



Parke-Davis

Medical & Scientific Affairs

Central Nervous System Specialty Group

TO: Medical Liaisons and Associate Medical Directors

FROM: Pat Woster, Pharm.D.
Chair

CC: Ken Massey, Pharm.D.; Marge Orwig

RE: Articles for distribution

May 16, 1999

This installment has something for everyone. ENJOY!!!

GABAPENTIN/PREGABALIN

- Field, et al. Gabapentin and pregabalin, but not morphine and amitriptyline, block both static and dynamic components of mechanical allodynia induced by streptozocin in the rat. *Pain* 1999; 80: 391-8.
- This article supports the use of gabapentin and pregabalin for treatment of neuropathic pain. The results show that gabapentin and pregabalin given orally dose-dependently blocked both static and dynamic allodynia. Morphine and amitriptyline dose-dependently blocked static allodynia, but not dynamic allodynia. The R-enantiomer of pregabalin was found to be inactive.
- Rosebush, P et al. Catatonia following gabapentin withdrawal. *J Clin Psychopharmacol* 1999;19:188-9. Interesting case report of a patient that developed catatonia within 48 hours after the last dose of a tapered gabapentin withdrawal regimen. The authors hypothesize that GABAergic systems may play a role in the syndrome of catatonia and that gabapentin may precipitate this in individuals with underlying mood disorders.
- Hatzimanolis, J. Gabapentin as monotherapy in the treatment of acute mania. *European Neuropsychopharmacology* 1999;9: 257-8. Two case reports of gabapentin being used to treat acute mania. The results are marginal, but the authors suggest further investigation is warranted.
- Vadivelu, N. et al. Neuropathic pain after anti-HIV gene therapy successfully treated with gabapentin. A report of successful treatment of neuropathic pain in a patient receiving anti-HIV gene therapy.

- Covington, E. et al. Use of gabapentin during sedative withdrawal. *Pain Medicine* 1997; 12: 1-4. The results of 7 chronic pain patients physically dependent on sedatives (mostly benzodiazepines) treated in a pain rehab program are reported. The patients underwent sedative detoxification with gabapentin to help minimize the withdrawal symptoms. There is a table in the text that outlines the type of pain and gabapentin doses used in each patient.
- Mikata, M. et al. Gabapentin in the treatment of refractory partial epilepsy in children with intellectual disability. *Journal of Intellectual Disability Research* 1998; 42: 57-62. This article reviews the use of gabapentin in 32 children (ages 2 - 17) with intellectual disability (n=26) and normal children (n=6) who have refractory partial epilepsy as an adjunctive medication to their regimen. The article provides some guidance for pediatric dosing. The authors conclude that gabapentin is effective in normal and intellectually disabled children, but children with disability who are also less than 10 years old with a baseline attention deficit may be at higher risk for behavioral side effects.
- Boyd, R. et al. Effects of age and gender on single-dose pharmacokinetics of gabapentin. *Epilepsia* 1999; 40: 474-9. Healthy subjects (aged 20 - 78) were given a single 400 mg dose of gabapentin. Serial blood samples and total urine output were collected. No change in C_{max}, T_{max} or VD with respect to age was noted. A significant decline in oral clearance, elimination rate constant and renal clearance was noted with increasing age. The total urinary recovery of unchanged drug did not change with age, therefore these declines can be explained by a decline in renal clearance with age. There was a significantly higher C_{max} in women versus men that the authors attribute to body size differences.
- Letterman, L. et al. Gabapentin: A review of published experience in the treatment of bipolar disorder and other psychiatric conditions. *Pharmacotherapy* 1999; 19: 565-72. Everything you ever wanted to know about the use of gabapentin in psychiatric conditions is referenced in this review. The authors do a nice job of reviewing the available published information regarding gabapentin in bipolar disorders, anxiety disorders, substance abuse, children and the elderly. The authors conclude that controlled trials are needed before gabapentin can be recommended first line in these patient populations.
- Gironel, A. et al. A randomized placebo-controlled comparative trial of gabapentin and propranolol in essential tremor. *Arch Neurol.* 1999;56:475-80. The results showed that both propranolol and gabapentin produced significant and comparable efficacy in reducing tremor in this small patient population studied.
- Bryans, J. et al. 3-substituted GABA analogs with central nervous system activity: a review. *Med Re Rev*, 1999; 19:149-77. A comprehensive reference for gabapentin and pregabalin questions. A review of the development of gabapentin as an anticonvulsant and other therapeutic uses is included. Pregabalin is also reviewed. The studies on the MOA are discussed.
- Pan, H. et al. Gabapentin suppresses ectopic nerve discharges and reverses allodynia in neuropathic rats. *JPET* 1999;288:1026-30. This study provides electrophysiological evidence that gabapentin is capable of suppressing the ectopic discharge activity from injured peripheral nerves.
- Leppik, I. et al. Treatment of epilepsy in women of childbearing potential. Issues in management. *CNS Drugs* 1999; 11: 191-206. For your files.

PHENYTOIN

- Yoshikawa, H et al. Extremely acute phenytoin-induced peripheral neuropathy. A case report of a patient that developed peripheral neuropathy a few hours after the initial administration of phenytoin.
- Steiner, T. et al. Lamotrigine monotherapy in newly diagnosed untreated epilepsy: a double-blind comparison with phenytoin. The patients were newly diagnosed patients with partial seizures or secondarily generalized tonic-clonic seizures. Both lamotrigine and phenytoin were similarly effective. Lamotrigine had a higher incidence of rash but a lower incidence of central nervous system side effects.

CITALOPRAM

- Pallanti, S. et al. Citalopram and sexual side effects of selective serotonin reuptake inhibitors. Letters to the editor. *Am J Psychiatry* 1999; 156:796. A letter to the editor describing the lack of sexual side effects in patients treated with citalopram that had previously experienced sexual dysfunction with other SSRIs.
- Ashton, A. Sildenafil treatment of serotonin reuptake inhibitor-induced sexual dysfunction. *J Clin Psychiatry* 1999; 60:194-5. Case reports of the use of Viagra to treat SSRI-induced sexual dysfunction. (This one is for you, Dr. Eudoric!).
- The Medical Letter. April 9, 1999. Drugs for depression and anxiety.
- The Medical Letter, December 4, 1998. Citalopram for depression. (Sorry, this one got "lost" on my desk).
- Comelius, J. et al. *J Clin Psychopharmacol* 1999; 2:183-4. Fluoxetine versus placebo to decrease the smoking of depressed alcoholic patients. The authors took patients involved in a study of the efficacy of fluoxetine vs placebo in depressed alcoholics and looked at their smoking history before and during the study. The patients did not receive counseling for smoking cessation or any pharmacologic therapies. There was a decrease in the number of cigarettes smoked in the fluoxetine treated group. Not scientific, but interesting.
- Michels, K. Problems assessing nonserious adverse drug reactions: antidepressant drug therapy and sexual dysfunction. *Pharmacotherapy* 1999;19:424-9. The author makes a plea for better reporting of nonserious ADRs. Citalopram is not mentioned, but it provides a nice review of what we know already....the inaccurate reporting of incidence rates of sexual dysfunction with the SSRIs.
- Evans, D. et al. Depression in the medical setting: biopsychological interactions and treatment considerations. *J Clin Psychiatry* 1999;60:40-55. An interesting article that looks at depression in coronary artery disease, cancer, HIV infection, Parkinson's, pain, and menopause. Citalopram is not included in the discussions regarding SSRI use in the various medical conditions. The authors suggest that depression is underdiagnosed and undertreated in various medical conditions and that treatment would improve morbidity and mortality in these conditions.
- Shelton, R. Treatment options for refractory depression. *J Clin Psychiatry* 1999;60:57-61. The article reviews treatment options for patients with refractory depression.
- Joffe, R. Substitution therapy in patients with major depression. *CNS Drugs* 1999;11:175-80. Another article that reviews the treatment options available to patients who have an

inadequate response to initial treatment. The options include optimization, augmentation/combination treatment and substitution.

- Gorman, J. et al. SSRIs and SNRIs: broad spectrum of efficacy beyond major depression. *J. Clin. Psychiatry* 1999;60: 33-8. The article reviews the support for these agents in the treatment for panic disorder, OCD, social phobia, PTSD, and bulimia. They also review their uses in dysthymia and GAD.
- Van Ameringen, M. et al. Selective serotonin reuptake inhibitors in the treatment of social phobia. The emerging gold standard. *CNS Drugs* 1999;11:307-15. This article is a useful review of the treatment of social phobia. There is a table of drugs other than SSRIs in the treatment of social phobia. There is also a table that reviews the studies using SSRIs for the treatment of social phobia. Citalopram is mentioned in the article.
- Emslie, G. et al. Depression in children and adolescents. A guide to diagnosis and treatment. *CNS Drugs*, 1999; 11:181-9. I thought I would include this as a reference for questions regarding dosing in children. Citalopram is mentioned in the article with dosing recommendations.
- Edwards, J.G. et al. Systematic review and guide to selection of selective serotonin reuptake inhibitors. *Drugs* 1999; 57: 507-33. A comprehensive review of the data available on the efficacy, tolerability and use of the SSRIs. There are tables available for quick reference. Citalopram is included.
- Gillman, PK. The serotonin syndrome and its treatment. *J of Psychopharmacology* 1999; 13: 100-9. For your files