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AN EVIDENCE BASED DRUG THERAPY RESOURCE

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The OHP Practitioner-Managed Prescription Drug Plan: Opportunities for Clinician Involvement

Senate Bill 819 was passed by the 2001 legislature and was signed into law by Governor Kitzhaber. The bill requires the Department of Human Services (DHS) to adopt a plan to ensure that Oregon Health Plan enrollees receive the most effective prescription drug available at the best possible price. The bill can be read at http://pub.das.state.or.us/LEG_BILLS/PDFs/ESB819.pdf.

The Health Resources Commission (http://www.ohppr.state.or.us/) is tasked with selecting drug classes to evaluate and eventually to make recommendations about drug inclusion in the plan. The Commission met on September 7 to organize and develop a work plan. Four drug classes were selected for initial evaluation. Those classes include: opioid drugs, non-steroidal anti-inflammatory drugs, cholesterol reducers and anti-ulcer drugs.

It was decided to form subcommittees to review a class and make recommendations to the HRC. In addition, subcommittees on mental health and cancer will be formed. Subcommittee composition will include physicians, pharmacists, other health care providers and consumer interests. Clinicians interested in participating on one of these subcommittees should contact Kelley Cullison at kelley.cullison@state.or.us or (503) 378-2422 Ext. 227 as soon as possible.

Literature evaluation and assessment will be provided by a contracted evidence-based medicine source and presented to the subcommittees. The subcommittees will also hear information from interest groups. Consensus recommendations of the subcommittees will be passed to the HRC for a final decision. DHS will then develop and write rules to implement the plan developed by the HRC. ▮

Use of Gabapentin in Oregon: The Evidence

By Ann Hamer, Pharm.D., OSU College of Pharmacy Clinical Pharmacy Specialist

Anticonvulsant drugs have long been used for a variety of indications from epilepsy to neuropathic pain and the treatment of psychiatric disorders. Both carbamazepine (Tegretol) and valproic acid (Depakote, Depakene) have found clinical roles beyond their use in epilepsy. The use of valproate and carbamazepine in bipolar disorder is well studied and clinical efficacy has been proven in placebo-controlled, double blind studies. In addition, carbamazepine has been used extensively with good documentation for the treatment of pain syndromes. An increasing amount of research has been dedicated to finding potential uses for the newer antiepileptics (e.g. gabapentin, lamotrigine, topiramate). Here, we will focus on the evidence supporting and refuting the use of gabapentin.

USE IN OREGON

Gabapentin use in Oregon has rapidly increased. From September 1999 to September 2000, the number of Oregon Medicaid patients taking gabapentin increased from 2498 to 7332. Currently, gabapentin is listed among the top 10 drug products by total cost for the Oregon Medical Assistance Program costing the state approximately $3.5 million in the year 2000.

A review of gabapentin utilization in primary practice clinics provided some valuable insight. Most prescriptions were for pain management followed by bipolar disorder and other mental health diagnoses. Very few prescriptions were written for epilepsy.

GABAPENTIN AND PAIN

As demonstrated in the literature, gabapentin has been used for a variety of indications. (Table 1) Controlled clinical trials of gabapentin in diabetic neuropathy and postherpetic neuralgia do support its use, with efficacy seen at doses ≥1800mg/day.1,2 Studies comparing gabapentin to tricyclic antidepressants (TCAs) suggest that both are comparable in terms of efficacy and tolerability.3 An effective dose of gabapentin has an AWP of $191 per month compared to $7 per month for amitriptyline. A major disadvantage of TCAs, however, is the risk of serious adverse events such as cardiac arrhythmias, which can occur in acute overdose or in high-risk patient populations.

GABAPENTIN AND PSYCHIATRIC DISORDERS

Current evidence does not support the use of gabapentin for psychiatric indications. Open label studies and case reports have suggested possible efficacy in the treatment of some psychiatric disorders. However 2 well-designed randomized trials of gabapentin for the treatment of bipolar disorder failed to demonstrate efficacy superior to placebo.4,5 In addition, no overall drug/placebo difference was observed in an 8-week randomized controlled trial of gabapentin in panic disorder.6

For other indications (e.g. anxiety, obsessive compulsive disorder, alcohol withdrawal), randomized trials have not been completed and the use of gabapentin cannot be recommended.

CONCLUSION

The utilization of gabapentin in Oregon has increased exponentially. Currently, beyond its use in epilepsy, evidence only supports the use of this drug for diabetic neuropathy or postherpetic neuraligia at doses ≥1800mg/day. Further, this costly drug should not be considered first-line for any indication. ▮

References:

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TABLE 1. SUMMARY OF STUDIES USING GABAPENTIN TO TREAT OFF-LABEL CONDITIONS

STUDY DESIGN	DOSE	POPULATION	RESULTS	REFERENCE
Neuropathic Pain				
RCT *7/96-3/97* *8 week trial*	3600mg/day (forced max 67% achieved) vs. placebo	Uncontrolled diabetics (75% Type2) n=84 gabapentin n=81 placebo	Difference in mean pain score at end point= -1.2 (p<.001) Difference in mean sleep interference score= -1.47 (p<.001)	*Backonja M, Beydoun A, et al. JAMA. 1998; 280:1831-1836*
RCT, crossover *3/97-12/97* *2, 6-week trials*	gabapentin= 900-1800mg/day amitriptyline: 25-75mg/day	Controlled diabetics n=19 Veterans completing both tx arms of cross-over trial	No statistically significant difference in pain intensity scores or in pain relief.	*Morello CM, et al Arch Intern Med. 1999; 159:1931-1937*
Open-label *1997* *12 week trial*	gabapentin= 2400mg/day amitriptyline= 90mg/day	Elderly controlled diabetics n=13 gabapentin n=12 amitriptyline	Gabapentin produced a meager reduction (1.9 point drop) from pain baseline compared to amitriptyline (1.3 point drop).	*Dallocchio C, Mazzarello P, et al J Pain Symptom Manage 2000; 20:280-285*
RCT, crossover *unknown date* *12 week trial*	900mg/day vs. placebo	Diabetics; control not mentioned n=19 gabapentin n=21 placebo	Statistical improvement in only 1 of 4 end points, the MPQ (McGill Pain Questionnaire) with a mean reduction of 8.9 pts compared to 2.2 pts placebo (p=0.03)	*Gorson KC, et al J Neurol Neurosurg Psychiatry. 1999; 66:251-252*
RCT *8/96-7-97* *8 week trial*	3600mg/day (65% achieved max dose) vs. placebo	Postherpetic Neuralgia n=113 gabapentin n=112 placebo	Decrease in average daily pain score=33% gabapentin, 7% placebo (p<0.001)	*Rowbotham M, et al Ann Pharmacother 2000; 34:802-807*
Bipolar Affective Disorder				
Open label, retrospective	200-3500mg/day	BAD or SAD Unresponsive or intolerant of standard mood stabilizers n=73	92% responded to gabapentin (unclear if other meds were used)	*Ryback, et al J Neuropsych Clin Neurosci. 1997;2:301*
RCT, crossover *3, 6 week monotherapy evaluations*	gabapentin = 3987±856mg/day lamotrigine = 274 ±128mg/day	Refractory BAD or unipolar mood disorder n=31	Gabapentin monotherapy is equivalent to placebo. (p=0.70) Primary outcome measure was the Clinical Global Impressions Scale (CGI).	*Frye M, Post RM, et al J of Clin Psychopharm. 2000; 20:607-14.*
RCT	adjunctive use of gabapentin 900-3600mg/day	BAD, type I, current symptoms despite ongoing therapy	Both decreased Young Mania Rating Scale, placebo significantly more than gabapentin (p<0.05). No significant difference between groups on HAM-D.	*Pande AC, et al Bipolar Disorders. 2000; 2:249-255. (abstract only)*
Spasticity/Tremor				
RCT, crossover and placebo-controlled *26 day trial*	gabapentin= 1200mg/day propranolol= 120mg/day	Essential Tremor n=16	No significant differences found between active treatments on Tremor Clinical Rating Scale. (p=0.20)	*Gironell A, et al Arch Neurol. 1999; 56:475-480*
RCT, crossover and placebo-controlled	gabapentin= 1800mg/day or 3600mg/day vs. placebo	Essential Tremor n=20	Patient global assessments (p<0.05), observed tremor scores (p<0.005), water pouring scores (p<0.05), and ADL scores (p<0.005) significantly improved. Low dose equivalent to high dose.	*Ondo W, et al Movement Disorders. 2000; 15:678-682. (abstract only)*
Open-label *9 month trial*	600-1600mg/day	Muscle Cramps n=30	May be helpful in the treatment of muscular cramps at dosages of 600-1200mg/day	*Serrao M, et al Clinical Neuropharm. 2000; 23:45-49*
RCT, crossover *26 day trial*	2700mg/day vs. placebo	Spasticity in MS n=21	Significant differences noted in spasm severity, interference with function, painful spasm, global assessment, Modified Ashworth Scale, and plantar stimulation response. There was no significant change in Digit Span, Digit Symbol, the adjective generation technique, or the EDSS.	*Cutter N, et al Arch Phys Med Rehabil. 2000; 81:164-9*
Panic/Anxiety				
RCT *14 week trial*	900-3600mg/day vs. placebo	Social phobia–unclear definition n=69	A significant (p<0.05) reduction in sx was seen in active vs placebo groups. Further studies are required to determine dose-response relationship	*Pande AC, et al Journal of Clinical Psychopharm. 1999; 19:341-348*
RCT *8 week trial*	600-3600mg/day vs. placebo	Panic disorder n=103	No overall drug/placebo difference was observed in scores on the Panic and Agoraphobia Scale. (p=0.606)	*Pande AC, et al Journal of Clinical Psychopharm 2000; 20:467-471.*

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