A comparison of pregabalin and gabapentin in the treatment of peripheral neuropathy

Priya Balakrishnan & Shannon Spangler*
Faculty: Patricia Bunton

Department of Physician Assistant

Abstract: *Background:* Peripheral neuropathy is a condition involving the nerves that carry information to and from the central nervous system. It is characterized by numbness, tingling, burning in the limbs, pain, and loss of sensation and muscle control. Diabetes mellitus is the most common cause in the United States. Two drugs recommended for treatment include gabapentin and pregabalin. *Study purpose:* To compare the efficacy of pregabalin to gabapentin in the treatment of peripheral neuropathy. *Methods:* An evidence based review was used to evaluate English language literature articles from 2003 to 2010. *Expected results:* Based on initial article reviews we expect to find that treatment of peripheral neuropathy with pregabalin is more efficacious than gabapentin in the treatment of peripheral neuropathy.

I. Introduction

Peripheral neuropathy is a condition characterized by the malfunctioning of the peripheral nerves. These nerves connect the skin, joints, muscles, and internal organs to the central nervous system. The disorder is characterized by numbness, tingling or burning in the hands and feet. It produces pain, loss of both sensation and muscle control. Diabetes mellitus is the most common cause of peripheral neuropathy and it is estimated that neuropathy affects about 30% of patients with diabetes mellitus [1], and approximately 2% of the population in the United States[2]. Treatment options are aimed at pain control or prevention of disease. Gabapentin is an antiepileptic drug that is widely used to treat painful neuropathies in patients with diabetic poly-neuropathy, post-herpetic neuralgia, and neuropathic pain in general. Pregabalin is a newer antiepileptic drug used for treatment of pain associated with diabetic peripheral neuropathy (DPN) and post-herpetic neuralgia (PHN). Few comparisons have been done to study the efficacy of these drugs in the treatment of peripheral neuropathy. The purpose of this study is to conduct an evidence based systematic review to compare the efficacy of pregabalin and gabapentin in the treatment of peripheral neuropathy.

2. Study, Results, Discussion, and Significance

A literature search for articles was performed using MEDLINE, CINAHL and Cochrane Library databases. Articles included were English language, randomized control trial articles dating from 2003-2010. The MeSH search terms included ‘neuropathic pain’, ‘peripheral neuropathy’, ‘gabapentin’, and ‘pregabalin.’ The articles were limited to randomized, double blind, placebo controlled clinical trials of pregabalin or gabapentin in the treatment of neuropathic pain. Studies by Lesser et al. [3] Tolle et al.[4] Rosenstock et al.[5] Tarride et al.[6] and Rodriguez et al.[7] evaluated the efficacy and safety of pregabalin in the treatment of DPN. In each of these studies pregabalin was found to significantly reduce patients’ pain scores when compared to placebo. The most common adverse effects were dizziness and somnolence. The efficacy and safety of pregabalin in the treatment of PHN was assessed in studies by authors Sabatowski et al.[8] Dworkin et al.[9] VanSeventer et al.[10] Toth et al.[11] Each of these studies found that pregabalin provided significant relief of symptoms when compared to placebo or gabapentin groups, with minimal adverse side effects. Most commonly occurring side effects were dizziness, somnolence, peripheral edema, headache, and dry mouth[8].
Tsavaris et al. [12] Sandercocck et al.[13] Ross et al.[14] compared the efficacy of gabapentin to placebo and all found that it was effective to treat neuropathic pain but Sandercock et al.[13] found that at doses required to treat DPN it had a high incidence of causing somnolence and dizziness.

3. Conclusion

Pregabalin’s linear pharmacokinetics results in a predictable dose-response relationship which allows it to be adjusted to the target dosage more rapidly. Gabapentin’s nonlinear pharmacokinetics results in decreasing absorption at higher doses and requires a long and slow adjustment to the effective dosage. Based on the studies in this review we found that pregabalin therapy is better tolerated with fewer adverse drug-related events, it is more

cost-effective than gabapentin, and can provide neuropathic pain relief in those patients who do not respond to gabapentin treatment.

Table 1: Comparison of gabapentin and pregabalin.

Structure	Gabapentin	Pregabalin
Indicated for	PHN in adults	DPN, PHN, seizures, fibromyalgia
Bioavailability	27%-60%	90%
Tmax (hrs)	2-3.2	1
Potency	+	++++++
$t_{½}$ (hrs)	6-8	5.5-6.7
Plasma protein binding	< 3%	0
Metabolism	None	None
Route of administration	Oral	Oral
Elimination	Renal (100% unchanged)	Renal (92-99%)
Dosing Schedule	TID	BID/TID
Controlled Substance	No	Schedule V
Neuropathic pain dose	1800-3600 mg/day	150-600 mg/day
Average cost per month	$188-$310	$164-$246

PHN=Post herpetic Neuralgia; DPN= Diabetic peripheral neuropathy; BID = Twice a day; TID = Three times a day.

References

[1] Jensen TS, Backonja MM, Jimenez SH, et al. New perspectives on the management of diabetic peripheral neuropathic pain. *Diabetes and Vascular Disease Research* 2006;3:108

[2] Mauermann ML, Burns TM. Pearl and Oy-sters: Evaluation of peripheral neuropathies, *Neurology* 2009;72;e28.

[3] Lesser H, Sharma U, LaMoreaux L, Poole RM. Pregabalin relieves symptoms of painful diabetic neuropathy: a randomized controlled trial. *Neurology* 2004:63:2104-2110.

[4]Tolle T, Freynhagen R, Versavel M, et al. Pregabalin for relief of neuropathic pain associated with diabetic neuropathy: A randomized double blind study. *European Journal of Pain* 2008:12:203-213.

[5]Rosenstock J, Tuchman M, LaMoreaux L et al. Pregabalin for the treatment of painful diabetic peripheral neuropathy: a double-blind, placebo-controlled trial. *Pain* 2004:110:628-638.

[6]Tarride JE, Gordon A, Dukes E, et al. Cost-effectiveness of pregabalin for the treatment for the management of neuropathic pain associated with diabetic peripheral neuropathy and postherpetic neuralgia: A Canadian perspective. *Clinical Therapeutics* 2006;28(11):1922-1934.

[7]Rodriguez MJ, Diaz S, Vera-Llonch, et al. Cost-effectiveness of pregabalin for the treatment for the management of neuropathic pain associated with diabetic peripheral neuropathy and postherpetic neuralgia. *Curr Med Res Opin* 2007;23(10):2585-2596.

[8] Sabatowski R, Galvez R, Cherry DA, et al. Pregabalin reduces pain and improves sleep and mood disturbances in patients with post-herpetic neuralgia: results of a randomized, placebo-controlled clinical trial. *Pain* 2004;109:26–35.

[9]Dworkin RH, Corbin AE, Young JP, et al. Pregabalin for the treatment of postherpetic neuralgia: a randomized, placebo-controlled trial. *Neurology*. 2003;60:1274–1283.

[10]VanSeventer R, Feister HA, Young JP, et al. Efficacy and tolerability of twice-daily pregabalin for treating pain and related sleep interference in post-herpetic neuralgia: a 13-week, randomized trial. *Curr Med Res Opin*. 2006;22:375–384.

[11]Toth C. Substitution of gabapentin therapy with pregabalin therapy in neuropathic pain due to peripheral neuropathy. *Pain Medicine*. 2010;11:456–465.

[12]Tsavaris N, Kopterides P, Kosmas C et al. Gabapentin Monotherapy for the treatment of Chemotherapy Induced Neuropathic Pain. *Pain Medicine* 2007;9:1209-1216.

[13]Sandercock D, Cramer M, Wu J, et al. Gabapentin Extended Release for the Treatment of Painful Diabetic Peripheral Neuropathy. *Diabetes Care* 2009;32(2):e20.

[14]Ross JR, Goller K, Hardy J, et al. Gabapentin is effective in the treatment of cancer related neuropathic pain: a prospective open label study. *J Palliat Med* 2005;8(6):1118-1126.