks decrease. Peak of aggravation potential was seen in early childhood population and maximum of effectiveness - in adult population.  
**Publication Type:** Journal: Conference Abstract  
**Source:** EMBASE

16. Efficacy and safety of topiramate depending on patient's age and forms of epilepsy
Abstract: Seven hundreds and twenty-two epileptic patients receiving topiramate (374 males, 348 females), aged from 3 month to 57 years, were followed with video-EEG control during the period of 2002-2012. Topiramate was effective in 465 (64.4%) patients, and among them the efficacy of monotherapy (72.2%) was higher compared to combined therapy (61.9%). The low efficacy was seen in 198 (27.4%) patients. The aggravation effect was noted in 59 (8.2%) of patients. Drug compliance (for >1 year) was 60.7%. In the group <1 year, the high efficacy was observed in 55.2%, low efficacy - in 34.5%, aggravation - in 10.3%. In the group 1-3 years, these indicators were 54.8%, 31.8% and 13.4%, respectively. In the pediatric population (>3 years), they were 67.3%, 26.2% and 6.5% as well as in the adult population (>18 years) - 82.1%, 16.6% and 1.3%, respectively. Thus, topiramate is a highly effective medication in the therapy of idiopathic generalized epilepsies without absences and in symptomatic/cryptogenic focal forms of epilepsy. The efficacy of topiramate raised with increasing of age while the aggravation risk decreased significantly.

Publication Type: Journal: Article
Source: EMBASE

17. Who gets side effects on antiepileptic drugs? Analysis of a large prospective cohort
Citation: Epilepsy Currents, 2012, vol./is. 12/1 SUPPL. 1, 1535-7597 (2012)
Author(s): Lowerison M.; Dykeman J.; Frolikis A.; Jette N.; Pillay N.; Federico P.; Murphy W.; Wiebe S.
Abstract: Rationale: There is controversy surrounding the association between increasing antiepileptic drug (AED) load and the occurrence of side effects (SE). We investigated the association of AED load and the occurrence of side effects (SE) in the context of AED types, psychosocial factors, and clinical factors. Methods: The outpatient epilepsy program in a large Canadian health region prospectively gathered data from adult patients' first assessments. Self-reported occurrence of SE was collected from patients on AED(s). AED load was calculated as the sum of the prescribed daily dose/defined daily dose (DDD) ratios where DDD is the assumed average maintenance daily dose of a drug for its main indication. Clinical factors included age, gender, medical comorbidity, history of epilepsy surgery, generalized versus focal seizures, epilepsy duration, mono or poly (>1) AED therapy, and seizure freedom in the prior year. Psychosocial variables included recreational drug use, alcohol use, current paid employment, presence of caregiver, having ever received psychiatric treatment, and history of learning disorder, anxiety, depression, and attention deficit disorder. AEDs were grouped into carboxamides (carbamazepine or oxcarbazepine), benzodiazepines (clonazepam or clobazam), barbiturates (primidone or phenobarbital), phenytoin, valproic acid, levetiracetam, topiramate, and gabapentin. The association between the risk of SE and these variables was investigated using Poisson regression with robust variance estimation. The results are expressed as risk ratios (RR, p-value). A sub-group analysis focusing on patients who had tried >1 AED investigated the factors associated with experiencing SE on all AEDs tried. Results: Of 963 patients taking AEDs the mean AED load was 1.32 DDD (SD=1.03 DDD) and 17.8% reported SE. Of patients who had tried >2 AEDs 13.7% had SE on all AEDs. After adjusting for confounders the risk of SE increased with AED load (16% per 1.0 DDD increase, p=0.029). DDD and current poly AED therapy were associated and so only DDD was included. SE were less likely in patients with a history of learning disorder (0.48, p=0.011); however, when adjusting for AED types, AED load was no longer associated with SE. Instead, SE were more likely with phenytoin (1.41, p=0.039) and topiramate (1.94, p=0.004), while a history of learning disorder remained protective (0.51, p=0.022). Patients having been on >2 AEDs were more likely to have SE on all AEDs if they used alcohol (1.88, p=0.012). Conclusions: Prior studies have concluded that AED load is not associated with increased risk of SE but that certain psychosocial factors are more important. However, this could be explained by high covariance between AED load and number of AEDs. We found that AED load is associated with increased risk of SE in addition to psychosocial factors. However, the type of AED is a more important determinant of SE than AED load alone. Further investigation is needed to determine whether AED types are associated with SE only in certain patients and if certain factors are protective of SE on given AEDs.

Publication Type: Journal: Conference Abstract
18. The pharmacokinetics of a novel, once-daily, extended-release formulation of topiramate (SPN-538) in the elderly

Citation: Epilepsy Currents, 2012, vol./is. 12/1 SUPPL. 1, 1535-7597 (2012)

Author(s): Vincent J.; Brittain S.; Stocks J.; Johnson J.; Baroldi P.

Abstract: Rationale: In general, aging is characterized by a progressive decline in the functional reserve of multiple organ systems. This decline in function may impact the pharmacokinetic (PK) profile of medications taken by the elderly. Supernus Pharmaceuticals, Inc. is developing SPN-538, a novel, once-daily, extended-release formulation of topiramate that may reduce the dose- and peak-related adverse events (AEs) that occur with twice-daily topiramate and may facilitate adherence to therapy. This study was conducted to compare the PK profile of a single dose of SPN-538 in young and elderly healthy adults. Methods: We conducted a single-center, single-dose, parallel-group, open-label study in healthy young and elderly adults. The study consisted of a 28-day screening period, administration of a single SPN-538 100-mg capsule under fasting conditions to study groups, followed by PK sampling for 7 days. Safety assessments and AE monitoring occurred throughout the study. Results: All 31 enrolled subjects completed the study and were included in the PK analysis. In the young adult group (n=18), the mean age was 33 (range: 19-45) and 11 (61.1%) were male. In the elderly group (n=13), the mean age was 75 (range: 71-84), and 3 (23.1%) were male. Topiramate plasma concentrations remained quantifiable throughout the 7-day PK sampling. After 100-mg SPN-538 capsule administration, the elderly group exhibited a 30% higher mean maximum plasma concentration (Cmax) and area under the plasma concentration-time curve from 0 to the last measurable concentration (AUC0-t) that was ~41% higher. While the elderly group exhibited faster absorption compared with young subjects (median time of observed maximum plasma concentration [Tmax] 16 vs 24 hours, respectively), the apparent first-order terminal elimination half-life (T1/2) was similar across age groups (49 vs 47 hours). All AEs were considered mild in severity and occurred more frequently in the elderly group (76.9%) compared with the young adult group (44.4%). No new or unexpected safety or tolerability signals were observed during the study. Conclusions: In elderly subjects taking a single 100-mg dose of SPN-538, higher maximum (~30%) and overall (~41-44%) drug exposures were found in comparison to young adults. Elderly subjects exhibited faster absorption of SPN-538 on average, but T1/2 was similar to that found in younger subjects. SPN-538 was generally well tolerated in the elderly group; all AEs were mild in intensity. In view of higher maximum and overall drug exposure in this population, individualizing the dosage of SPN-538 in elderly subjects with epilepsy may be prudent, as is also the case with the originally formulated, twice-daily, immediaterelease version of topiramate (Topamax).

Publication Type: Journal: Conference Abstract

Source: EMBASE

Full Text: Available from National Library of Medicine in Epilepsy Currents

19. Review of topiramate for the treatment of epilepsy in elderly patients

Citation: Clinical interventions in aging, 2010, vol./is. 5/(89-99), 1178-1998 (2010)

Author(s): Sommer B.R.; Fenn H.H.

Abstract: Individuals over 65 years of age experience the new onset of seizures at a prevalence rate of roughly twice that of younger adults. Differences in physiology, need of concomitant medications, and liability for cognitive deficits in this population, make the choice of anticonvulsant drugs especially important. This paper reviews topiramate (TPM), a treatment for many types of seizures, with the above risks in mind. In particular, we discuss efficacy and pharmacokinetics with emphasis on the older patient, and adverse events in both the younger and older adult. With most studies of TPM-induced cognitive deficits having been performed in younger adults and volunteers, we discuss the implications for the older adult. Even in studies of younger individuals, up to 50% discontinue TPM because of intolerable cognitive deficits. Most studies find specific declines in working memory and verbal fluency. In conclusion, we give recommendations for use of this antiepileptic drug in this population.

Publication Type: Journal: Review

Source: EMBASE

Full Text: Available from National Library of Medicine in Clinical Interventions in Aging
20. Efficacy of topiramate in adult patients with symptomatic epilepsy: An open-label, long-term, retrospective observation

Citation: CNS Drugs, 2009; vol./is. 23/4(351-359), 1172-7047 (2009)

Author(s): Lu Y.; Yu W.; Wang X.

Abstract: Background: Topiramate is a newer generation antiepileptic drug with a wide range of antiepileptic efficacy as monotherapy or as adjunctive therapy, and which has shown positive activity in intractable epilepsy and newly diagnosed epilepsy. Topiramate has also been shown to exert good seizure control with a low incidence of adverse effects in brain tumour-associated epilepsy. However, there have been few reports on the efficacy of topiramate in the treatment of symptomatic epilepsy of varying aetiologies. Objective: The aim of the present study was to evaluate the efficacy of topiramate in the treatment of adult patients with symptomatic epilepsy of various aetiologies. Methods: This was an open-label, long-term, retrospective observation. 227 patients with symptomatic epilepsy (110 male, 117 female) were enrolled into this study. The underlying aetiologies included low-grade brain tumour, head trauma, cerebrovascular diseases, infection, diabetes mellitus, hydrocephalus and parasitosis. Topiramate was titrated up to a target dosage of 200 mg/day and maintained for at least 1 year. Response to topiramate was defined as >50% reduction in seizure frequency compared with baseline. Seizure free was defined as no seizure occurring during 1 year of topiramate therapy. Results: 157 (69.2%) patients were responders and 124 (54.6%) patients were seizure free with topiramate administration. Responders by subgroup included 40 patients (74.0%) with low-grade brain tumour, 32 (55.2%) with trauma, 30 (90.9%) with cerebrovascular disease, 21 (55.3%) with infection, 18 (81.8%) with diabetes, 12 (85.7%) with parasitosis and 4 (50.0%) with hydrocephalus. The percentage of seizure-free patients by subgroup was 61.0% with brain tumours, 31.0% with trauma, 78.8% with cerebrovascular disease, 44.7% with infection, 59.0% with diabetes, 85.7% with parasitosis and 50.0% with hydrocephalus. The incidence of adverse effects was 36.1%. The most commonly reported adverse effects were weight loss, memory impairments, paraesthesia, headache and dizziness; most were mild to moderate in severity and transient. Sixty-eight (30.0%) patients withdrew from topiramate treatment in this study: topiramate was discontinued in 56 patients because of lack of efficacy and in 12 patients because of adverse effects. At the end of the study, 109 patients received topiramate monotherapy, including 52 newly diagnosed patients and 57 subjects who transferred to topiramate monotherapy successfully; another 118 patients received add-on topiramate therapy. The percentage of patients responding to topiramate was 85.3% in the monotherapy group and 54.2% in the topiramate add-on therapy group; the percentage of seizure-free patients was 68.8% in the topiramate monotherapy group and 45.1% in the topiramate add-on therapy group. Conclusion: When administered either as a single drug or as an add-on drug, topiramate is effective and well tolerated in adult patients with symptomatic epilepsy of various aetiologies. 2009 Adis Data Information BV. All rights reserved.

Publication Type: Journal: Article

Source: EMBASE

Full Text: Available from EBSCOhost in CNS Drugs

21. Exploring efficacy and tolerability outcomes in patients with difficult-to-treat epilepsy receiving adjunctive topiramate at different titration rates - An exploratory study

Citation: Acta Neurologica Scandinavica, August 2009, vol./is. 120/2(80-87), 0001-6314;1600-0404 (August 2009)

Author(s): Kurth C.; Schauble B.; Schreiner A.; Rettig K.; Steinhoff B.J.

Abstract: Exploring efficacy and tolerability outcomes in patients with difficult-to-treat epilepsy receiving adjunctive topiramate at different titration rates - an exploratory study. Acta Neurol Scand 2009: 120: 80-87. 2009 The Authors Journal compilation 2009 Blackwell Munksgaard. Objective - To compare rapid vs regular titration of topiramate concerning efficacy and safety. Materials and methods - Open-label, prospective, single-center study exploring efficacy and tolerability of two adjunctive dosing regimens of topiramate (TPM) in adult patients with difficult-to-treat epilepsy. Based on investigator judgment, 21 of 50 consecutive patients received a rapid titration (starting dose 50 mg/day, stepwise increase with 50 mg/day after 3 days each until reaching the target dose), while the other 29 patients received titration according to the German prescribing information (starting dose 25 mg/day, stepwise increase with 25-50 mg/day every 7 days). Patients were observed until the target dose was reached and 3 months thereafter. Results - Mean final dosages were 136 mg/day (regular titration) and 213 mg/day (rapid titration). Efficacy and tolerability measures did not differ significantly. Forty-six percent of all patients
experienced a seizure reduction of >50%; 14% became seizure free. No serious adverse events occurred. The most common adverse effects were tiredness (20%), memory and language difficulties (18% each), slowness in thinking and speech (10%), psychomotor disturbance (8%) and paresthesia (8%). Conclusions - This study suggests that rapid and conventional titration generate similar tolerability, safety and effectiveness in selected patients. 2008 Blackwell Munksgaard.

Publication Type: Journal: Article
Source: EMBASE
Full Text: Available from EBSCOhost in Acta Neurologica Scandinavica

22. Attention changes in epilepsy patients following 3-month topiramate or valproate treatment revealed by event-related potential
Citation: International Journal of Psychophysiology, June 2008, vol./is. 68/3(235-241), 0167-8760 (June 2008)
Author(s): Sun W.; Wang Y.; Wang W.; Wu X.
Abstract: The present study was designed to reveal changes of cognitive processes in epilepsy (EP) patients with Topiramate (TPM) or Valproate (VPA) treatment using Wechsler Adult Intelligence Scale (WAIS-CR) and event-related potential (ERP). Thirty untreated epilepsy patients were randomly divided into two groups receiving TPM or VPA, respectively. Fifteen healthy volunteers were included as controls. All the patients were examined by WAIS-CR and ERP before and 3 months after drug treatment. Controls were examined by ERP at the time recruited into the study and 3 months later. Unfamiliar grey-scale photographs of faces (front view) were used as stimuli. ERP were recorded at the same time. Mean Intelligence Quotient (IQ) in TPM group decreased after the 3-month treatment (90.40 vs. 81.00, P < 0.05). One component of ERP-P300 was smaller in epilepsy patients than controls (P < 0.05), but remained unchanged after TPM or VPA treatment (P > 0.05). A delayed and smaller N270 was detected in patients compared to controls (P < 0.05). After 3 months TPM treatment, it decreased further compared to before treatment (P < 0.05). N170 was lower in patient groups, and it became lower after TPM treatment than before. Our results demonstrate that in all epilepsy patients with mild cognitive impairment ERP changes were found. TPM affected the cognitive functions in epilepsy patients reflected by the decreased full-scale intelligence quotient (FIQ). The imperative effects of TPM on visual perception function reflected by N170 were more obvious than that of VPA. Attention reflected by N270 was impaired after TPM treatment. 2008 Elsevier B.V. All rights reserved.

Publication Type: Journal: Article
Source: EMBASE

23. Effects of topiramate versus other antiepileptic drugs on the cognitive function of patients with epilepsy
Citation: Neural Regeneration Research, February 2007, vol./is. 2/2(95-98), 1673-5374 (February 2007)
Author(s): Xu F.; Feng Q.H.; Yu L.; Liu J.; Sun H.B.
Abstract: Background: Only very large dose of topiramate has neurotoxicity, indicating that topiramate has low neurotoxicity and high safety. The residual rate of topiramate is affected by many cognitive-related adverse effects. Patients who take topiramate often accompany with thought slowness, difficulty in finding words, dyscalculia, blunt reaction, attention decreasing, memory deterioration, etc. Objective: To compare the effects of topiramate with traditional anti-epileptic drugs (including carbamazepine and Valproic acid (VPA) on cognitive function of patients with epilepsy. Design: Observational experiment, self-control and intergroup comparison. Setting: Sichuan Academy of Medical Science. Participants: Eighty-seven inpatients and outpatients with newly diagnosed epilepsy who received preliminary diagnosis and follow-up in the Department of Neurology, Sichuan People's Hospital between January 2004 and June 2006 were involved in this survey. They were diagnosed according to disease history and electroencephalogram (EEG). The onset type was diagnosed following the definition of epilepsy and epileptic syndrome in 1989 International Anti-epileptic League. The involved patients and their relatives were informed of detection and therapeutic regimen. The patients were assigned into two groups according to table of random digit: traditional antiepileptic drugs group (AEDs group, n =44) and topiramate (TPM) group (n =43). Methods: 1 Among the patients in AEDs group, carbamazepine was the first choice for 21 patients with partial seizures or partial secondarily generalized seizures, and VPA for 23 patients with generalized seizures. The initial dose of carbamazepine was 300 mg/d, and
that of VPA was 500 mg/d. Patients in the TPM group took TPM with the initial dose of 25 mg/d, increased by 25 mg/d each week to target dose 150 mg/d within 8 weeks. 2 Curative effect was graded into 4 degrees: markedly effective, effective, ineffective and aggravated. Total effective rate was calculated. 3 Cognitive function of patients was tested before and 6 months after administration by using Wechsler Adult Intelligence Scale(WAIS) or Wechsler Intelligence Scale for Children (WISC, Chinese edition), (Higher scores indicated better cognitive function), Stroop color word interference, test of memory of past numbers, test of telling the names of fruits and vegetables within 1 minute (Shorter time for reading word, telling color and memory of past numbers demonstrated better cognitive function. Less errors in reading words, telling colors and memory of past numbers, numbering and telling the names of fruits and vegetables within 1 minute indicated better cognitive function), etc. totally 22 items. 4 t test and paired t test were used for measurement data. Main Outcome Measures: Clinical curative effects and adverse reactions as well as neurological tests. Results: Eighty-four patients participated final analysis and 3 dropped out. 1 In the AEDs group and TPM group, total effective rate was 86% and 99%, respectively. 2 In the AEDs group, there were no significant changes in the scores of each test of WIS before and after treatment (P > 0.05). In the TPM group, total IQ, word scores, verbal IQ and digit span scores were significantly decreased (t =2.097 -4.423, P < 0.05-0.01). Following treatment, the time for reading word and telling color for patients in the AEDs group was prolonged in Stroop color interference test (t = -2.304, -2.454, P < 0.05), and time for reading word and memory of past numbers for patients in the topiramate group was significantly prolonged (t=-3.054, 2.272, P < 0.01, 0.05). 3 There were no significant differences in scores of WIS before and after treatment in AEDs group and TPM group (P > 0.05). Following treatment, verbal IQ, word scores, total IQ, digit span of patients in the TPM group were significantly lower than those in the AEDs group (t =2.052 -3.297, P < 0.05 - 0.01). There were no significant differences in Stroop color word interference, memory of past numbers and telling the names of fruits and vegetables within 1 minute before and after treatment in AEDs group and TPM group (P > 0.05). Conclusion: 1 Moderate and small doses of both TPM and AEDs may lead to mild cognitive function impairment of patients, mainly presenting delayed reaction and decreased sensitivity. 2 TPM mainly influences attention, language comprehension ability and fluency, while AEDs cause delayed reaction easily, but influence executive function mainly.

**Publication Type:** Journal: Article  
**Source:** EMBASE

### 24. Psychiatric and behavioral side effects of the newer antiepileptic drugs in adults with epilepsy

**Citation:** Epilepsy and Behavior, February 2007, vol./is. 10/1(105-110), 1525-5050;1525-5069 (February 2007)  
**Author(s):** Weintraub D.; Buchsbaum R.; Resor Jr. S.R.; Hirsch L.J.  
**Abstract:** Objective: Psychiatric/behavioral side effects (PSEs) are common in patients taking antiepileptic drugs (AEDs). The objective of the study described here was to compare the PSE profiles of the newer AEDs. Methods: We examined the charts of 1394 adult outpatients seen at the Columbia Comprehensive Epilepsy Center who had taken one of the newer AEDs. We compared the rate of AED-related PSEs in patients newly started on the newer AEDs both before and after controlling for non-AED predictors of PSEs. Results: Overall, 221 of 1394 (16%) patients experienced PSEs. The average rate of AED-related PSEs for a single AED was 8.4%, with 6.1% resulting in dosage change and 4.3% resulting in AED discontinuation. Significantly fewer PSEs were attributed to gabapentin (n = 160, 0.6% incidence, P < 0.001) and lamotrigine (n = 547, 4.8% incidence, P < 0.001), and significantly more PSEs were attributed to levetiracetam (n = 521, 15.7% incidence, P < 0.001; 8.8% discontinued LEV because of PSEs). Vigabatrin, felbamate, and oxcarbazepine were associated with similarly low rates of PSEs in many analyses but with fewer of patients. Tiagabine was associated with high PSE rates (similar to those for levetiracetam), but was used much less commonly at our center. Intermediate rates of PSEs were attributed to topiramate and zonisamide (both nonsignificant). Psychiatric history was the most significant nondrug predictor of AED-related PSEs (PSEs occurred in 23% of patients with a psychiatric history vs 12% of patients without such a history, P < 0.001). The relative rates of AED-related PSEs were similar when controlling for non-AED predictors and when analyzing only patients on monotherapy. Conclusions: There are significant differences between the newer AEDs in terms of their PSE profiles. Patients taking levetiracetan experience significantly more PSEs than
average, and patients taking gabapentin and lamotrigine experience significantly fewer PSEs. Even with the medication with the highest rate of PSEs (levetiracetam), less than 10% of patients discontinued it because of PSEs. A past psychiatric condition is the most significant nondrug predictor of AED-related PSEs. 2006 Elsevier Inc. All rights reserved.

**Publication Type:** Journal: Article  
**Source:** EMBASE

**25. Topiramate: A prospective study on the relationship between concentration, dosage and adverse events in epileptic patients on combination therapy**

**Citation:** Epileptic Disorders, September 2005, vol./is. 7/3(237-248), 1294-9361 (September 2005)  
**Author(s):** Froscher W.; Schier K.R.; Hoffmann M.; Meyer A.; May T.W.; Rambeck B.; Rosche J.  
**Abstract:** Rationale. The relationship between topiramate (TPM) concentration, dosage and adverse events in patients with epilepsy is still controversial. We therefore performed a prospective study in patients with poorly controlled epilepsy treated with TPM, predominantly in combination with other antiepileptic drugs. The goal of the study was to investigate the relationship between the occurrence of adverse events due to TPM and its serum concentration or dosage, respectively. Methods. The relationship between the occurrence of adverse events and TPM serum concentration or dosage, respectively, was examined in a group of 42 young adult and adult patients with poorly controlled epilepsy. Within 22 months, all patients treated with TPM had been included in the study. The 8 adverse events occurring most frequently (difference > 10%) in TPM-treated patients in 5, double-blind, placebo-controlled, parallel group studies, were checked regularly. This side effect profile has been presented by Reife et al. (1995a). Other possible or probable adverse events were also documented. Results. The difference in TPM serum concentrations and TPM dosages (mg/kg) for patients without an adverse event and patients with a given adverse event was statistically significant for "abnormal thinking, impaired concentration, weight loss, dizziness, speech problems, somnolence, ataxia, increased seizure frequency and paresthesia". To avoid adverse events, we recommend an initial "maintenance serum concentration" of below 4 µg/mL. As regards the TPM dosage, our results suggest initial maintenance dosages of 100 TPM or lower, 1.5 mg/kg or lower, respectively. These conclusions are limited by the relatively small number of patients.

**Publication Type:** Journal: Article  
**Source:** EMBASE

**26. Treatment of epilepsy in adults: Expert opinion, 2005**

**Citation:** Epilepsy and Behavior, September 2005, vol./is. 7/SUPPL. 1(S1-S64), 1525-5050;1525-5069 (September 2005)  
**Author(s):** Karceski S.; Morrell M.J.; Carpenter D.  
**Abstract:** Rationale: Over the past decade, there has been a proliferation of new therapies for the treatment of epilepsy. Faced with this growing list of options, clinicians must decide what therapy, or combination of therapies, is best for a given individual. Although controlled clinical trials exist for each treatment option, the answer to these questions may remain unclear. In 2000, a survey of expert opinion was done to address questions concerning which treatment options might be best in a number of clinical situations. We surveyed a group of US epileptologists again in 2004 and compared the results of the two surveys. Methods: We sent a questionnaire on the treatment of adolescent and adult epilepsy syndromes to a group of opinion leaders in the field of epilepsy. The questions were formatted to simulate real-world clinical situations in the treatment of symptomatic localization related epilepsy (SLRE) and idiopathic generalized epilepsy (IGE). The experts were asked to rate treatment options based on a modified RAND 9-point scale (with "9" most appropriate and "1" least appropriate). Statistical analysis of data was performed as defined by the expert consensus method. The results were used to develop user-friendly recommendations concerning overall treatment strategies and choice of specific medications. Results: Of the 48 experts to whom the survey was sent, 43 (90%) responded; 29 (67%) of the respondents had also participated in the first survey. For initial monotherapy for IGE (generalized tonic-clonic [GTC], absence, and myoclonic seizures), valproate was rated as treatment of choice. For IGE-GTC seizures, lamotrigine and topiramate were also identified as usually appropriate for initial monotherapy. For IGE-absence seizures, ethosuximide was also a treatment of choice, and lamotrigine was
usually appropriate. For SLRE, the experts were again asked to rate treatment options based on seizure type: simple partial seizures (SPS), complex partial seizures (CPS), and secondarily generalized tonic-clonic seizures (SGTC). In SLRE-SPS and SLRE-SGTC, carbamazepine and oxcarbazepine were treatments of choice, with lamotrigine and levetiracetam also usually appropriate. In SLRE-CPS, carbamazepine, lamotrigine, and oxcarbazepine were treatments of choice, while levetiracetam was also usually appropriate. For women who are pregnant or trying to conceive, lamotrigine was treatment of choice for both syndrome types. In the elderly, whether medically stable or ill, the treatment of choice was lamotrigine, while levetiracetam was also usually appropriate (along with gabapentin for persons with comorbid medical illness). In persons with HIV and epilepsy, lamotrigine and levetiracetam were usually appropriate. In people with both epilepsy syndromes who have depression, lamotrigine was treatment of choice. In a person with seizures and renal disease, lamotrigine was usually appropriate for both syndromes, with valproate also usually appropriate for IGE. In patients with hepatic disease, levetiracetam and lamotrigine were usually appropriate for IGE; in SLRE, levetiracetam was treatment of choice, with gabapentin also usually appropriate.

Conclusions: Although the panel of experts reached consensus on many treatment options, there are limitations to these types of data. Despite this, the expert consensus method concisely summarizes expert opinion, and this opinion may be helpful in situations in which the medical literature is scant or lacking. The information in this report should be evaluated in conjunction with evidence-based findings. 2005 by Comprehensive Neuroscience, Inc. All rights reserved.

**Publication Type:** Journal: Review

**Source:** EMBASE

27. Evaluation of health status in epilepsy using the EQ-5D questionnaire: A prospective, observational, 6-month study of adjunctive therapy with antiepileptic drugs

**Citation:** Current Medical Research and Opinion, May 2005, vol./is. 21/5(733-739), 0300-7995 (May 2005)

**Author(s):** Selai C.E.; Trimble M.R.; Price M.J.; Remak E.

**Abstract:** Aims: The aims of this project were to evaluate the impact of adjunctive treatment with an anti-epileptic drug (AED) on the health status of people with epilepsy and to investigate how seizure frequency affects their health status. Methods: Adult epilepsy patients, refractory to current treatment, were included in this prospective observational study. Patients commencing adjunctive therapy with one of five AEDs (topiramate, lamotrigine, gabapentin, clobazam, vigabatrin) were eligible for inclusion. The study took place at the outpatient clinics of the National Hospital for Neurology and Neurosurgery, Queen Square, London. Patients completed the EQ-5D, a generic health status measure, at baseline and again after 3 and 6 months. Information was also collected on medications and seizure frequency. Results: In total, 125 patients entered the study and were followed up for 6 months. Patients treated with topiramate had a significant increase (p < 0.05) in EQ-5D score from baseline, indicating an improvement in their health status whereas scores for lamotrigine, clobazam and gabapentin all showed a non-significant decline. When the data were analysed according to seizure frequency, only patients who became seizure-free on adjunctive treatment had a significant increase in their health status. The group who had a 50% reduction in seizure frequency did not have increased health status. Conclusions: In summary, adjunctive treatment with topiramate significantly increased health status as measured by the EQ-5D. These data also suggest that achievement of seizure-freedom is the key to improving health status in this patient group. 2005 Librapharm Limited.

**Publication Type:** Journal: Article

**Source:** EMBASE

28. The choice of antiepileptic drugs in newly diagnosed epilepsy: A national French survey

**Citation:** Epileptic Disorders, December 2004, vol./is. 6/4(255-265), 1294-9361 (December 2004)

**Author(s):** Semah F.; Picot M.-C.; Derambure P.; Dupont S.; Vercueil L.; Chassagnon S.; Marchal C.; Thomas P.; Ryvlin P.

**Abstract:** The choice of an antiepileptic drug (AED) in patients with epilepsy is mainly based on efficacy and safety of each drug. However, these criteria of drug selection should...
be further evaluated according to the epileptic syndromes, and adjusted to the sex and age of the patient. Unfortunately, very few studies have been conducted based on these latter criteria. We conducted a survey on the management of epilepsy treatment in adults. This survey was undertaken in France, and led to the establishment of a French consensus on antiepileptic drug treatment in adult patients with newly diagnosed epilepsy. Patients were grouped into 18 categories according to the epileptic syndrome (absence epilepsy, juvenile myoclonic epilepsy, undetermined idiopathic generalized epilepsy, symptomatic or cryptogenic partial epilepsy and unclassified epilepsy), and to the patient’s gender and age. Our survey suggests that there is a consensus among French epileptologists for the choice of AEDs, mainly based on the epilepsy syndrome. Gender also plays a crucial role. Sodium valproate and lamotrigine are the two drugs of choice for generalized epilepsies, as well as for undetermined epilepsies. Lamotrigine is often preferred for women of childbearing age. First line AEDs in partial epilepsy are carbamazepine (particularly for men), lamotrigine (particularly for women), and gabapentin (in the elderly). In cases of failure and/or intolerance to one of these AED, the principal alternatives are oxcarbazepine, sodium valproate and topiramate.

**Publication Type:** Journal: Article

**Source:** EMBASE

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29. Impact of traditional antiepileptic and topiramate on the quality of life of adult epileptic patients

**Citation:** Chinese Journal of Clinical Rehabilitation, September 2004, vol./is. 8/25(5386-5388), 1671-5926 (September 2004)

**Author(s):** Xu N.-G.; Zhu D.-T.; Xiao B.; Xie G.-J.

**Language:** English

**Abstract:** Background: Topiramate has been widely applied in the clinical treatment of all types of epilepsy at present. However, there are few reports about its impact on the quality of life(QOL) of domestic adult epileptic patients. Objectives: To compare the impact of traditional antiepileptic and Topiramate on the QOL of adult epileptic patients for the discussion of the relative mechanism. Design: A randomized controlled clinical trial. Setting and participants: There were 102 epileptic patients newly diagnosed in the Outpatient Department of Xiangya Hospital and the Second Xiangya Hospital of Central South University, of which there were 60 males and 42 females aged from 16 to 60 years old. Interventions: There were 102 newly clinical diagnosed adult epileptic patients randomly allocated into two groups: One group was treated by traditional antiepileptic single medication systemic therapy (traditional antiepileptic group, n = 54) and the other group was treated by Topiramate single medicine therapy (Topiramate group, n = 48). The attack frequency and adverse effect of the two groups were compared after one month and the QOL of these 102 epileptic patients were evaluated with QOLIE-30 scale. Main outcome measures: (1) attack frequency(AF) and adverse reaction and side effect of two groups. (2) QOL score. Results: The AF and AE of the Topiramate group were significantly lower than that of the traditional antiepileptic group, of which there were 11 cases effective, 7 cases showing effect and 16 cases in control of the former group, and 13 cases effective, 5 cases showing effect and 13 cases in control in the latter group. The QOL score of the Topiramate group was significantly higher than that of the traditional antiepileptic group, which were 60 +13 and 53 + 15 respectively, especially in the first 5 items. Conclusion: Topiramate can improve the QOL of epileptic patients, which realizes its improvement of QOL through controlling the attack and reducing AE.

**Publication Type:** Journal: Article

**Source:** EMBASE

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30. The relationship between treatment with valproate, lamotrigine, and topiramate and the prognosis of the idiopathic generalised epilepsies

**Citation:** Journal of Neurology, Neurosurgery and Psychiatry, January 2004, vol./is. 75/1(75-79), 0022-3050 (January 2004)

**Author(s):** Nicolson A.; Appleton R.E.; Chadwick D.W.; Smith D.F.

**Abstract:** Objective: To examine a large population with idiopathic generalised epilepsy (IGE), and estimate the overall remission rates for the IGEs and subsyndromes in a clinic based sample. Remission rates on valproate, lamotrigine, topiramate, and combinations of these antiepileptic drugs were estimated and factors predicting outcome examined. Methods: All patients with IGE were identified from a computerised database and EEG records at large adult and paediatric epilepsy clinics. Data were recorded retrospectively on demographics and clinical information, seizure types and syndrome diagnosis,
antiepileptic drug treatment details, and remission rates. Results: 54.3% of 962 patients had achieved a one year period of remission; this was most likely with valproate monotherapy (52.1%), with lower rates for lamotrigine and topiramate (16.7% and 34.6%, respectively). The combination of valproate and lamotrigine achieved a remission rate of 15.3%. The factor most predictive of a response to a particular antiepileptic drug regimen was the rank order in which it was given. Relapse rate was high (79.9%) after antiepileptic drug withdrawal in remission, particularly with juvenile myoclonic epilepsy (93.6%). Conclusions: Valproate may be the most effective antiepileptic drug in the treatment of the IGEs. Combination therapy should be initiated if an adequate trial of valproate monotherapy is not effective, rather than switching to alternative monotherapy. Antiepileptic drug treatment needs to be lifelong in many adult patients with IGE.

Publication Type: Journal: Article
Source: EMBASE
Full Text: Available from EBSCOhost in Journal of Neurology, Neurosurgery & Psychiatry

The next entries are taken from the Cochrane Review. There may be others which you will find useful – too many to include in this document!

   A randomised observer-blind clinical study comparing the cognitive effects of topiramate versus valproate in a first-line add-on design
   Epilepsia, 1999, Vol 40, issue suppl 2.94

   A multicentre, randomised clinical study to evaluate the effect of cognitive function of topiramate compared with valproate as add-on therapy to carbamazepine in patients with partial-onset seizures
   Epilepsia, 2000, 41 (9) 1167 – 78

33. Blum D, Meador K, Biton V et al
   Cognitive effects of lamotrigine compared with topiramate in patients with epilepsy
   Neurology, 2006, 67, 400 – 6

34. Edwards J, Privitera M, Neto W, Wu SC
   Topiramate vs Carbamazepine and valproate in newly diagnosed epilepsy: effectiveness according to seizure type
   Epilepsia, 2004, 45 (7) S127

35. Fritz N, Glogau S, Hoffman J et al
   Efficacy and cognitive side effects of tiagabine and topiramate in patients with epilepsy
   Epilepsy and Behavior, 2005, (6) issue 3, p373-81

36. Isojarvi JI, Kero SP, Caldwell PT et al
   Double-blind evaluation of the cognitive effects of lamotrigine vs topiramate adjunctive therapy
   Epilepsia, 2005, Vol 46, (8) 176

37. Marson A, Smith D, Tudour Smith C et al
   Carbamazepine vs gabapentin, lamotrigine, oxcarbazepine and topiramate for epilepsy: results from arm A of the SANAD trial
   Epilepsia, 2006, Vol 47. 272

38. Marson AG, Al-Kharusi AM, Alwaidh M et al
   The SANAD study of effectiveness of carbamazepine, gabapentin, lamotrigine, oxcarbazepine or topiramate for treatment of partial epilepsy: an unblended randomised controlled trial
   Lancet, 2007, 369 (9566) 1000 – 1015
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*From 1st page of results:*

**G1. Cognitive effects of topiramate, gabapentin, and lamotrigine in healthy young adults**

R Martin, R Kuzniecky, S Ho, H Hetherington,

Neurology, 1999, Vol 52 (2) 321

**G2. Effects of topiramate on cognitive function**

PJ Thompson, SA Baxendale, JS Duncan


**G3. The effects of adjunctive topiramate on cognitive function in patients with epilepsy**

S Lee, V Sziklas, F Andermann, S Farnham, G Risse


**G4 Cognitive effects of lamotrigine compared with topiramate in patients with epilepsy**

D Blum, K Meador, V Biton, T Fakhoury, B Shneker

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**G5 Neuropsychological effects of epilepsy and antiepileptic drugs**
G6 Effect of antiepileptic drugs on cognitive function in individuals with epilepsy

L Brunbech, A Sabers


G7 Cognitive and behavioral effects of antiepileptic drugs

KJ Meador, FG Gilliam, AM Kanner, JM Pellock


G8 Effect of topiramate on attention

LA Burton, C Harden

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